Year book

2023

Blog Heart Surgery Today

Coordinator
José Manuel Martínez Comendador

Editors
Elio Martín Gutiérrez/José Manuel Martínez Comendador/ Bunty Ramchandani

SECCE
Sociedad Española de Cirugía Cardiovascular y Endovascular

Blog

Heart Surgery Today

Year book **2023**

Summarized comments of the main publications in cardiovascular and endovascular surgery

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Heart Surgery Today 2023

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Foreword

It is with great pleasure that we present the second edition of the book *"Heart Surgery Today".* This volume compiles all the articles published on our blog from November 2022 to December 2023. Due to the outstanding success of the 2023 edition in Spanish, we were encouraged to create an English edition of the first volume to reach a broader international audience. This initiative stems from a recognized need for a comprehensive source that consolidates, analyzes, and disseminates key scientific publications in the field of cardiac surgery.

Month by month, we have curated the most relevant scientific articles within our specialty, providing summaries and critical analyses with a rigorous scientific approach. Through our commentary, we have consistently aimed to include an educational and critical perspective, with the ultimate goal of advancing scientific knowledge in the most objective manner possible.

Another key objective of the *"Heart Surgery Today"* blog is to foster participation from the entire cardiac surgical community—not only cardiac surgeons but also other professionals involved in the broader cardiac field. While this project has been primarily developed by Spanish-speaking contributors, we warmly invite cardiac surgeons from around the world to join us in this collaborative effort, sharing their perspectives and enriching the global dialogue on cardiac surgery. This collaborative approach has been well-received, as evidenced by over 170 comments from 40 different authors and the thousands of visits to the blog. These metrics have positioned the blog as one of the most sought-after resources on the Spanish Society of Cardiovascular and Endovascular Surgery's (SECCE) website in recent times. I hope that from now on, it will also become a valuable resource for the international community, as we now offer an English version of the website featuring all the articles. I wish to extend my deepest gratitude to all contributors and invite all our readers to actively engage by providing their insights and comments. Additionally, the presence of our articles on social media has greatly enhanced their visibility and dissemination.

The format of this book includes six clearly defined sections: aortopathies; ischemic heart disease; congenital heart disease; heart failure and circulatory support devices; aortic, mitral, and tricuspid valve diseases; and a miscellaneous section. Within each of these categories, topics have been organized according to their relevance and frequency in the current literature, ensuring a logical structure that facilitates efficient navigation for readers seeking specific articles of interest.

I would also like to express my sincere appreciation to SECCE and its Board of Directors, particularly to its former president, Dr. Jorge Rodríguez-Roda Stuart, and its current president, Dr. Juan José Legarra Calderón, for their unwavering support in bringing this project to fruition. Furthermore, I wish to acknowledge the invaluable contributions of Dr. Elio Martín Gutiérrez and Dr. Bunty Ramchandani, whose relentless dedication to editing and

drafting these commentaries has consistently upheld the highest standards of excellence for the *"Heart Surgery Today"* blog.

Our heartfelt hope is that this book proves to be a useful resource for our readers and that it brings them great satisfaction.

Dr. José Manuel Martínez Comendador
Coordinator of *Cardiac Surgery Today* blog, 2023

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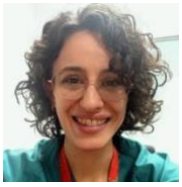

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Blog
Heart Surgery Today

Index of sections

Section I: Aortopathies

Left main disease

CABG

CABG vs. PCI

Miscellaneous

Section IV: Heart failure, heart transplant and mechanical circulatory support devices

- V B: Mitral valve disease

<u>Surgical mitral valve repair</u>

Surgical mitral valve replacement

Percutaneous mitral valve repair and transcatheter mitral valve implantation

- V C: Tricuspid valve disease

Tricuspid valve surgery

Tricuspid regurgitation and risk stratification

- V D: Other valvulopathies

Valve prosthesis

Other

Section VI: Miscellaneous

Cardiac electrical stimulation

Atrial fibrillation and surgical ablation

Oral anticoagulation

Infective endocarditis

Cancer and cardiac tumours

Perfusion

Postoperative course

Other

Section I:

Aortopathies

José Manuel Martínez Comendador

A Tailored Strategy for Acute Type A Aortic Dissection: Is It Really Necessary?

This study, conducted at a specialized aortic surgery center, examines the short- and long-term outcomes of surgical repair for type A aortic dissection based on whether a conservative or more extensive repair strategy was chosen.

The surgical techniques for acute type A aortic dissection (ATAAD) vary significantly. While indications for certain approaches are sometimes clear, in other cases, selecting the optimal surgical strategy is more complex.

The aim of this study was to analyze outcomes based on the chosen surgical approach for ATAAD: a conservative approach with ascending aorta and hemiarch replacement in higher-risk patients, or a more aggressive technique with root and/or total aortic arch replacement in lower-risk patients. Patients undergoing conservative repair (group 1) were compared to those undergoing extensive repair (group 2) using univariable and multivariable analysis. From 1997 to 2019, 343 patients underwent ATAAD repair. Of these, 240 received conservative repairs, while 103 received extensive repairs. Group 1 was older and presented more comorbidities such as hypertension, previous myocardial infarction, and renal dysfunction. Group 2 had a higher prevalence of connective tissue disease (2.1% vs. 12.6%; $p = 0.01$), aortic insufficiency, and longer intraoperative times. The incidence of individual postoperative complications was similar regardless of approach. However, the composite of significant adverse events (surgical mortality, myocardial infarction, stroke, dialysis, or tracheostomy) was higher in the conservative group (15.1% vs. 5.9%; $p = 0.03$). Surgical mortality was 5.6% and showed no difference between groups. Ten-year survival rates were similar with either surgical approach. The cumulative 10-year reintervention risk was higher in group 2 (5.6% vs. 21%; $p < 0.01$). In multivariable analysis, ejection fraction and diabetes were predictors of major adverse events, but extensive repair was not. Extensive repair was, however, a predictor of late reintervention (OR = 3.03; $p = 0.01$).

The authors conclude that a customized conservative approach for ATAAD leads to favorable surgical outcomes without compromising durability.

COMMENTARY:

There is no doubt that treating type A aortic dissection represents a surgical challenge with significant mortality. Both the chosen surgical strategy and the expertise of the surgeons play a decisive role in the outcome. Lau et al. present their personal experience from a specialized aortic surgery center, encompassing a considerable number of patients over a 22-year period. In two-thirds of cases, a conservative strategy was adopted, avoiding root and total arch replacement, primarily in elderly, frail patients with significant comorbidities. The remaining group of patients underwent a more extensive root and/or aortic arch surgery. Notably, regardless of the chosen surgical strategy, the observed operative mortality was very low, and the long-term results were excellent.

When reviewing the literature comparing hemiarch surgery versus complete aortic arch replacement in ATAAD, there is a wide variation in outcomes. Pending results from the first randomized trial (HEADSTART) underway, the latest meta-analysis shows no significant differences in mortality or long-term reoperation rates. However, other studies present diverse outcomes, likely due to the challenge of homogenizing study groups in this type of disease. In the series analyzed by Lau et al., the conservative approach group showed, somewhat paradoxically, a higher incidence of adverse events than the extensive repair group. This outcome highlights the appropriate decision to limit

aggressive surgery in higher-risk patients. In terms of long-term outcomes, ten-year survival was notably high in both groups, exceeding 60%, which is commendable. On the other hand, the higher incidence of late distal reintervention in the extensive surgery group reflects a more severe pathology rather than incomplete treatment. Conversely, the lower reoperation rate during follow-up in the conservative group might be attributed to unknown factors such as deaths from non-aortic causes, contraindications for reintervention due to age/comorbidities/frailty, or other factors.

Achieving these excellent outcomes required a combination of factors that are not always possible. The systematically adopted strategy of performing less aggressive surgery in older patients with severe comorbidities is a key component, but probably more crucial was the degree of specialization achieved at this center in the surgical treatment of aortic dissection. This allowed the surgeons to acquire all necessary skills (surgical experience, consistent decision-making, etc.) to optimize these results. Increasingly, many cardiac surgery centers have begun establishing multidisciplinary teams specialized in this pathology, enabling them to gain experience with a relatively rare condition that involves continuously evolving technological resources and complex surgical treatment.

In any case, as with many things in life, these decisions are rarely black and white but rather shades of gray. A long, complex surgery, even if performed technically to perfection, may not be tolerated by an elderly and frail patient. Conversely, a more conservative approach might not be sufficient long-term in a younger patient with connective tissue disease. This article reflects the philosophy followed by many centers, where the approach should be guided by the patient's condition rather than the disease itself, and the primary goal in cases of aortic dissection should always be, above all, to save the patient's life.

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José Manuel Martínez Comendador

Importance of Distal Residual False Lumen Size After Surgery for DeBakey Type I Aortic Dissection: Is It What We All Suspect?

This study aimed to evaluate if, in patients undergoing surgery following DeBakey Type I aortic dissection, the maximum area of the false lumen in the distal thoracic aorta predicts late aortic dilation and the need for reintervention.

Historically, open surgery for acute ascending aortic dissection (AAAD) of DeBakey Type I has primarily focused on resecting the ascending aorta segment containing the primary intimal tear to survive this catastrophic emergency. Surgeons have accepted that if the remaining dissected distal aorta dilates in the future, complex reoperation could be performed in an elective context. In the past decade, mortality rates and complications such as stroke and malperfusion after this emergent procedure appear to have improved. In contrast, long-term complications due to residual aortic dilation remain an unsolved issue. The primary underlying causes of aortic dilation include intimal tears allowing reentry into the proximal thoracic aorta and false lumen (FL) patency. Most studies on FL after AAAD surgery focus on FL diameter and/or thrombosis. However, the FL in the aorta has complex, dynamic, and three-dimensional features, and such studies may not accurately capture its true characteristics.

The aim of this study was to investigate whether the ratio of the maximum false lumen area (MFLA) in the distal aorta predicts late aortic dilation and reintervention following open repair of DeBakey Type I AAAD. For this, 309 patients with DeBakey Type I AAAD treated with proximal aortic repair between 1994 and 2017 were analyzed. In 230 patients with non-thrombosed FL in postoperative computed tomography (CT), the MFLA ratio (MFLA/aortic area) in the descending thoracic aorta was measured via postoperative CT. Patients were divided into three groups based on MFLA quartiles: low MFLA, <0.62 (n = 57); intermediate MFLA, 0.62 to 0.81 (n = 116); and high MFLA, ≥0.82 (n = 57). The aortic expansion rate was significantly higher in the high MFLA group (11.1 ± 21.2 mm/year) compared with the intermediate group (3.0 ± 7.4 mm/year; $p < 0.01$) and the low group (0.6 ± 6.6 mm/year; $p < 0.01$). A high MFLA ratio was found to be an independent risk factor for significant aortic expansion (HR = 5.26; $p < 0.01$) and aorta-related reintervention (HR = 4.99; $p < 0.01$), and the MFLA ratio was significantly associated with reentry tears in the proximal descending thoracic aorta.

The authors conclude that a high MFLA ratio in the descending thoracic aorta following DeBakey Type I AAAD repair is associated with a greater risk of late aortic reintervention and distal aortic dilation. A high MFLA ratio is strongly associated with reentry tears in the proximal descending thoracic aorta.

COMMENTARY:

In this retrospective study by Kim et al., 309 DeBakey Type I AAAD cases over 20 years were analyzed. This study is rare and genuine as it includes long-term information on both clinical outcomes and imaging follow-up. The three most relevant findings would be: 1) a growth rate >10 times higher in the high FL ratio group compared to the low FL ratio group; 2) a significantly higher incidence of reintervention in the high FL ratio group with an HR of 4.99; and 3) a clear association between aortic growth and proximal reentry tears.

Most surgeons would not be surprised by these findings, which would seem quite expected, though, before this article's publication, they were merely conjectures. This data has been substantiated by the large annual patient volume and the excellent and

detailed follow-up of both clinical and imaging outcomes. Additionally, the study is highly relevant due to the current availability of hybrid open and endovascular techniques in cardiovascular surgery teams.

To my knowledge, this is the most comprehensive study demonstrating that residual FL following DeBakey Type I AAAD repair is a risk factor for aneurysm formation. These results lead to further questions: Are there preoperative factors that can help predict which patients will have a larger FL? Should early intervention be considered in cases of a high FL ratio, even if they do not meet the surgical criteria for aortic diameter? What is the best technique to treat the residual aorta given the range of available hybrid procedures? Is it increasingly necessary to establish specialized aortic teams, and if so, which patients should be referred to these centers of excellence?

To date, most information on the safety of complete aortic arch surgery in DeBakey Type I AAAD comes from retrospective studies, mainly conducted, like this one, in Asia. Currently, the first randomized study in North America (HEADSTART) is underway to compare standard hemiarch surgery with more extensive aortic surgery in patients with DeBakey Type I AAAD, which may provide answers to many of these questions.

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María Nieves de Antonio Antón

The Value of Time, Even in Type A Aortic Dissection

A retrospective study examining the impact on morbidity and mortality of the time elapsed from symptom onset to surgical intervention in patients with acute type A aortic dissection complicated by malperfusion of one or more regions.

Acute type A aortic dissection is a condition with a high mortality rate. Without immediate intervention, mortality increases by 1-2% per hour from the onset of symptoms. The treatment of choice is emergency surgery, where rapid diagnosis and the implementation of urgent medical management are essential to optimize the patient's condition upon arrival for surgery.

Despite advances in surgical outcomes over the years improving survival rates, mortality remains high. Malperfusion signs at diagnosis present a major complication that greatly impacts short- and long-term surgical outcomes, resulting in poorer morbidity and mortality outcomes.

This study's objective is to determine whether the elapsed time from symptom onset to surgery and the location of malperfusion syndrome influence survival in type A aortic dissection surgery. A 300-minute cutoff was established to divide patients into two groups: those who underwent early versus delayed intervention. All patients presenting to the hospital with acute type A aortic dissection between 2003 and 2019 at the Japanese Red Cross Kobe center were studied. In total, 463 subjects were included, excluding those who died in transit and those who were not operated on. Among the remaining 331 patients, 25% (84) presented with malperfusion syndrome, diagnosed clinically and by CT angiography upon arrival at the emergency department.

Kaplan-Meier analysis with a log-rank test was used to evaluate survival. Cox proportional hazards analysis was performed to identify predictive elements, focusing on factors with a $p < 0.1$ level of significance in the univariable analysis (shock upon emergency department arrival, coronary malperfusion, time exceeding 300 minutes until intervention, and preoperative cardiopulmonary arrest).

No statistically significant differences were found in preoperative variables between groups. In patients with malperfusion, the time from symptom onset to transfer to the operating room was significantly longer (209 vs. 976 minutes). Comparing patients presenting without malperfusion symptoms to those with them, the latter group experienced higher postoperative morbidity and 30-day mortality. However, despite this, no long-term survival differences (mean follow-up of 5 years) were observed among survivors, with higher survival among patients transferred to the operating room early, regardless of clinical malperfusion presentation. Multivariate analysis indicated that patients with coronary malperfusion and shock upon emergency department arrival experienced higher long-term mortality.

The authors concluded that, in patients diagnosed with acute type A aortic dissection associated with malperfusion, those who underwent early surgical intervention—within five hours from symptom onset—demonstrated higher long-term survival. Additionally, among the regions affected by malperfusion syndrome, coronary ischemia was associated with higher short- and long-term mortality. Finally, patients who experienced shock prior to surgery had poorer long-term survival.

COMMENTARY:

Malperfusion syndrome encompasses all situations that compromise blood flow to an organ, resulting in ischemia and/or dysfunction. It can arise from various causes: dissection of aortic branches, dynamic or static obstruction, thrombosis in the false lumen, or a combination thereof. Multiple therapeutic options have been described to address this issue, such as fenestration or extra-anatomical arterial bypasses, but their efficacy remains uncertain. Whether coronary intervention should precede ascending aorta repair in malperfusion patients is particularly contentious, as suggested by the authors of this study. This action could worsen outcomes, as it delays patients' transfer to the operating room and does not seem to offer a clear survival advantage. Therefore, caution is needed when extrapolating this approach to our practice, since preoperative coronary angiography is not customary, and, in most cases, ischemia arises from ostial-proximal coronary vessel involvement by the dissection itself. Aortic surgery resolves dynamic obstruction in a large proportion of cases by redirecting flow into the true lumen. This underscores the importance of minimizing delays in transferring a patient with acute ascending aortic dissection to the operating room.

This study highlights the importance of early surgical intervention, yet this should always align with rapid diagnosis and a hospital protocol that facilitates effective, safe, and efficient patient transfers. The tolerance for malperfusion varies between organs, affecting postoperative morbidity differently. For example, myocardial or cerebral tolerance times are generally shorter. However, visceral organs have better tolerance, although established mesenteric involvement has a very high mortality rate in these patients.

The number of patients included in the study is remarkable, yet one limitation of this article is the small number of patients with mesenteric, renal, peripheral, and spinal malperfusion; this would have helped to clarify specific management for each type of pathology and its impact on short- and medium-term survival. The same research group published results in 2011 on surgical intervention for acute aortic dissection complicated by cerebral coma, again demonstrating the importance of early surgical intervention despite the presence of cerebral malperfusion with a comatose neurological state.

In conclusion, acute type A aortic dissection with associated malperfusion syndrome is a pathology with high morbidity and mortality. Additionally, it can trigger severe systemic complications, with emergency surgery being one of the few effective options to prevent fatal complications and improve long-term outcomes. We must aim for the earliest possible surgical intervention from diagnosis in these patients and minimize decision-making time.

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Daniel Martínez López

Modified Frozen Elephant Trunk in the Treatment of DeBakey Type I Aortic Dissection: Is It Time to Change the Current Approach?

Unicentric, retrospective study adjusted by propensity analysis from the Cleveland Clinic group comparing the traditional treatment of aortic dissection (limited to ascending aorta replacement with/without extension to the aortic arch) with the modified frozen elephant trunk technique in Stanford Type A, DeBakey Type I dissection.

Aortic dissection is a severe condition with high mortality from its diagnosis, despite technological improvements and advances in radiodiagnosis. Surgical mortality with new techniques has been reduced from 33% in 1999 to approximately 22% in international records. This reduction in mortality and the development of new prostheses have led many surgeons to pursue a more aggressive approach in this emergency surgery, focusing on reducing the amount of aorta with residual dissection, particularly extending the treatment to the aortic arch. Recent studies have warned of the consequences of systematic extension of treatment to the aortic arch and descending thoracic aorta in this patient population, claiming an increase in postoperative stroke, as well as an increase in spinal ischemic injuries and 30-day mortality. All this makes it still a controversial topic, and no standard surgical treatment exists for these patients.

The present study analyzes data recorded in one of the most experienced centers worldwide (Cleveland Clinic) since 1978, with a total of almost 900 patients. To establish a more rigorous analysis, potential significant differences between patient groups were eliminated through propensity analysis adjustment. Comparisons were made between patients with treatment restricted to the ascending aorta only, patients with ascending aorta and aortic arch treatment according to conventional techniques, and those in whom the ascending aorta and aortic arch were replaced using the modified frozen elephant trunk technique. The outcomes of each group were analyzed in relation to aortic clamping and circulatory arrest times, survival, need for reintervention, neurological events, and renal failure.

Regarding surgical times, there were no significant differences in mean aortic clamping or circulatory arrest times. No significant differences were found in postoperative bleeding between the frozen elephant trunk and ascending aorta surgery, but significant differences emerged compared with conventional aortic arch surgery ($p = 0.01$). Renal failure was lower in patients undergoing modified frozen elephant trunk when compared to those receiving only ascending aorta replacement ($p = 0.006$), but no significant differences were found in other group comparisons. Neurological events were similar across the three groups, with no significant differences in spinal ischemia rates. Reinterventions for growth of the remaining aortic segments were only 47% in the frozen elephant trunk group, compared to 71% in the group where only the ascending aorta was treated and 75% in the conventional aortic arch approach. All reinterventions in the frozen elephant trunk group could be performed endovascularly.

Finally, the authors highlight that, when comparing survival between groups, greater mortality was observed in the extended classical arch approach compared to the group with ascending aorta replacement only ($p = 0.0005$). However, there were no significant mortality differences between the modified frozen elephant trunk and isolated ascending aorta treatment groups.

COMMENTARY:

Thanks to propensity analysis adjustment, the heterogeneity of populations observed since the 1980s in this Cleveland Clinic cohort could be rigorously studied. This study observed that patients undergoing modified frozen elephant trunk have similar ischemic times to classical approaches, with similar neurological complications but lower rates of renal failure and reintervention for bleeding when compared to the ascending aorta-only approach or the conventional aortic arch approach. Most importantly, a significant difference in terms of survival was found in favor of the modified frozen elephant trunk compared to the conventional aortic arch approach, with a non-significant trend when compared to ascending aorta-only treatment. Likely, a larger sample size would have achieved statistical significance. In conclusion, in expert hands, the modified frozen elephant trunk in acute DeBakey Type I aortic dissection surgery may show favorable outcomes when compared to more classic approaches and contradicts publications by other groups and international registries.

However, the study is not without criticism or limitations. Aortic dissection is a pathology with a limited number of annual events. The sample size collected spans a long period, during which different technical and technological advances were not considered in the propensity analysis, which may have influenced the results. Extending treatment to the aortic arch, in early stages, would have been adopted as an obligation (due to the presence of tear or entry at that level) where mere ascending aorta replacement was not feasible, while in recent stages, adopting the elective approach with modified frozen elephant trunk was the result of experience and availability of this type of prosthesis. This and other inherent biases in the retrospective nature of the study, such as follow-up losses, may limit the validity of the conclusions drawn. Thus, while the results are interesting, they should be taken with great caution.

The modified frozen elephant trunk is a complex procedure that adds even more difficulty to a surgery that is already highly demanding in an emergency situation. Therefore, to clarify its role in elective application in this context, registries and collaboration between centers will be essential to shed light on these issues.

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José Manuel Martínez Comendador

Oral Anticoagulation After Surgical Repair of Type A Aortic Dissection: Does it Impact Prognosis and False Lumen Patency?

A single-center retrospective study analyzing the effects of chronic oral anticoagulation (OAC) on long-term outcomes after surgical repair of acute type A aortic dissection (A-AAD), as well as its impact on false lumen (FL) evolution.

Acute type A aortic dissection (A-AAD) is associated with high in-hospital mortality, exceeding 20% according to the International Registry of Aortic Dissection (IRAD). Five-year survival stands at approximately 63%. Predictors of long-term morbidity and mortality include advanced age, female sex, atherosclerosis, and renal impairment. A recent meta-analysis by Li et al. demonstrated that the size of the residual patent FL is associated with poorer long-term survival compared to complete FL thrombosis. Therefore, residual flow in the FL is considered to promote dilation and, ultimately, rupture of the aorta. Additionally, partial FL thrombosis has also been independently associated with worse long-term survival in type B aortic dissection.

Many survivors of aortic dissection may have an indication for long-term oral anticoagulation (OAC) therapy. Currently, there are no clear recommendations for OAC use in patients undergoing A-AAD repair. The study by Song et al. found an association between early initiation of anticoagulation and a higher incidence of FL patency, yet paradoxically observed better overall long-term clinical outcomes. Other studies have reported conflicting results, failing to demonstrate a clear clinical impact, whether negative or positive of OAC in this context.

The aim of this study was to investigate the long-term clinical impact of OAC and its effects on FL patency in patients who underwent surgery for A-AAD. The study analyzed 188 patients (median age, 62 years; 74% male) who underwent A-AAD repair, comparing patients who received chronic postoperative OAC (n = 59) with those who received antiplatelet therapy alone (n = 129). The median age was similar between groups, 60 years (range: 18–79 years; anticoagulated group) vs. 64 years (range: 22–86 years; non-anticoagulated group) (p = 0.11); anticoagulated patients were more frequently male (88% vs. 67%, p = 0.003). After a median follow-up of 8.4 years (range: 2 months–30 years), 58 patients died, 18 due to aortic-related causes, and 37 patients underwent aortic reintervention. After multivariable analysis, anticoagulation did not show a significant effect on long-term survival or reintervention risk. Analysis of 127 postoperative CT scans showed a patent FL in 53% of anticoagulated patients vs. 38% of non-anticoagulated patients (p = 0.09). The FL was also partially thrombosed in 8% vs. 28% (p = 0.01) and fully thrombosed in 39% vs. 34% (p = 0.63), respectively. Among patients with follow-up CT scans, there were 6 late aortic-related deaths, 1 among anticoagulated patients and 5 among non-anticoagulated patients.

The authors concluded that chronic anticoagulation following A-AAD repair favors long-term FL patency, which is not associated with an increased risk of late mortality or reintervention in this study. Chronic anticoagulation can be safely administered to patients with repaired A-AAD regardless of specific indications.

COMMENTARY:

Current scientific evidence indicates that in chronic aortic dissection, FL patency and even partial thrombosis are associated with disease progression and a poor long-term prognosis compared to patients with complete FL thrombosis. This association also applies to surgically treated A-AAD cases. However, it is noteworthy that the incidence

of long-term FL patency has significantly decreased due to advancements in surgical techniques, such as the increasingly frequent use of frozen elephant trunks. Therefore, it could intuitively be assumed that anticoagulant use in these patients would reduce the incidence of FL thrombosis, which would be linked to a poorer prognosis. However, the study by Vendramin et al. suggests that oral anticoagulation (OAC) does not have as unfavorable an effect as might initially be assumed. In this retrospective single-center analysis, a higher proportion of patients with persistent FL patency was observed in the OAC group, but this was not associated with an increase in adverse events. These findings provide a degree of reassurance when chronic anticoagulation therapy is required in patients who have undergone surgical intervention for A-AAD, especially those with comorbidities and a higher risk of thromboembolic events, such as the presence of mechanical valve prostheses or concomitant atrial fibrillation.

The overall mortality of treated type A dissections over time was 24%. Of the 188 patients who survived until discharge, FL evolution could be accurately evaluated in 127, thanks to appropriately timed imaging follow-ups. Among these patients, 39 received oral anticoagulation therapy with warfarin, mainly due to the presence of mechanical prostheses, while the remaining 88 did not receive oral anticoagulation. Therefore, it is important to interpret the results of this study with caution, as it includes a limited number of evaluated patients. Although the baseline characteristics of the two groups were very similar, the type of surgery performed differed significantly. The non-anticoagulated group had a much higher proportion of isolated hemiarch replacements compared to the anticoagulated group (87% vs. 29%). Consequently, this study may present a selection bias, as a relationship between the extent of repair and FL thrombosis seems to exist. In cases where more residual aorta was left, there was a higher likelihood of FL patency (44% vs. 34% in this study) and a lower incidence of complete thrombosis (31% vs. 48%) compared to more aggressive and extensive surgeries.

A notable aspect of this study is that, although a slightly higher but non-significant incidence of FL patency was observed in the OAC group compared to the non-anticoagulated group (54% vs. 38%), and a significantly higher incidence of partial thrombosis was observed in the non-anticoagulated group (28% vs. 8%), the incidence of complete FL thrombosis was comparable between the two groups. From another perspective, one could also argue that if FL patency is considered as the combination of both completely and partially patent FL cases, there was no difference between the groups, with 62% in the OAC cohort and 66% in the non-anticoagulated cohort. Conversely, if thrombosis is considered as the combination of complete and partial thrombosis, then it occurred in 46% of the OAC group and in 62% of those without anticoagulants. Therefore, it could be inferred that OAC does not promote FL patency per se but rather prevents thrombosis.

In addition to flow rate and duration of FL patency, other factors influence thrombus formation and growth of the residual dissected aorta. Recent computational modeling studies suggest that the geometry of the aortic dissection and its evolution over time also play influential roles. Therefore, while OAC may favor the persistence of FL patency, it is insufficient alone to lead to a poorer prognosis compared to patients who are not on anticoagulants. The long-term prognosis of patients undergoing A-AAD repair and the mechanisms involved are determined by multiple factors, requiring a multifaceted approach.

The findings of the study by Vendramin et al. add further complexity to the debate on the effect of oral anticoagulation on FL patency, and its interpretation may vary depending on how FL patency or partial thrombosis is defined. However, the true value of this study lies in its demonstration that OAC use in this patient group does not seem to have a

significant impact on mortality or the incidence of reoperations. This has substantial intrinsic value and a direct practical implication for the care of our patients.

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Begoña Bernal Gallego

Management of the Aortic Root in Aortic Dissections: Less is More?

This is a single-center retrospective study comparing mortality and reintervention rates between conservative treatment (limited to the ascending aorta) and aggressive treatment of the aortic root in acute Stanford type A aortic dissection.

Acute type A aortic dissection (AAD) is an emergency associated with high morbidity and mortality, requiring immediate surgical intervention in most cases. Over the years, advancements in diagnosis and surgical treatment have reduced early mortality rates to approximately 10%–15%. Traditionally, surgical management has been limited to exclusive replacement of the ascending aorta, even in cases involving the aortic root. In such cases, the root is preserved, usually reinforcing it and resuspending the aortic valve. Alternatively, aortic root replacement can be performed, either with valve preservation or replacement with a valved conduit. Late reinterventions following aortic dissection are common in both proximal (aortic root) and distal (aortic arch) parts of the aorta. Conservative management of type A AAD repair is associated with progressive root dilation, repeated dissections, or involvement of the aortic valve, leading to a higher reintervention rate. This rate is reduced with a comprehensive treatment of the root; however, the net effect of an aggressive approach to the aortic root in type A AAD and its outcomes remains insufficiently explored.

The aim of this study is to compare early and late mortality and reoperation rates between aggressive and conservative treatment of the aortic root in type A AAD. To achieve this, an analysis was conducted on patients operated on between 1992 and 2020 at Leiden University Medical Center (n = 322). Comparisons were made between patients who received treatment limited solely to the ascending aorta, those with ascending aortic treatment including interventions on the root (reinforcement, valve resuspension), and those with aortic root replacement, with or without valve replacement. Additionally, a subgroup analysis was conducted for patients operated on in three different periods: 1992–1999, 2000–2012, and post-2012. The median follow-up duration was 5.1 (0–21) years and 7.1 (0–25) years for the root replacement and conservative surgery groups, respectively. Outcomes in each group were analyzed with respect to early mortality, overall survival, and the need for reintervention due to complications in the root or aortic valve. The frequency of comprehensive aortic root approaches increased over the years, from 19% in earlier periods to 78% more recently. Early mortality decreased over the years, despite the adoption of a more aggressive approach, and remained lower in the subgroup of patients who underwent aortic root replacement. The conservative approach was associated with a higher risk of late mortality and reintervention, with aortic valve insufficiency being the most common cause.

Based on these results, the authors conclude that aortic root replacement is a safe approach and can be applied in type A AAD with good long-term clinical outcomes without an increase in in-hospital mortality.

COMMENTARY:

The treatment of type A AAD is one of the most complex and unpredictable surgeries we can face. Improvements in diagnosis, perioperative management, and surgical techniques play a crucial role in reducing mortality in recent years. This, along with the development of new prostheses, has encouraged many surgeons to opt for a more aggressive approach, even in emergency surgery, aiming to minimize the amount of residual dissected aorta both distally and proximally. This is reflected in the group of Arabkhani et al., who significantly increased the rate of aortic root replacement in aortic

dissections over the past two decades. Although aortic root surgery inevitably entails a longer surgical time and greater procedural complexity, no detrimental effect on postoperative complication rates was observed; indeed, better outcomes were achieved in terms of mortality and reintervention rates. This could be explained by advances over time in perioperative management, including earlier diagnosis and better monitoring; additionally, they noted a shift in cannulation techniques over the decades, moving from femoral to axillary access. The early mortality observed was comparable to data from the International Registry of Acute Aortic Dissection, ranging from 16% to 27%.

However, the study is not without limitations. This research pertains to a single center with a heterogeneous patient population, spanning a very long timeframe and involving various degrees of aortic dissection that were not taken into account. Furthermore, they acknowledge data loss, especially in the group of patients operated on during the initial period (1990s). Most importantly, no reference is made to the criteria guiding the choice of surgical strategy. Surgery must be tailored to the patient's profile; an elderly patient with comorbidities might not withstand extensive surgery, whereas a conservative approach in a younger patient may not provide long-term resolution, necessitating a second intervention with the added risk that entails. This could lead to interpretations that are not necessarily applicable to other populations or to daily clinical practice.

Aortic root replacement is a procedure that adds complexity to a surgery that is already challenging in emergency situations. In expert hands, it may yield even better outcomes compared to more traditional approaches, but we must remember to select the best option based on each patient’s comorbidities and characteristics. Therefore, further studies are needed to explore strategies tailored to individual cases.

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Paula Liliana Torres Gómez

Chronic Type A Aortic Dissection: Durable Repair with Acceptable Risks?

This article examines the characteristics and postoperative outcomes of patients who underwent surgical intervention for chronic type A aortic dissection (over 60 days post-symptom onset) between 1990 and 2021.

The management of aortic disease, in both its chronic and acute presentations, has always been a fascinating challenge for the cardiac surgeon. This complexity stems from its multifaceted diagnostic nature, its potential simultaneous involvement of various sections of the aorta (ascending, aortic arch, and/or descending), and the time constraints it imposes on precise surgical planning. Consequently, it is essential to approach it optimally in the shortest possible timeframe.

The preferred approach for acute type A aortic dissection is strongly endorsed by the consensus of various medical societies, with surgical intervention considered an immediate necessity. This urgency elevates perioperative morbidity and mortality rates. Without intervention, the natural course of the disease results in a short-term mortality rate ranging from 70% to 90%.

However, there is a subset of patients who progress unusually to a chronic stage without undergoing acute management, deviating from the typical natural course of the disease. In these cases, the condition is often incidentally detected due to diagnostic failure or the absence of medical consultation after the initial acute episode. This variation in presentation results in histopathological changes in the affected tissues, notably fibrosis development, which imparts greater stability. This phenomenon could predict more favorable perioperative outcomes in both short and long-term periods.

In previous years, Elefteriades et al. described certain clinical situations where medical management prevails over surgical intervention, which is deferred or disregarded. These scenarios include a critical condition at initial assessment (with multiorgan involvement) associated with severe comorbidities, patients in their eighties, and a "delayed" presentation, defined as hospital consultation occurring 48-72 hours after symptom onset, and/or a history of previous aortic surgery (vascular or valvular).

The article “Contemporary Midterm Outcomes After Primary Repair of Chronic Type A Aortic Dissection” retrospectively analyzes data from a cohort of 205 patients obtained from a single center between 1990 and 2021. These patients underwent primary repair for “chronic” type A dissection, defined as repair conducted over 60 days after symptom onset or when the onset time was uncertain, based on imaging or intraoperative findings that suggested chronicity.

The technical aspects of the procedures varied considerably over the long period covered by this cohort. Nonetheless, all patients were approached via median sternotomy. A recommendation is made for arterial cannulation at the innominate artery, offering the advantage of selective antegrade systemic or cerebral perfusion. However, femoral cannulation was the primary site in 41% of the cohort, with only 14% undergoing cannulation at the innominate, likely reflecting the historical nature of the cohort. Hypothermia and circulatory arrest were used in 91% (186) of cases, with 44% receiving antegrade cerebral perfusion, 31% retrograde, and the remaining patients managed with bilateral or combined perfusion at low temperatures between 22 and 24ºC. The extent of resection was tailored to the diseased aorta section, with most patients undergoing ascending aorta and hemiarch replacement (72%), unless additional criteria for full arch replacement were met, accounting for 18% of cases:

- Arch diameter exceeding 5 cm.
- Severe compression of the true lumen by the false lumen within the arch.
- Tear originating in or affecting the major curvature or supra-aortic trunk region.

Results showed a relatively young patient population, with a median age of 66 years. Most patients presented with DeBakey type I dissection (52% of the cohort) and were generally younger than those with type II (64 vs. 68 years; $p < 0.01$). Males were predominant (73%), and 64% had a symptomatic clinical course. Initial acute episodes led to a chronic classification in 40% of patients. Regarding history, 46% had prior cardiac surgeries, with significant differences between DeBakey classifications (type I: 37% vs. type II: 57%; $p < 0.05$). Among these, 35% had previously undergone coronary revascularization, the most common prior procedure. Ischemia and perfusion times showed no statistical significance between dissection types; however, circulatory arrest time varied by DeBakey classification (type I: 31 minutes vs. type II: 27 minutes; $p < 0.01$).

Early postoperative outcomes did not show significant adverse event differences among DeBakey types, except for postoperative arrhythmia rates (type I: 28% vs. type II: 42%; $p < 0.04$). The overall mortality was 7%, which was notably lower than the rates reported in the literature. Absence of complications such as paraplegia, very low rates of paraparesis, and minimal persistent renal dysfunction requiring replacement therapy were remarkable findings. Long-term follow-up (median of five years, ranging from 2 to 11 years) documented a reoperation rate of 3% and reoperation-free survival of 61%.

The authors conclude that durable repair is achievable with acceptable perioperative risks. Although some postoperative variations are noted between aortic dissection subtypes, mid-to-long-term outcomes are comparable. They emphasize the need for individualized therapeutic approaches. However, the management of “evolved” aortic dissection is associated with reduced rates of persistent neurological complications, even lower than in the acute management of this pathology.

COMMENTARY:

This article is highly valuable as it establishes a clear definition of the “chronic” or delayed phase of this pathology, providing crucial insights for patients presenting in this manner. The extensive timeframe of the study and large cohort enable observations of evolving surgical techniques. Despite this, global analysis shows no statistically significant sociodemographic or clinical differences, indicating that these factors did not influence postoperative outcomes or have any significant clinical impact.

The percentage of patients experiencing an episode of type A aortic dissection with a prior surgical history is noteworthy. This is uncommon in routine clinical practice and may be linked to specific surgical techniques used in this single-center cohort (cannulation strategies, clamping, proximal coronary anastomoses, perioperative blood pressure control, etc.).

Due to the single-center retrospective nature of the data analysis, some results should be interpreted cautiously. Nevertheless, this remains one of the most extensive series examining this form of type A dissection, where “natural selection” yields superior outcomes not directly comparable to those in acute presentations.

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José Manuel Martínez Comendador

Aortic Pseudoaneurysm After Type A Aortic Dissection: When to Consider Conservative Management?

This article retrospectively analyzes a cohort of 39 patients who developed an aortic pseudoaneurysm following surgery for Type A aortic dissection, comparing the long-term outcomes of conservative management versus surgical treatment.

Acute Type A Aortic Dissection (ATAAD) represents a medical emergency with high mortality if not surgically addressed within the initial hours. During the hyperacute phase, the aortic tissues enter an inflammatory state, rendering them particularly fragile, which may lead to long-term complications necessitating subsequent interventions. These interventions may be required for various reasons, such as the development or progression of aortic insufficiency, a gradual increase in residual native aortic diameters, false lumen expansion, graft infection, and the formation of aortic pseudoaneurysms (PA).

The incidence of PA following ATAAD repair is estimated at 10-24%, making it a feared and poorly understood complication. Clinical guidelines vary on when and how to address them. For example, the Canadian Cardiovascular Society recommends surgery when PA reaches a maximum diameter of 2 cm, regardless of cause. In contrast, the European Society of Cardiology suggests open surgery without consideration of size or cause, albeit without a specific level of evidence recommendation. Despite this, scant attention has been paid to the natural history of PA, its prognosis, and treatment in uncomplicated or asymptomatic patients following aortic replacement for any reason.

The objective of this article was to examine the safety and efficacy of a conservative approach to PA and compare this approach with standard surgical treatment. We retrospectively examined 39 patients who presented an aortic pseudoaneurysm after ATAAD surgery to evaluate outcomes (baseline characteristics, presentation, and freedom from aortic events and mortality). Initially, 31 patients were identified for conservative treatment (CT). After close follow-up, 5 of them underwent surgery, bringing the total number of surgically treated patients (ST) to 13 for long-term analysis, while 26 remained in the conservative group. The mean follow-up for the entire cohort was 7.9 years. Freedom from aortic-related mortality at 1, 5, and 10 years was 100%, 83.3%, and 72.9% for the ST group and 95.8%, 77.3%, and 77.3% for the CT group ($p = 0.35$).

In light of these results, the authors conclude that a conservative approach for aortic pseudoaneurysms may be justified in asymptomatic patients with high surgical risk. Close follow-up by specialized clinicians is essential to refer patients for surgery when necessary.

COMMENTARY:

Chaud et al. present in this article the evolution of a series of 39 patients with aortic pseudoaneurysm as a complication following repair of acute Type A aortic dissection. Traditionally, the general belief has been that aortic pseudoaneurysms require surgical intervention. However, the authors challenge this premise by offering a thorough comparison of long-term outcomes between conservative management and surgery in these cases. The most remarkable finding in this study is the objective lack of significant differences in aortic and all-cause mortality at 10 years. This represents a milestone by justifying, for the first time, the feasibility of a conservative approach for a specific population of asymptomatic patients with pseudoaneurysms. Furthermore, this finding highlights the importance of close and rigorous follow-up for these patients.

This article rests on three fundamental pillars that underscore its importance. Firstly, it presents a patient series with PA that exceeds any previous study in size. Secondly, by excluding patients with infections, the study achieves a notable degree of cohort homogeneity regarding pseudoaneurysm etiology. Finally, the study's groundbreaking contribution lies in its innovative approach to conservatively addressing pseudoaneurysms, marking a milestone in the understanding and treatment of this complication.

Nonetheless, to avoid premature conclusions, it is essential to highlight several aspects related to the size of the pseudoaneurysms in each of the analyzed groups. Patients managed conservatively, comprising two-thirds of the cohort, presented a mean pseudoaneurysm size of 10 mm, whereas the surgical group showed an average size of 18 mm. Notably, those initially opting for conservative management who later required surgical intervention displayed a pseudoaneurysm size of 20 mm at the time. It is crucial to consider that the existing literature on pseudoaneurysms after aortic dissection is sparse and often limited to isolated case reports. Consequently, recommendations tend to be ambiguous and contradictory. Certain guidelines and scientific societies, such as the Canadian Cardiovascular Society consensus, suggest intervention for pseudoaneurysms larger than 20 mm, despite limited solid scientific evidence to support this threshold. Chaud et al.'s study, within this context, may bolster the size threshold proposed in the consensus document.

However, if we factor in the variable of time, the study's results should be interpreted with caution. On the one hand, the time elapsed from the initial aortic dissection repair to the pseudoaneurysm diagnosis in conservatively treated patients is shorter than for those undergoing surgical treatment (1.4 years versus 6.3 years). On the other hand, the follow-up duration after diagnosis in the conservative treatment group was only 5.1 years. This implies that pseudoaneurysms in the conservative group were diagnosed shortly after surgery, and the follow-up period was significantly shorter compared to the mean cohort follow-up duration, which was 8.1 years. In summary, while initial follow-up and observation with conservative treatment may be a suitable strategy, prolonged monitoring is necessary to ensure pseudoaneurysms do not continue to increase in size over time.

Another intriguing aspect is addressing the issue from the perspective of the relationship between PAs and the use of different materials during emergency surgery to treat aortic dissection, particularly the application of Teflon felt or the use of biological surgical adhesives such as BioGlue®. BioGlue®, composed of bovine serum albumin and glutaraldehyde, is used to enhance suture hemostasis and strengthen delicate aortic tissue and was approved by the FDA in 2001 for use in aortic dissection cases. In the study, the authors found no statistically significant differences in the prevalence of Teflon felt use (60% in the conservative group vs. 36.4% in the surgical group) or BioGlue (12% vs. 27% between conservative and surgical management groups, respectively). Teflon felt is widely recognized as a well-established protective agent against pseudoaneurysm formation, while BioGlue®, due to its glutaraldehyde content, has been studied for its potential cytotoxicity and association with pseudoaneurysm formation in prior research. The lack of a statistically significant relationship in this study between BioGlue® use and pseudoaneurysm progression toward a poor prognosis requiring surgery might be attributed to the relatively small cohort size. Although other studies have explored the role of BioGlue®, firm conclusions remain elusive. Should the hypothesis of glutaraldehyde-induced cytotoxicity hold true, BioGlue® could mask leaks under a seemingly successful hemostasis, ultimately progressing in the absence of an intact aortic wall to contain them as PA. Therefore, it is currently impossible to issue a recommendation on BioGlue® use in ATAAD surgery.

Infections are widely recognized as a significant etiological factor in PA formation. In this study, all patients showing evidence of infection were meticulously excluded to maintain cohort homogeneity, as any infection alone would necessitate surgical intervention.

Endovascular treatment has shown to be an effective option with acceptable outcomes for managing pseudoaneurysms in the descending aorta. However, in the ascending aorta, endovascular options are generally limited to exceptional cases involving small pseudoaneurysms located in zone 0 with suitable landing zones, and they are documented only as rare clinical cases. In the present article, the possibility of endovascular treatment has yet to be considered. It is likely that in the coming years, the development of branched or fenestrated stent grafts will enable the preservation of supra-aortic trunks, thus allowing more widespread endovascular management of this complication. Nevertheless, this perspective remains unexplored within this study.

The study's findings merit special recognition, firstly because it constitutes the largest series of patients with PA post-aortic dissection surgery; and secondly, due to the outstanding outcomes achieved through both conservative and surgical treatment. One of the most noteworthy takeaways lies in the choice of conservative management, emphasizing the importance of close clinical and radiologic follow-up. This is crucial to detect potential signs of new symptoms, such as angina suggesting left coronary trunk compression, heart failure secondary to fistulas into other cavities, among others. Additionally, rapid PA growth or sizes exceeding 20 mm should be closely monitored, as these indicators could signal the need for surgical intervention. Further study with extended follow-up of these patients will likely clarify lingering questions about this feared complication.

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Elio Martín Gutiérrez

Neomedia of Bioglue® in Type A Aortic Dissection Repair: From Myth to Science

An in vitro study on the mechanical properties of BioGlue® sealant applied to neomedia reconstruction in type A aortic dissection repair.

Many surgical techniques we perform are carried out almost automatically, with an assumption of correctness. Since it's not always feasible to question the underlying scientific basis (and it likely doesn't exist for everything), habits are formed through imitation and learning from peers. While a surgical profession like ours involves a significant amount of practical learning, the distinction between merely "tailors" stitching structures together and "physicians who operate" lies in the scientific basis of much of what we do.

In cases where such a scientific foundation doesn't exist, we must create and disseminate it. This approach inspired the British team in today's article to investigate the mechanical properties of BioGlue® when used for repairing the aortic wall in type A dissection, by creating a neomedia on which the Dacron conduit anastomoses could be performed. Many of us have performed this practice, adopting it more through craft than study. Notably, the product has certification for this use, in addition to being an anastomotic sealant. This adoption is driven more by craft than by study, given the extensive collection of studies delving into the so-called "black legend" surrounding this sealant. The presence of glutaraldehyde, which denatures bovine albumin to form the characteristic "caramel" layer, has led to accusations of polypropylene suture rupture, tissue necrosis, regional inflammation, and other complications resulting in pseudoaneurysms. Numerous reports also document embolization of gelatin fragments, either from accidental application into the circulatory stream or after using it in reconstructing the aortic wall, with resulting redissections.

Regarding pseudoaneurysm formation, a previous blog post analyzed BioGlue®'s potential role. However, none of the studies proved conclusive enough to warrant the removal of FDA and CE markings, with a usage history extending over 50 years in aortic dissection contexts.

The authors developed a porcine aorta model in which 42 tissue samples were dissected into two layers through the tunica media, replicating pathological conditions. A layer of product was applied, keeping the two layers of dissected aorta pressed together for two minutes, as per the manufacturer's instructions. Groups were created with varying levels of pressure maintained on both layers after adhesive application, alongside a group with no applied pressure. Twenty-eight non-dissected aorta samples served as comparative controls.

Adhesive function was assessed using a T-Peel test, a standard method for evaluating the mechanical properties of adhesives across industries. The addition of BioGlue® with some degree of pressure (particularly when applied using Borst clamps specifically designed for this purpose) showed greater wall resistance compared to cases with no pressure application. In fact, compared to the non-dissected controls, the wall resistance of BioGlue® applied with pressure was similar to that of a healthy aorta. Conversely, when no pressure was applied, the wall resistance was significantly lower than that of the non-dissected controls.

Histological analyses, including optical and electron microscopy, and cell culture tests were conducted to assess cellular viability in the context of BioGlue®. Microscopy confirmed the differentiation between tissue and adhesive layers, suggesting no

penetration of the product into the tissue. While no tissue or cellular damage was observed, a reduction in smooth muscle cell growth in the tunica media was noted in BioGlue-exposed environments compared to non-dissected controls.

The authors concluded that the application of the T-Peel test methodology is novel in evaluating the properties of various surgical adhesives. This study confirms the efficacy of BioGlue® in reconstructing the dissected aortic wall. However, it also emphasizes that achieving this effect requires maintaining pressure for at least two minutes.

COMMENTARY:

This study reminds us not to take anything for granted. BioGlue® is effective in aortic wall repair, but only when used correctly. Excessive product application, spilling into the intraluminal space, failure to wait for the two-minute setting time, and, as newly highlighted, maintaining continuous pressure—preferably using Borst clamps—seem to be the usage guidelines for this indication. In cardiovascular surgery practice, especially in intraoperative scenarios like circulatory arrest, these guidelines may not always be strictly followed, which can undermine the intended effect and, ultimately, be harmful. Indeed, the apparent uniformity in its application may mask diverse usage practices that could explain inconsistent results and many reported adverse events.

In summary, this is an elegant study with inherent limitations of in vitro analyses. However, its lesson transcends a mere call to use any product or device correctly. It shows that disparate outcomes can arise from heterogeneous practices and a lack of scientific rigor in seemingly simple acts like applying a surgical adhesive. This study encourages us to keep researching and questioning every technical step we take, especially if it doesn't yield satisfactory results. After all, chance, myths, tradition, "this is how it's always been done," "we do it this way here," or "I was taught to do it this way" have no place in modern surgery.

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Elio Martín Gutiérrez

TEVAR for Acute Type B Uncomplicated Aortic Dissection: The Key Is in the Details

American registry of 5-year outcomes in patients with acute type B uncomplicated aortic dissection treated within the first 30 days with TEVAR vs. conservative management.

The therapeutic management of acute type B uncomplicated aortic dissection holds a class I recommendation in the 2014 European guidelines for medical management and IIa for interventional management, whereas in the American guidelines of 2022, medical management receives a class 1 indication and the interventional approach, only for anatomies with a high risk of developing complications, 2b. Nevertheless, these patients exhibit a significant mortality during follow-up, raising questions whether early endovascular treatment could offer any benefit over the natural history of the disease and prevent the development of complications that have not initially occurred.

The highest quality evidence, available so far, comes from the European studies INSTEAD and ADSORB. Both presented low statistical power (n=140 and 61 patients, respectively), although in the first, a sample size calculation was performed. The included patients presented with acute type B uncomplicated aortic syndromes, but at different evolutionary phases, and none of them demonstrated a true short-term benefit or at the 5-year follow-up. It was the extension of the follow-up in the INSTEAD study beyond 5 years (INSTEAD-XL) that determined a benefit of TEVAR in patients with type B uncomplicated dissection treated in the subacute phase by adding cases of mortality in the medical treatment group, without new randomized works proving this until now (mortality 19.3% vs 6.9%, p<0.0045).

The following work attempts to shed light in this respect. It involves a study of historical cohorts that included patients with acute type B uncomplicated aortic dissection treated in American centers affiliated with Medicare and Medicaid programs, between 2011 and 2018, with maximum follow-up until 2019. The results included all-cause mortality, and the need for hospitalization due to cardiovascular and/or aortic causes, including the need for new interventions/interventionism. Treatment cohorts were compared between those patients managed with optimal medical treatment and those who received TEVAR in the acute phase of the disease.

Of 7,105 patients with acute type B dissection, 1,140 (16%) underwent initial TEVAR (first 30 days) and 5,965 (84%) received medical treatment. The assignment to one type of therapy or another was adjusted based on idiosyncratic care reasons of the centers (which included differences in the type of care coverage), the presence of comorbidities such as arterial hypertension (OR 1.2), peripheral vascular disease (OR 1.24) or frailty (OR 0.09), and the year (increase in procedures from 2011) were related in the multivariate analysis to a different probability of having received TEVAR vs. medical treatment.

One of the main criticisms of the work (for the purpose of homogenizing both groups, argue the authors) comes from having excluded patients who died in the first 30 days or who did not have sufficient health coverage for that period were excluded. The observed mortality with both strategies up to the 5 years of follow-up did not show significant differences in mortality, nor in hospitalizations related to aortic pathology, nor the need for new therapeutic procedures. For the purpose of amending the bias with the exclusion of the deceased in the first 30 days, a sensitivity analysis was included that suggested that initial TEVAR was associated with lower mortality during a period of the first year (adjusted HR = 0.86; 95% CI 0.75-0.99; p=0.03), at 2 years (adjusted HR = 0.85; 95%

CI 0.75-0.96; p = 0.008) and at 5 years (adjusted HR = 0.87; 95% CI 0.80-0.96; p = 0.004).

COMMENTARY:

This new study on TEVAR treatment in type B aortic dissection provides highly relevant information on a topic with a clear lack of solidity in terms of evidence. It also represents one of the main experiences in American practice published regarding the management of uncomplicated type B dissection. The procedure rate remains low and adherence to clinical guidelines remains the norm in clinical practice, in light of the 16% of patients who received TEVAR in the initial phase. Although the results of adverse events observed in the follow-up are not published, broken down for each of the treatment cohorts, the authors recognize the lack of benefit for indicating TEVAR in early phases. Indeed, they argue that the potential benefit of changing the natural history of the disease (aneurysm formation of the dissection) is countered with the aggregation of short-term complications (retrograde dissection, stroke, paraplegia) and long-term (treatment of endoleaks, progression of native disease). This uncertainty continues to make necessary the selection of those cases with a high risk of complication: hypertension or uncontrolled pain, maximum aortic diameter ≥40 mm, maximum diameter of the proximal false lumen ≥22 mm, true lumen dwarfing without malperfusion, progression of periaortic hematoma, large single entry tear ≥10 mm proximal and especially if located in the lesser curvature and/or distal “cul-de-sac” with partial thrombosis of the false lumen, as candidates to benefit from TEVAR in the acute-subacute phase of the uncomplicated type B dissection.

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José Manuel Martínez Comendador

Endovascular Treatment in Uncomplicated Type B Aortic Dissection: Has the Time Come?

A retrospective analysis of the GREAT registry comparing short- and medium-term results of endovascular treatment in acute type B aortic dissection complicated with uncomplicated dissection.

Currently, the most widely accepted treatment for uncomplicated acute type B aortic dissection (UATBAD) is conservative management through optimal medical therapy (OMT), reserving thoracic endovascular aortic repair (TEVAR) for complications such as rupture, malperfusion syndrome, refractory or recurrent pain, and uncontrolled hypertension. TEVAR is a procedure not free of risks, which can lead to complications such as retrograde dissection to the ascending aorta, "bird beak" phenomenon leading to prosthetic collapse or type IA endoleaks, among others, especially when additional procedures on the supra-aortic trunks (SAT) are required. However, the benefits in medium- and long-term survival of implanting these endoprostheses in the presence of complications in UATBAD seem to outweigh perioperative morbidity and mortality. The use and indications of TEVAR in UATBAD are not as clear and continue to be a subject of ongoing debate.

The objective of this study was to analyze the results of TEVAR performed in complicated and uncomplicated UATBAD in the Global Endovascular Aortic Treatment Registry of WL Gore (GREAT). A total of 5014 patients were retrospectively analyzed, of whom 172 underwent TEVAR in a UATBAD situation. Of these procedures, 102 were complicated UATBAD and 70 were uncomplicated. There was a greater involvement of procedures involving the SAT in complicated UATBAD vs. uncomplicated (45.1% vs. 21.4%, p = 0.002). Patients in the complicated UATBAD group also had a longer average hospital stay (14.3 vs. 9.8 days, p = 0.002). There were no significant differences in 30-day mortality (2.9% in complicated UATBAD and 1.4% in uncomplicated) or in aortic complications (8.8% vs. 5.7%). The three-year aortic event-free survival was similar in both groups (62.9% vs. 70.6%).

The authors conclude that patients with UATBAD in the GREAT registry treated with TEVAR, whether they were complicated or uncomplicated cases, had a low and similar incidence of perioperative complications and mortality. The medium-term results in both groups were satisfactory.

COMMENTARY:

The guideline on the management of type B aortic dissection of the STS/AATS published in 2022 is clear. TEVAR is unequivocally the treatment of choice in complicated UATBAD, just as OMT is in uncomplicated UATBAD. On the other hand, TEVAR in uncomplicated UATBAD continues to be a controversial issue. Over time, TEVAR in this scenario has been gaining ground in recent years; however, the level of recommendation in this last guideline is still not high (recommendation class IIb), stating that prophylactic TEVAR may be considered in uncomplicated UATBAD to reduce the risk of death and long-term adverse events related to the aorta.

OMT, which primarily consists of controlling blood pressure below 120/80 mmHg and a heart rate less than 70 beats per minute, has shown excellent intrahospital and 1-year survival results in uncomplicated UATBAD. However, numerous registries and a clinical trial have shown that these patients over time develop aneurysms in a proportion close to 70% and a mortality between 3-5 years of 25-30%.

The only two clinical trials that compare OMT with TEVAR in uncomplicated UATBAD provide very relevant data in favor of TEVAR, but still insufficient. The INSTEAD XL study showed that TEVAR performed between week 2 and 52 after acute aortic syndrome (subacute and chronic phase) improves 5-year survival and delays disease progression compared to isolated OMT. On the other hand, the ADSORB study, which does compare OMT with TEVAR without waiting for the subacute phase, showed a reduction in diameter and thrombosis of the false lumen with the use of endoprosthesis, but we still do not have information on the impact of this in the long term. Observational studies that compare OMT with TEVAR in this scenario are scarce and provide unclear and sometimes contradictory results.

Spinelli and colleagues, in this study conducted with patients from the GREAT registry, contribute their bit by adding evidence in favor of the safety and effectiveness of TEVAR in uncomplicated UATBAD. The results of the GREAT registry are the result of the analysis of real-world patients. A total of 172 patients with UATBAD treated with TEVAR with Gore TAG prostheses between 2010 and 2016 were analyzed. In the group with complicated UATBAD, TEVAR is confirmed as the treatment of choice. However, the real value of this study is provided by the results in patients with uncomplicated UATBAD. Mortality at 30 days, 1 and 3 years was 1.4%, 3.2%, and 9.6%, respectively, figures equivalent or better than the results of other studies that analyze OMT in isolation. Additionally, the aortic event-free survival (composite event that includes reintervention, stroke, spinal damage, aneurysm growth, retrograde dissection, or persistence of the false lumen) was 77% and 71% at 1 and 3 years, respectively. These data confirm the perioperative safety of TEVAR for patients with uncomplicated UATBAD, and demonstrate that TEVAR is not inferior to OMT in the short term. Unfortunately, the average follow-up of this study was relatively short (2 years), and there is little information available to assess the effectiveness in aortic remodeling, such as changes in the false and true lumen. On the other hand, for years it has been known that there are a series of anatomical characteristics such as an aortic diameter > 40 mm, initial diameter of the false lumen > 22 mm, intimal tear near subclavian artery, among others that, when present, the patient is classified as high risk for developing late complications. In this study, it would have been of great interest to know which patients had these risk factors and their evolution based on the treatment.

In the absence of randomized clinical trials, the information from this subgroup of patients that comes from registries like this one is invaluable for advancing knowledge of the best therapy. In patients with low-risk uncomplicated UATBAD, it seems prudent to first advocate for OMT, and at a second yet to be determined time, assess elective TEVAR based on the circumstances of each case. However, given the poor long-term results of OMT in uncomplicated UATBAD and the growing evidence of the safety and effectiveness of TEVAR in this group of patients, in some cases endovascular therapy, especially in those patients labeled as high risk for late complications, could be the first therapeutic option. This would be the true metamorphosis of the management of uncomplicated UATBAD; change is the only constant thing, and in this field it would be no exception.

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Elio Martín Gutiérrez

Uncomplicated Type B Aortic Dissection: TEVAR or Not TEVAR... and When to TEVAR

A retrospective study involving 91 patients with uncomplicated type B aortic dissection, initially managed with medical treatment, assessing the rate, indications, and characteristics of patients who required invasive procedures during follow-up compared to those who continued with optimal medical treatment.

Uncomplicated type B aortic dissection (uTBAD) has traditionally been assigned to conservative management through intensive pharmacological therapy from diagnosis, continuing during follow-up if clinical-radiological stability is maintained in successive controls. However, the evolution of progressively increasing evidence reflects a scenario where a considerable volume of patients benefits from or needs invasive procedures to correct the progression of their aortopathy or to prevent potentially lethal complications.

Research in this field is plagued by heterogeneity (patients at different stages of the disease, different follow-up durations, and different goals: mortality, aortic remodeling, etc.) and studies with limited statistical power. The generation of evidence began, firstly, from the INSTEAD and ADSORB studies, where TEVAR was compared to optimal medical treatment (OMT) in the subacute and acute phases, respectively, of patients with uTBAD. In none of the cases was a benefit obtained with respect to OMT. It was the INSTEAD-XL study that first demonstrated a survival benefit at 5 years related to aortic events in patients treated with TEVAR in relation to a limitation of disease progression and better aortic remodeling. Since then, different observational works supported this thesis, proposing different predictors that would allow selecting the best candidates for TEVAR in subacute and chronic phases. The culmination of this work was provided by the analysis of the GREAT registry, showing good results for the application of TEVAR in patients with uTBAD in the acute phase, where new predictors were identified.

The work by Kreibich et al. (from Czerny's team in Freiburg, Germany) describes the natural history of uTBAD. They selected 91 patients affected between 2012 and 2018, all of them initially managed with OMT. They performed a 5-year follow-up finding that, at a median follow-up of 4 months, 33% had required some invasive procedure. The indications for this were the progression of aortic diameters >5 mm/year (67%), dynamic obstruction or claudication (23%), recurrent pain (7%) and one case of aortic rupture. The invasive procedure that was mainly performed was TEVAR (83%) with/without left subclavian artery bypass. Elephant trunk surgery was reserved for those cases with involvement of the aortic arch in the pathology (10%) and repair was performed via a thoracoabdominal approach in those where the involvement extended distally to the thoracic aorta (7%). TEVAR was also rejected for those patients in whom a sufficient landing zone could not be obtained despite the transposition of the left subclavian artery or carotid-subclavian bypass when the diameters of the ascending aorta and/or arch exceeded 40 mm or there was some underlying connective tissue disorder. There was no periprocedural mortality, and the mortality during follow-up was 3 patients for non-cardiovascular reasons. In the univariate analysis, different factors, which we will mention below, were presented significantly more frequently in the patients who required an interventional/surgical/hybrid strategy compared to those in whom management continued with OMT. In the multivariate analysis, only an aortic diameter >45 mm was shown as an independent predictor of having an indication for performing some interventional/surgical procedure.

The authors concluded that in patients with uTBAD, initially managed with OMT, the need for additional endovascular, surgical or hybrid procedures was substantial. It is necessary to establish new management criteria based on the available evidence that optimize the assignment of patients to the best treatment strategy at each evolutionary moment of their pathology.

COMMENTARY:

The work of Kreibich et al. perfectly describes the natural history of uTBAD in the context of modern OMT and calls for an update of the consensus documents that do not reflect the reality of the available evidence. Reviewing the predictors that indicate benefit in survival and aortic wall remodeling with TEVAR compared to OMT, which are discussed in this work and in subsequent comments on it, we have:

- In the acute phase (<14 days), defined as "high-risk" uTBAD, currently included in the 2020 SVS/STS clinical guidelines: poorly controlled pain, refractory arterial hypertension, pleural effusion, radiological evidence of arterial obstruction without signs or symptoms compatible with malperfusion.
  In the subacute phase (2 weeks - 3 months): entry door on the lesser curvature and >10 mm, false lumen diameter >22 mm and aortic diameter >40 mm in the first diagnostic angiography, partial or absent thrombosis of the false lumen, elliptical true lumen (instead of circular, which is a good prognosis), false lumen without exit door in "cul-de-sac" and rehospitalization for aortic cause in the first 30 days after diagnosis.

- In the follow-up with OMT (>3 months) proposed in the work of Kreibich et al. and concordant with the previous literature: partial or absent thrombosis of the false lumen, greater length of dissection extension, greater amount of communications between lumens (this criterion has not been constant in the literature or has been considered a protective factor), greater proximity of the entry door to the left subclavian artery, size of the entry door >10 mm and location on the lesser curvature (although these last ones were not significant in the work of Kreibich et al.), larger diameters of thoracic and abdominal aorta with a cut-off point at 45 mm (other works have suggested 40 mm), non-A non-B dissection (entry door in the aortic arch) and diameter of the false lumen >22 mm.

The number of predictors makes one consider the almost oxymoron "dissection" and "uncomplicated". Indeed, this justifies that in a third of the patients a conservative strategy is not enough, and its perpetuation, harmful. After all, OMT only delays the natural evolution of the disease; TEVAR achieves a high rate of correction with a favorable risk/benefit balance thanks to the advancement of technology and the experience of the teams. Therefore, that procedure still assigned to a class of evidence IIb, conceived as prophylactic, probably has to be reconsidered in the therapeutic algorithm of these patients, apparently, uncomplicated.

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Elio Martín Gutiérrez

Type B Aortic Dissection: Masters in the Field Share Insights

Review Article from the Houston Methodist DeBakey Heart & Vascular Center Updating Knowledge on Classification and Management Recommendations for Type B Aortic Dissection.
Type B aortic dissection has recently seen renewed interest in the literature, prompting updates to concepts, classifications, therapeutic management strategies, and outcomes. It is a severe and complex pathology as it affects the body's main artery where repair options are limited. With advances in technology and medical team experience, the endovascular approach has become preferred over open approaches due to its less invasive nature and higher success rates.

In our country, this pathology affects over 2,000 patients annually (incidence 3.5-6/100,000/year) and continues to pose a therapeutic challenge with certain management uncertainties. Traditional classification by the Stanford criteria and those proposed by DeBakey, as well as its categorization as "complicated" and "uncomplicated," have guided therapeutic attitudes for decades. However, recent times have brought numerous considerations regarding this pathology. Authors from the center named after the pioneer of this pathology's study and treatment, Dr. Michael Ellis DeBakey, as well as one of its survivors, review and propose innovative concepts on classification, pathophysiology, and treatment of this disease. Here, we proceed to synthesize these concepts.

COMMENTARY:

Various novel aspects are detailed in the work, highly recommended for reading and archiving:

Modification of classification criteria:

- Anatomical classification: Anatomical classification holds particular importance in determining prognosis and therapeutic management of patients with aortic dissections, especially type B. These classifications have undergone modifications and adaptations to the current criteria:
    - Stanford classification: This is a clinically oriented classification that has undergone significant modifications over time. Traditionally, it distinguished two types of acute aortic syndrome (AAS), type A (involving the ascending aorta with an entry tear at this level) and type B (not involving the ascending aorta nor presenting the entry tear at this level, typically appearing in the proximal portions of the descending aorta). Determining the involvement of the ascending aorta has a pronounced prognostic importance as the risk of developing heart failure, cardiac tamponade, and/or coronary malperfusion significantly worsens the prognosis compared to AAS type B. However, with the emergence of concepts like retrograde dissection, which could affect an aortic territory proximal to the entry tear, and those forms where the involvement is exclusive or starts at the aortic arch, left some patients outside the classification, which led to the description of AAS type non-A non-B. The authors propose a further evolution of this classification, combining it with the landing zones of endoprostheses in the 11 segments into which Ishimaru divided the aorto-iliac territory, likely indicating future endovascular therapeutic intentions. The classification would consider the entirety of the affected territory, both by dissection and adjacent intramural hematoma, naming it A or B depending on whether the entry tear is located at the ascending aorta (zone 0) or any of the remaining 11 segments (1-11),

respectively. Thus, the typical dissection with an ascending aorta flap would be known as AAS type A, indicating with a subscript the most distal segment to which it extends (for example, up to the common iliac artery would be A10). Similarly, a descending aorta dissection reaching below the renal arteries and flap at 2 centimeters from the left subclavian artery would be described as AAS type B3-9. And a dissection, with a flap under the left carotid artery extending with an intramural hematoma to the brachiocephalic trunk and distally to the external iliac would be named B1-11). Retrograde extension affecting the ascending aorta would not change the designation to A, as the letter would be determined by the entry point, so it would be called B0-11 (one of the forms of the previous non-A non-B AAS). Finally, the letter I followed by two subscripts (for example, I3-5) would correspond to those cases of intramural hematoma where the entry tear is not evident (in the example, intramural hematoma extending from the segment within the 4 centimeters distal to the subclavian artery to the portion of the thoracic aorta below the sixth thoracic vertebra).

- DeBakey classification: This is another of the classic classifications that, paradoxically, the authors of the work chose not to adapt to our times as they did with the previous one. It comprises three types of aortic dissection: I (involving the ascending aorta to the descending); II (limited to zone 0); and type III, subdivided into IIIA and IIIB when the involvement extends from zone 3 to the distal 4 (IIIA) or from 5 onwards (IIIB). Although with a clear anatomical focus, like the first version of the Stanford one, it had gaps in describing certain forms of AAS, particularly those originating or exclusively involving the aortic arch.
- TEM classification: This is the most recently proposed and combines anatomical and clinical features. It includes three concepts: T for "type" according to the modified Stanford classification (A: affects the ascending aorta, B: only affects the descending aorta, non-A non-B: involvement of the arch with/without descending aorta, not affecting the ascending aorta), E for "entry" according to the location of the entry tear (0: indeterminate, intramural hematoma; 1: ascending aorta, zone 0; 2: aortic arch, zones 1 and 2; 3: descending aorta, zones 3-11) and M for malperfusion (0: absent, 1: coronary, 2: cerebral; 3: spinal, iliac and/or limbs; +: with the presence of clinical signs, -: without the presence of clinical signs). This constitutes the main competitor of the first, and it must be determined by scientific organizations which of them is considered more recommendable for clinical practice. Much of this decision will fall on whether to continue recognizing the form of AAS type non-A non-B.

- Chronological classification: Comprises hyperacute forms (<24 hours), acute (from 24 hours to 14 days), subacute (from 2 weeks to 3 months), and chronic (>3 months). These cut-off points are marked by pathophysiological aspects of maturation of both the medio-intimal membrane and the free wall of the false lumen. Both aspects have therapeutic value in terms of the possibility of remodeling the true lumen and the pertinent circulatory adaptations (irrigation through the true or false lumen, situations of subclinical malperfusion); and prognostic value in terms of the development of serious or fatal complications.

Therapeutic decision:

The clinical classification must consider type B aortic dissection as "complicated" and "uncomplicated". The former is described as that form with the development of rupture or clinical threat of the same and/or malperfusion (clinical or not) and corresponds to a therapeutic emergency. On the other hand, an intermediate concept of "high-risk" dissection has been described, applicable to the acute phase, where a therapeutic

attitude also urgently applies, analogous to the complicated situation. Otherwise, although "uncomplicated" dissection has traditionally been considered for conservative treatment, multiple works highlighted by the authors (INTEAD, INSTEAD-XL, ADSORB) describe poor outcomes in almost half of these patients. Selecting candidates is crucial, with the subacute phase being the choice for carrying out endovascular treatment that allows correcting aortic remodeling and preventing both future complications and the aneurysm process, which would limit subsequent therapeutic action, impacting survival. Some of these predictors have been described in previous entries of this blog, to which we refer you (Uncomplicated type B aortic dissection: TEVAR or not TEVAR... and when to TEVAR [https://secce.es/diseccion-aortica-tipo-b-no-complicada-tevar-o-no-tevar-y-cuando-tevar/]). Not addressing these predictors, leaving patients with potential poor evolution to the only alternative of medical treatment, entails an accumulation of adverse events in the follow-up and aortic dilation that, reaching the 55-60 mm proposed as an indication in clinical guidelines, frequently makes complete percutaneous treatment difficult. As recognized by Mani et al., it often requires adopting a thoracoabdominal approach with FEVAR (fenestrated-EVAR) and BEVAR (branched-EVAR), where in less than 50% of cases a reduction in aortic diameter is achieved. Other authors have reported low success rates of the procedure and complications during follow-up (endoleaks, migration). In addition to the aforementioned predictors, the authors expose different odds ratios from the analysis of the IRAD (International Registry of Aortic Dissection) of the main prognostic factors in patients with type B aortic dissection that would be clinical markers to cement the decision of a surgical/interventional/hybrid treatment instead of the conservative one in the acute/subacute phase. Among them, limb ischemia (OR = 3), periaortic hematoma (OR = 3), aortic diameter >5.5 cm (OR = 3), acute renal failure (OR = 3.6) stand out.

Technical aspects:

- Positioning regarding cerebrospinal fluid (CSF) drainage: the authors indicate that CSF drainage is recommended as a therapeutic option (in the presence of spinal neurological symptoms) rather than prophylactic (application prior to procedures). It is considered the best risk-benefit balance of the procedure, as a rate of spinal neurological events <5% has been described, which balances with an equivalent rate of adverse events (epidural hematoma, subarachnoid hemorrhage, infection, malfunction of the drainage system due to obstruction, malposition, migration, etc.) if applied systematically prophylactically. In fact, they consider that, in the presence of spinal neurological symptoms, permissive arterial hypertension may have a greater therapeutic benefit than drainage.

- Treatment of complicated aortic dissection: the reasons why complicated aortic dissection requires emergency treatment are rupture or the threat of the same and the presence of malperfusion (clinical or subclinical).

    - Rupture: In the presence of hemothorax, decompression with thoracic drainage is not recommended until complete control of the leak has been achieved, due to the risk that it may progress. In fact, it is recommended to maintain a shock situation with permissive hypotension without excessive use of crystalloids in resuscitation in order to limit hemodilution and related hemostatic alterations. Coverage of the leak site by deploying an endoprosthesis in the true lumen that obliterates the false lumen should be the objective and treatment of choice, in accordance with current clinical guidelines. Although the criteria for considering technical success in aortic dissection require the presence of good proximal sealing (absence of type IA endoleak) and between endoprosthesis modules (absence of type III endoleak), the presence of collateral branches or distal re-entries (type II and IB endoleaks, respectively), could maintain the patency of the

false lumen and perpetuate the bleeding in this context. Mere expansion and pressurization of the true lumen may be sufficient to redirect aortic remodeling in other contexts, but not in the case of rupture. Strategies such as the "candy-plug" (endoprosthesis in napkin ring parallel to the previous one but housed in the false lumen with obliteration within the narrow area with an Amplatzer® device), the "Knickerbocker" (which will be described later) or embolization with coils (of the false lumen and/or collateral branches) will pursue achieving thrombosis of the portion of false lumen isolated between the proximal sealing and the distal level of the endoprosthesis housed in the true lumen.

- Malperfusion: can affect different levels (cerebrovascular, visceral, and/or limbs) and can be classified as static (when there is a permanent obstruction of distal flow due to obliteration of the true lumen by the pressurized false lumen and/or thrombosis) or dynamic (when the compromise of flow depends on hemodynamic aspects such as coverage of the ostium of the vessel by the medio-intimal membrane or exists a variable compression of the true lumen by the false lumen dependent on its pressurization). The first therapeutic option consists of expanding the true lumen by deploying an endoprosthesis with coverage of the entry tear and redirection of flow inside it, without type IA or III endoleaks, since in 4 out of 5 cases the dynamic mechanism predominates over the static one. If the malperfusion situation persists (which is recommended to be checked by IVUS), treatment with direct stenting channeling the true lumen of the tributary vessel may be considered. The authors do not contemplate fenestration percutaneous treatment strategies or creation of new re-entries in the medio-intimal membrane, suggesting surgical alternatives such as open fenestration or extra-anatomic bypasses.

- Treatments to prevent aneurysmal degeneration: one of the main reasons for aneurysmal degeneration is because adequate treatment has not been applied in earlier stages that would have favorably conducted aortic remodeling. However, even when applying it, due to the possibility that distal re-entries to the treated dissection at the thoracic level remain and perpetuate the patency of the false lumen, different techniques have been proposed to potentiate favorable aortic remodeling. Among them, the authors highlight:

  - "Knickerbocker": consists of a specific oversized point with a compliant balloon at the mid-distal level of the endoprosthesis module, until it obliterates the false lumen at that level. This alternative emerged as a rescue from an acute rupture situation where hemorrhage was perpetuated from distal re-entries to the false lumen. However, it may be applied in the prevention of aneurysmatization of the residual false lumen at the treated segment level and could even lead to the loss of proximal sealing. It was proposed the development of a prosthesis with a bulboid zone prepared to be expanded in case it is necessary to perform this procedure, but it did not have diffusion in practice.

  - PETTICOAT (Provisional ExTension To Induce COmplete ATtachment): emerged as an evolution of the initial idea of an open-cell stent Djumbodis expanded by a compliant balloon. This system intended to expand the true lumen until obliterating the false one. The implants were carried out in open surgery (precursor of the "frozen elephant trunk") and endovascular in the aortic arch, descending aorta or visceral trunks, these latter in the era prior to the development of BEVAR and FEVAR. The discrete results and cases of stent fracture led to the development of new systems, such as the Cook® Zenith® (stent composed of a portion of covered endoprosthesis followed by an open-cell stent distally) or the Jotec® E-XL® (independent open-cell stent) that replaced it.

The STABLE trial showed a success rate in thrombosis of the thoracic false lumen in 70% of the patients, but only in 10% of the abdominal one, using the composite stent Cook® Zenith®, which is why a third of the patients required reintervention at 5 years. The discouraging results of the STABLE trial were improved by repeated non-randomized studies, including one that used the Jotec® prosthesis that achieved a 54% successful remodeling rate compared to 18%, by extending the treatment with an open-cell endoprosthesis with stent. Finally, and despite the benefit demonstrated in aortic remodeling, since it did not translate into a survival benefit, a review of the Cochrane collaboration and a meta-analysis by Qui et al. limited the generalization of PETTICOAT therapy.

- STABILISE (STent-Assisted Ballon-Induced intimaL dISruption and rElamination): consists of a more aggressive variation of PETTICOAT, where following a scheme of a consecutive and/or overlapped endoprosthesis and open-cell stent, the false lumen is obliterated by direct balloon dilatation, instead of depending on the spontaneous expansion of the open stent due to its radial force and material properties (nitinol). This action may even condition the rupture of the medio-intimal membrane, especially from the chronic phase. The technique has demonstrated good results, with complete aortic remodeling at the thoracic level in 100% of the cases and 83% at the abdominal level. However, the experience remains very limited.

- Embolization of the false lumen: which includes direct embolization, collateral branches or techniques such as the previously described "candy plug". In short, aortic dissection is a dynamic entity, both in its pathophysiology and in the scientific evidence around its knowledge. The efforts of the reference groups will continue to deepen the treatment alternatives. The legacy of pioneers like Michael DeBakey who initiated the principles of its study and approach, is assured.

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José Manuel Martínez Comendador

Urgent TEVAR with occlusion of the left subclavian artery: Is it safe in most patients?

A retrospective study analyzing morbidity and mortality associated with urgent thoracic endovascular aortic repair (TEVAR) in acute aortic syndromes, focusing on the effects of occluding or not the left subclavian artery.

The 2014 European guidelines recommend a maximum aorta diameter of 40 mm and a minimum proximal landing zone length of over 20 mm to ensure the success of thoracic endovascular aortic repair (TEVAR), thus minimizing the risk of type Ia endoleaks. However, this criterion presents a challenge in acute aortic syndromes (AAS) affecting the distal aortic arch. In these situations, it is common to need to completely or partially occlude the left subclavian artery (LSA) to achieve adequate proximal sealing.

Partial occlusion of the LSA could, theoretically, increase turbulences, the risk of embolisms or even cause a retrograde aortic dissection, not A-not B and even type A. On the other hand, complete occlusion of the LSA carries the risk of ischemia in the upper limb and may affect the flow in the cerebral artery, with possible adverse consequences for the brain or spinal cord. It is noteworthy that the European guidelines already in 2009 recommended the revascularization of the LSA. Since then, this type of surgical procedure has experienced a notable increase, reflecting its growing importance in clinical practice.

This study aims to evaluate the optimal management of the LSA during TEVAR involving the distal aortic arch in an urgent context. For this purpose, a total of 52 patients with AAS underwent TEVAR (from March 2017 to May 2021) requiring a proximal landing zone in the distal aortic arch. The decision to partially or completely cover the ostium of the LSA with an endoprosthesis, with or without additional bypass, was based on aortic pathology (if there was sufficient proximal neck) and vascular anatomy (based on the patency of the circle of Willis and the unilateral dominance of a carotid or vertebral artery). 35% underwent complete LSA coverage (complete LSA group) and 17% partial coverage (partial LSA group), while in 48% there was no need to occlude the LSA (control group). 22% of the complete LSA group underwent an LSA bypass before TEVAR, while 11% underwent cerebrospinal fluid drainage. The primary endpoints were 30-day and 1-year mortality, stroke, spinal cord ischemia (SCI), and malperfusion syndrome.

Technical success was achieved in 96% of the procedures. The length of the endoprostheses was 171 mm (complete LSA group) versus 151 mm (partial LSA group) vs. 181 mm (control group), covering 6±2 vs. 5±1 vs. 7±2 intercostal arteries. The 30-day mortality, stroke, and SCI rates did not differ. A patient with arm malperfusion underwent an LSA bypass after TEVAR. After 1 year, aortic interventions occurred in 6% (complete LSA group) versus 22% (partial LSA group) versus 13% (control group). Mortality at one year (0% vs. 0% vs. 8%), stroke (6% vs. 0% vs. 4%) and SCI (0% vs. 0% vs. 4%) were similar between groups.

The authors conclude that, after adequate analysis of vascular anatomy, the coverage of the LSA for TEVAR is safe and may offer similar results to TEVAR that starts distal to the LSA.

COMMENTARY:

The outstanding results of this study, achieved in the group of patients with partial or total occlusion of the LSA, are highlighted by the absence of deaths and neurological

complications, along with a single case of arm hypoperfusion. This case was timely identified and effectively treated, demonstrating that these achievements are not due to chance. The implementation of a decision-making algorithm specially designed for TEVAR cases in AAS, combined with the vast experience of a hospital specialized in these procedures, are the fundamental pillars behind these successful results.

Emergency TEVAR requiring proximal anchorage in zones Z1 or Z2 involves the total or partial occlusion of the subclavian artery. It is crucial to ensure that after implantation the blood flow to the brain, the anterior spinal cord (SC) and the left arm is not compromised. This involves meticulous preoperative assessment to identify any vascular anomalies that may affect blood flow, such as a pronounced dominance of the left vertebral artery (VA), a hypoplastic right VA, carotid artery stenosis, or a non-patent circle of Willis. In addition, in cases of endoprosthesis that occlude 7 intercostal arteries, or those exceeding 20 cm or covering more than a third of the descending thoracic aorta, prophylactic cerebrospinal fluid (CSF) drainage is recommended. The implementation of this practice should be personalized and performed with care, as it can improve blood flow in the SC through the anterior spinal artery, potentially reducing the incidence of SCI from 9% to 2%, although the complication rate is not negligible, ranging between 6 and 7%. The execution of the procedure in several stages would facilitate ischemic conditioning of the paravertebral collateral network after the occlusion of the first intercostal arteries, as well as the development of collaterals in the vascularization of the affected SC. This staged approach, particularly in the treatment of aortic aneurysms, has proven effective in reducing the incidence of SCI.

This team establishes, first and foremost, that if the indication for TEVAR is urgent and the patient is hemodynamically unstable or in hypovolemic shock, performing a carotid-subclavian bypass prior to TEVAR is not practical or realistic.

The visual algorithm for decision-making they propose is practical and easy to follow. If the patient is hemodynamically stable but exhibits symptoms (persistent pain, paraplegia or other neurological deficits), the first step should be to obtain detailed images of the supra-aortic vessels, including the vertebral arteries, the basilar artery, and the circle of Willis. Furthermore, they emphasize that, depending on the location and extent of the aortic pathology, it is essential to make a pre-procedure decision on whether to partially or completely cover the LSA, the estimated length of the endoprosthesis, and the likely number of intercostal arteries to be occluded. Therefore, they suggest the following recommendations:

Partial coverage of the LSA is viable as long as it does not compromise and ensures the safety of the proximal anchorage zone. In cases where TEVAR requires an endoprosthesis with a total length greater than 200 mm, they recommend performing prophylactic CSF drainage 48 hours before the procedure and consider performing TEVAR in two stages. This same strategy applies if it is necessary to cover more than 7 intercostal arteries, although this entails some risk of type Ib leakage (which could be treated in a secondary procedure). In case of complete coverage of the LSA, a carotid-subclavian bypass could be avoided if the circle of Willis is confirmed to be intact, the vertebral arteries are compensated and there is no significant stenosis of the left carotid artery. A prophylactic carotid-subclavian bypass should be performed if these conditions are not met, as well as in cases where the left vertebral artery is dominant or emerges directly from the aortic arch. In this study, only 22% of complete LSA occlusions required prior bypass. To assess arm ischemia, the decision to perform revascularization post-TEVAR is primarily based on the detection of clinical symptoms of malperfusion during the first hours after the intervention.

However, in the case of elective surgeries involving endoprosthesis with occlusion of the LSA, this team prefers to perform a carotid-subclavian bypass prophylactically in most patients, regardless of the specific vascular anatomy they present.

In the recent multicenter study by Luehr et al., which has included the largest number of patients to date to assess the impact of LSA occlusion after TEVAR, based on whether they underwent LSA revascularization, it was observed that, although only 50% of the procedures were emergencies, there were no significant differences in terms of mortality (12.7% vs. 19.8%), incidence of stroke (5.5% vs. 7.4%) and paraplegia rates (5.5% vs. 6.6%). However, it is important to note that the rate of arm malperfusion was 10 times higher in those patients who did not receive subclavian revascularization. This study, unlike the one we are analyzing today, obtained worse clinical outcomes, was multicenter and did not have homogeneous action protocols, which makes extrapolation and interpretation of these results difficult.

On the other hand, prophylactic open revascularization of the LSA could increase the risk of minor perioperative complications (such as seroma, nerve damage, lymphatic leakage) and major (neurological) ones. It is known that this practice is associated with an operative mortality that ranges from 1.2% to 5%. For this reason, some researchers propose prophylactic revascularization of the LSA only when there is a high risk of neurological complications, especially stroke or SCI, predicted by angioCT. Additionally, given the difficulty that can entail performing a carotid-subclavian bypass prophylactically in an emergency context with the patient unstable, it seems reasonable to refrain from performing such in these circumstances.

Although it is a retrospective study with a relatively limited patient sample, the most significant finding that emerges from this study is that, in an urgent context, TEVAR with partial or complete occlusion of the LSA can be safely performed without a prophylactic carotid-subclavian bypass, as long as the angioCT predicts that cerebral and spinal vascularization will be sufficient to prevent complications. Therefore, following decision-making algorithms like the one presented in this study is very valuable, safe and its implementation should be recommended in any hospital that handles this type of pathology.

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José Manuel Martínez Comendador

Innominate Artery Cannulation versus Axillary in Proximal Aortic Arch Surgery: ACE CardioLink-3 Study

A multicenter randomized study evaluating the efficacy of antegrade cerebral perfusion (ACP) through innominate artery cannulation compared to axillary artery during hypothermic circulatory arrest in elective proximal aortic arch surgery.

Cerebral protection during aortic arch surgery requiring open repair remains crucial for favorable clinical outcomes. Right axillary artery cannulation has been the method of choice for many surgeons to achieve ACP during hypothermic circulatory arrest (HCA) in such procedures; however, consensus on the optimal strategy has yet to be reached.

The aim of this study was to compare the safety and efficacy of innominate trunk cannulation versus axillary artery for providing antegrade cerebral protection during elective proximal aortic arch surgery.

The ACE CardioLink-3 study (The Aortic Surgery Cerebral Protection Evaluation CardioLink-3 trial) is a randomized, multicenter clinical trial that includes patients undergoing elective ascending aorta and proximal aortic arch surgery requiring open distal anastomosis for hemiarch replacement. A total of 111 patients were assigned to either right axillary artery or innominate artery cannulation for ACP infusion during the moderate HCA period (nasopharyngeal temperature 25.7°C). The primary safety outcome was neuroprotection, with postoperative severe ischemic lesions on diffusion magnetic resonance imaging (MRI) occurring in 38.8% of patients in the axillary group versus 34% in the innominate trunk group (*p* for noninferiority = 0.0009). The primary efficacy outcome was total operative time, with no significant difference observed between both arms. Other secondary outcomes, including 30-day mortality (3.9% in the axillary artery group versus 3.7% in the innominate artery group), stroke/transient ischemic attack (7.1% vs. 3.6%), radiographic or analytical markers, and neurocognitive evaluations between the two different ACP cannulation methods, were similar across both groups.

It was concluded that ACP with direct innominate trunk cannulation is safe and provides neuroprotection similar to axillary cannulation during aortic surgery, though the burden of new neurological lesions (as evaluated by diffusion MRI) is high in both groups.

COMMENTARY:

The ACE CardioLink-3 trial is the first rigorously conducted randomized study to provide evidence of the non-inferiority of direct innominate trunk cannulation versus right axillary cannulation for ACP in hemiarch aortic surgery.

The efficacy of cerebral protection measures during aortic arch surgery is the most decisive factor in favorable postoperative neurological outcomes. The results of deep hypothermic circulatory arrest (DHCA) served as a reference for years. However, the limited duration of “safe” cold ischemia without neurological sequelae, along with the deleterious systemic effects of deep hypothermia, prompted surgeons to experiment with circulatory arrest at milder hypothermic levels combined with ACP through the supraaortic trunks or retrograde cerebral perfusion via the superior vena cava. Despite numerous existing studies, most of which are retrospective, it remains unclear which cerebral perfusion method (antegrade or retrograde) is optimal for effective brain protection.

Initially, ACP was directly and simultaneously employed through the ostia of the innominate and left carotid arteries with the aortic arch open during DHCA. One of the major drawbacks of this strategy is the discomfort caused by the perfusion cannulas interfering within a confined surgical field. Consequently, selective ACP through right axillary artery cannulation became prevalent, providing cerebral perfusion via the right carotid artery with excellent clinical results due to the high percentage of patients with an intact circle of Willis. However, axillary artery access requires an additional incision distinct from the sternotomy, partial dissection of the pectoralis major and minor muscles, careful isolation of the brachial plexus, and manipulation of the axillary artery (which has notably fragile walls). This is where direct innominate artery cannulation offers a more robust alternative, as it allows access through the same sternotomy incision (possibly extending it slightly cranially) and a simpler dissection process compared to the axillary approach.

Several studies and a meta-analysis have compared axillary versus innominate artery cannulation results, generally finding no significant differences between the two techniques except for a shorter operative time favoring the innominate approach. This randomized study thus holds significant relevance in providing scientific evidence to support what has been previously suspected.

On the other hand, some surgeons argue that direct innominate artery cannulation, being more proximal than the axillary, could pose a higher risk of embolization through the right common carotid and vertebral arteries. Depending on the surgeon's preferences, some may contend that there is no justification for a secondary cannulation site when perfusion can be achieved directly through the ostium of the innominate artery (when the arch is open and exposed). Axillary cannulation should remain the preferred choice for total arch surgery, mainly because it leaves the innominate artery free for anastomosis with the branch of a four-branched Dacron graft, and the axillary cannula can be used to resume CPB during the rewarming phase. Axillary cannulation should also be the preferred method for acute type A dissections to avoid cannulating a frequently dissected and friable innominate artery, as recommended by the 2014 European Society of Cardiology guidelines on aortopathies.

In contemporary aortic arch surgery, stroke incidence in elective cases is around 5%, while in emergency contexts, it is approximately 12%. This study, with an average stroke incidence of 5.4%, aligns with previously published data. One limitation of this work was that the neurological damage classification was not performed by a neurologist but by clinical follow-up carried out by the cardiac surgeon, potentially underestimating the incidence of neurological events. On the other hand, a high incidence of new severe silent ischemic lesions was detected via MRI in both groups. It is known that new MRI-detected lesions may often not result in clinically significant neurological deficits in the immediate postoperative period. Still, studies with long-term cognitive assessments are required to understand their true influence on brain function. In fact, studies already exist correlating total infarct volume on MRI with specific levels of cognitive impairment in patients undergoing aortic valve replacement.

To date, the optimal cerebral protection strategy for hemiarch replacement remains undetermined. The next step would involve randomized, prospective studies of cerebral protection strategies that, like this study, incorporate thorough and rigorous neurological evaluation.

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Ramón Aranda

Unilateral antegrade cerebral perfusion as a neuroprotective strategy in aortic arch surgery

Review article and meta-analysis comparing different cerebral protection techniques in aortic arch surgery.

Aortic arch surgery represents a field with considerable clinical variability within cardiac surgery. Owing to its low incidence and the relatively small number of cases per center compared to other pathologies, despite a broad range of strategies and therapeutic options, experience is minimally represented in the literature. Cerebral protection in arch surgery is a critical component in the surgical management of this pathology. Following the implementation of deep hypothermic circulatory arrest (DHCA), two other types of cerebral protection have emerged. Firstly, retrograde cerebral perfusion (RCP), often associated with DHCA, involves cerebral perfusion from the venous system via cannulation in the superior vena cava. Secondly, anterograde cerebral perfusion (ACP), which can be executed under deep or moderate hypothermia, encompasses unilateral perfusion (PCAu), typically on the right side through cannulation of the axillary or innominate arteries, where contralateral flow depends on the presence and patency of the Circle of Willis; and bilateral ACP (PCAb), which can leverage the PCAu setup and incorporate one or more perfusion cannulas to directly perfuse the supra-aortic trunks. The choice between these cerebral protection techniques primarily depends on the surgical team's experience.

In 2022, Abjigitova and colleagues published in *Interactive Cardiovascular and Thoracic Surgery* the most comprehensive meta-analysis to date comparing various cerebral protection methods in aortic arch surgery. Over 43,500 patients undergoing aortic arch repair through median sternotomy were included, sourced from 222 observational studies and two randomized trials, and divided into four groups based on the employed cerebral protection strategy: RCP, PCAu, PCAb, and isolated DHCA. Results were pooled using a random-effects model to estimate inter-study variance, assessing perioperative mortality as the primary outcome and the incidence of paraplegia, disabling stroke, renal failure, and respiratory failure as secondary outcomes. Additionally, the authors conducted a sub-analysis stratifying results by underlying pathology: degenerative aneurysms and type A aortic dissection.

The PCAu group exhibited lower postoperative pooled mortality (6.8%) compared to the other groups. RCP showed a mortality rate of 7.1%, while the DHCA and PCAb groups each had a 9% mortality rate. Regarding intraoperative technique characteristics, surgery with ACP was performed under moderate hypothermia compared to the DHCA used in the other two groups (25.8°C vs. 20.4°C). The incidence of disabling stroke was also lower in the PCAu group (4.8%) compared to 7.3% and 6.3% in the PCAb and other groups, respectively. The incidence of paraplegia stood at 2.5% in both types of PCA compared to 3.4% and 4.7% in RCP and DHCA. On the other hand, the incidence of renal failure was notably high in the PCAu group (15%), particularly when compared to the DHCA group (0.8%); however, the need for postoperative dialysis was similar across all groups.

The authors conclude that their work summarizes the outcomes of various neuroprotection techniques in arch surgery over recent decades. Nevertheless, they acknowledge that their data should be cautiously interpreted within the context of their study's limitations.

COMMENTARY:

The article by Ablitgova et al. summarizes the existing literature on neuroprotection techniques in aortic arch surgery up to the current date. They report the PCAu technique as yielding the best outcomes in their analysis, marking it as the first meta-analysis to date to identify significant differences between unilateral and bilateral anterograde perfusion, despite several limitations that must be highlighted.

We are discussing heterogeneous groups where the lack of matching in the majority of the observational studies contributing to the work results in imbalances. This imbalance appears to disadvantage the PCAb technique based on the reported data. For instance, considering the assessed neurological outcomes, the PCAb group includes more patients with a history of cerebrovascular disease than other groups, exceeding twice the frequency of the PCAu group (14.6% vs. 6.4%). Additionally, the PCAb group was more frequently associated with complex surgeries: in 62% of patients with PCAb, total arch replacement was performed compared to 28.7% in DHCA, and PCAb was associated with longer cardiocirculatory arrest times (48 minutes compared to 27.7 and 23.1 minutes in PCAu and DHCA).

Another significant limitation of the study is the unspecified rate of crossover between techniques. This is particularly crucial when comparing unilateral or bilateral PCA, where many surgeons might switch the perfusion technique to bilateral following an asymmetric drop in NIRS readings. Ultimately, factors such as temperature, times, etiology (aneurysmatic vs. SAA), and the type of procedure (hemiarch vs. total arch replacement) seem to act as confounders in this article.

Over the past year, two new studies have retrospectively compared PCAu and PCAb using moderate hypothermia (28°C) in patients with aortic dissection. The study by Piperata et al. found significant differences between the groups with shorter cardiocirculatory arrest times and a lower incidence of neurological events in the PCAu group, arguing that "blind" insertion of perfusion catheters into the left carotid artery might cause disruption or mobilization of atherosclerotic plaques, increasing the risk of periprocedural stroke. The study by Song et al. found no differences between groups, even though the perfusion techniques were similar in both studies. Additionally, some centers employ a combination of retrograde and anterograde neuroprotection strategies, yet this has been scarcely studied in the literature, and one study showed no superior results compared to RCP. While some literature supports the use of PCAu with moderate hypothermia, it should be noted that other meta-analyses have not highlighted the differences underscored in this article.

As with other cardiac procedures, time matters in arch surgery. Angleitner et al. reported lower long-term mortality in PCAb than in PCAu if the cardiocirculatory arrest exceeded 50 minutes, and a meta-analysis by Angeloni et al. showed an increase in mortality in patients with longer times, but only if unilateral protection was used. Based on these findings, the 2022 American guidelines suggest that in cases of cardiocirculatory arrest times over 30 minutes, PCAb may be advantageous.

In my view, this study helps us understand where we stand, where the literature is as of today, and it opens new avenues for analysis. However, its results are inconsistent, with high heterogeneity that prevents extrapolation to clinical practice, a point already emphasized by the authors themselves. The answer to the question posed in the title requires conducting studies that evaluate perfusion techniques by differentiating the type of pathology (acute aortic syndrome vs. aneurysm), conducting a radiological analysis of the Willis polygon anatomy, estimating the crossover rate between PCA techniques, and

developing a comprehensive neurological analysis that includes neuroimaging and neurocognitive tests.

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José Manuel Martínez Comendador

Comprehensive management of aortic arch emergencies

An essential review that provides a complete therapeutic approach for aortic arch emergencies, based on the latest classifications and treatment options available.

Acute aortic syndromes (AAS) are potentially life-threatening conditions that require urgent and meticulously planned attention. The emergency management of these cases, particularly when involving the aortic arch, encompasses the entire spectrum of cardiovascular surgery, from traditional open surgery procedures to hybrid and endovascular interventions. To determine the most effective therapeutic strategy, surgeons must rely on a uniform nomenclature supported by radiological and anatomical parameters. This review article examines in detail the different anatomopathological types of AAS with aortic arch involvement, offers guidance on key preoperative studies, and provides essential guidance for addressing each case, considering the new classifications and available procedures.

Common nomenclature

It is absolutely essential before addressing each case to use uniform terminology to describe the extent of the disease and the clinical conditions. For this, several classifications are mentioned that we should be familiar with:

- Ishimaru Zones: Used to describe the extent of the disease. They are divided into a range from 0 to 11, where Zone 0 corresponds to the ascending aorta, including the brachiocephalic trunk. Zones 1 and 2 encompass the aortic arch, with Zone 1 covering the involvement of the left carotid, and Zone 2 including the left subclavian.

- Azizzadeh classification: Used in cases of traumatic thoracic aortic lesions, it describes four levels of severity ranging from grade I with simple intimal tear to grade IV which equates to rupture.

- TEM Classification (Type, Entry, Malperfusion): Used to summarize the extent of the disease in any acute aortic dissection and commented on in a previous blog entry. It consists of three key concepts: T (type), according to the modified Stanford classification (A for ascending aorta, B for descending aorta, non-A non-B for involvement of the arch with/without descending aorta not affecting the ascending aorta). E (entry) according to the location of the entry door (0: undetermined, intramural hematoma; 1: ascending aorta, zone 0; 2: aortic arch, zones 1 and 2; 3: descending aorta, zones 3-11). Finally, M (malperfusion) (0: absent, 1: coronary, 2: cerebral, 3: spinal, iliac and/or limbs; +: with presence of clinical signs, -: without presence of clinical signs).

- GERAADA score: A new scoring system to estimate the 30-day mortality in cases of acute type A aortic dissection.

Anatomopathological types of AAS

In addition to these classifications, the pathophysiology of the different types of AAS is addressed and explained, defining each one with its particularities and explaining the frequent transition from one to another, as occurs in the case of intramural hematomas (IMH) that can evolve towards dissections:

- Aortic Dissections: It defines aortic dissection as a rupture of the intimal layer that forms a false lumen. A crucial detail is the retrograde component that every dissection has to a greater or lesser extent, which is decisive for the treatment strategy.
- Aortic Aneurysm: Isolated aortic arch aneurysms are rare, but are common in the descending thoracic aorta. The focus is on this latter group, especially if a chronic aortic syndrome turns acute. Thoracic endovascular aortic repair (TEVAR) is the first treatment option in practically all cases of AAS of the descending aorta with arch involvement, but with the peculiarity that the proximal and distal anchoring zones necessary for the implantation of the endoprosthesis are almost never ideal in cases of aneurysms.
- Blunt Traumatic Aortic Injuries: These are generally due to a sudden deceleration and usually occur in the transition from the aortic arch to the descending aorta. This group of patients tends to be younger and therefore the vessel dimensions are smaller, which has implications in the treatment strategy, so many times it is necessary to resort to endoprostheses used in iliac extensions.
- IMH: Currently, evidence indicates that the predominant underlying mechanism is a tear of the arterial intima layer, as opposed to the previously accepted theory of a rupture of the vasa vasorum. Identifying the precise location of this initial tear can be a challenging task and delay diagnosis by imaging tests. It is generally located in the proximal part of the descending aorta or in the distal aortic arch. It is important to note that when the IMH is located in the lesser curvature, it increases the risk of developing a retrograde type A dissection, since, unlike its location in the greater curvature, there are no supra-aortic trunks that serve as a physical barrier to progression. In any case, TEVAR proves to be effective and sufficient in most cases to close the primary intimal flap in these cases with retrograde involvement.
- Penetrating Aortic Ulcer (PAU): Unlike other syndromes, PAUs are usually associated with coronary artery disease and peripheral occlusive arteriopathy. The lesions may span several segments and often present an IMH component. All these features can pose challenges when considering the use of TEVAR. Moreover, the decision to intervene should be based more on morphology and progression than on diameter, unlike what is most useful in the case of aortic aneurysms.

Preoperative study and intraoperative considerations

The key to planning an adequate operation or intervention is imaging techniques. Therefore, an electrocardiographically synchronized computed tomography angiography (angioCT) of the entire aortic lumen, including the circle of Willis, with fine cuts is recommended. A preoperative echocardiogram and a carotid ultrasound complement the basic diagnostics.

Interventions on the distal aortic arch and/or proximal descending aorta can reduce blood flow to the spinal cord by compromising the network of collateral branches or occluding segmental arteries, leading to spinal ischemia. Continuous monitoring of cerebrospinal fluid (CSF) pressure and pressure-dependent CSF drainage can counteract this. If the short version of the frozen elephant trunk (frozen-elephant-trunk [FET]) of 100 mm is used, the resulting risk of symptomatic spinal cord injury is very low, therefore the authors do not recommend CSF drainage in this case. In the case of metachronous TEVAR extension or single TEVAR procedure, CSF drainage is used as standard, with excellent results. Contraindications for CSF drainage include blood coagulation disorders. In the event of ischemic spinal cord injury occurring postoperatively without the placement of CSF drainage, for the reasons mentioned, immediate placement of CSF drainage is recommended after optimizing coagulation. It is attempted to maintain cerebrospinal perfusion pressure high enough, and if CSF pressure is high (>20 mmHg) or is

increasing, intermittent drainages of several milliliters of CSF should be performed. The goal would be to maintain the recommended CSF pressure between 8 and 10 mm Hg.

In open surgery, monitoring and protection of the organs are fundamental for a successful operation or intervention. Blood pressure should be measured at three sites, including bilateral radial arteries and unilateral femoral artery. These measurements are essential to anticipate poor perfusion and its resolution through individual treatment approaches, such as the FET technique. The brain and spinal cord are the most vulnerable organs, and stroke is one of the most disabling complications in surgery or interventions on the aortic arch, making the perfusion strategy a cornerstone for neuronal protection. The standard protocol recommended is unilateral anterograde cerebral perfusion (PCA) through the right axillary or subclavian artery and the carotid artery with the brachiocephalic trunk occluded during lower body hypothermic circulatory arrest (PCH). Bilateral perfusion, by additional cannulation of the left carotid artery, would be necessary in case of irregular collateralization through the Willis circle. If a dominant left vertebral artery is detected in the preoperative ATC, even trilateral PCA perfusion should be established through the left subclavian artery. Lower body PCH is usually set at 26 °C, which leaves a sufficient margin for arch replacement. Temperature should be measured centrally (usually by intravesical thermometer) and at the surface (usually by nasopharyngeal or tympanic thermometer). Infrared spectroscopy should be used in all cases, whether surgery is open, hybrid, or endovascular. In the case of a single TEVAR procedure or a simultaneous FET and stent-graft extension, spinal cord monitoring should be extended, when possible, by checking motor evoked potentials and somatosensory evoked potentials. Current research has reported that neurophysiological monitoring of motor and somatosensory evoked potentials is a useful tool for detecting early perioperative paraplegia in an anesthetized patient.

As for the type of arterial cannulation to establish extracorporeal circulation, we speak of central cannulation (ascending aorta and/or axillary/subclavian artery) and peripheral (femoral artery) cannulation. Evidence seems to indicate that the best results are obtained if possible, with axillary cannulation as the first option, as recommended in the 2019 clinical guidelines of the European Society of Vascular Surgery.

Another problem during the FET procedure is placing the stent-graft in the true lumen. In most cases the stent-graft should be placed under visualization in the true lumen. In cases where the true lumen cannot be clearly defined or when the dissection begins distally from the aortic arch, it is advisable to use a guide under fluoroscopy to ensure that the stent-graft is implanted in the true lumen. Having a hybrid operating room is extremely valuable when performing arch surgery and for this group is almost indispensable in endovascular procedures, although, in our environment, the use of a radioscopic arch may be sufficient.

Treatment options

- Treatment of pathologies involving Zones 0 to 1: The standard approach for any proximal thoracic aortic pathology involving zones 0 to 2 is open replacement, usually in PCH of the lower body and selective PCA for brain protection. The extent of the disease determines the extent of treatment. The FET technique is very frequently used in case of lack of a sufficient proximal anchoring zone and in case of previous replacement of the ascending aorta when the progression of the disease has led to the formation of aneurysms in zones 0 to 3 with various distal extensions. Endovascular techniques are feasible, but due to the limited number of devices available on the market (for example, Nexus® prostheses), endovascular repair of the aortic arch with branching in the acute setting remains exceptional.

- Treatment of pathologies involving Zones 2 to 4: In the absence of an adequate proximal anchoring zone, bypass or transposition of the left subclavian artery to the left common carotid artery is the first-choice option to create a sufficient proximal anchoring zone and to be able to perform a TEVAR with guarantees. New endovascular revascularization techniques of the left subclavian artery have emerged showing promising prospects for the future, although they are still in the research phase. If extensive proximalization is required, double transposition, whether autologous or alloplastic, is an elegant method to obtain an adequate anchoring zone, especially for atherosclerotic aneurysms. In type B and non-A non-B aortic dissections, more extensive proximalization of the anchoring zones beyond zone 2 should be avoided, due to the exponentially increased risk of type A retrograde aortic dissection, which occurs due to the presence of a proximal thoracic aorta inherently diseased, regardless of diameter. Precisely, if carotid-subclavian bypass or transposition does not create a sufficient proximal anchoring zone, the FET technique is generally applied through open surgery to avoid this increased risk of retrograde aortic dissection associated with TEVAR.
- Treatment of more distal pathologies: In the vast majority of acute aortic syndromes, TEVAR is the method of choice. In acute aortic dissection it is vitally important to avoid oversizing the distal component of the endoprosthesis, and it is recommended that these have a conical shape to prevent the formation of a new entry induced by the endoprosthesis at the distal level. In addition, the importance of CSF drainage is emphasized, a standard tool that the article's authors recommend in all cases of TEVAR.

COMMENTARY:

In summary, this review is presented as essential reading for cardiac surgeons, especially those of us facing the challenges of AAS, with a particular focus on those involving the aortic arch. Understanding the pathophysiology and origin of AAS, as well as their classification based on clinical and radiological criteria, is essential for effectively addressing them and ensuring optimal treatment in each case. In this article, all therapeutic options are addressed in a comprehensive and practical way, ranging from classic open surgery procedures to hybrid and endovascular interventions. Lastly, it is important to highlight the valuable contribution of a table that simplifies the process of choosing between hybrid/endovascular treatment and conventional surgery. This table is based on the presence of clinical and morphological factors, which facilitates decision-making in this complex pathology.

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Daniel Martínez López

Twenty Years of Aortic Valve Reimplantation with Valsalva Graft: Does Preserving the Sinuses of Valsalva Make a Difference?

A retrospective analysis of aortic valve reimplantation outcomes over the last 20 years, using the "Valsalva graft" at the center that introduced its clinical application.

Aortic root replacement surgery with preservation of the native aortic valve has established itself as a solid alternative to Bentall surgery by avoiding the complications related to valve prostheses and lifelong anticoagulation required by mechanical valves. However, since its description over 30 years ago, unanswered questions remain, such as the role of the Valsalva sinuses (VS) and the sinotubular junction in the hemodynamics of the ascending aorta, as well as the importance of their preservation. Various modifications of the technique have been developed to maintain the anatomical structure of the aortic root, including the Valsalva graft—a specially designed Dacron graft developed by this team in Rome to achieve anatomical reconstruction of the aortic root.

In this article, the authors review 20 years of results using David's technique with the "Valsalva graft." This Dacron graft is specifically designed for these surgeries, featuring a wider lower portion to simulate the VS area that transitions to a smaller diameter conduit, mimicking a sinotubular junction. The authors analyzed a cohort of 265 patients over the past two decades, with an average follow-up exceeding 7 years (minimum 1 month, maximum 21 years). Survival, freedom from reintervention, and development of significant aortic insufficiency were assessed in this cohort. The surgical mortality was 0.8% (two cases), with a 3-month mortality of 0.8% (two cases). Cardiovascular event mortality remained stable across the years at 0.4% over 15 years. Total mortality was 13 deaths during the follow-up, accounting for 4.9% of the sample, with only 5 of these attributed to cardiovascular causes. Residual aortic insufficiency (grade ≥ 3+) was 5.9% at 5 years, stabilizing at 7.8% at both 10 and 15 years. Fourteen patients (5.4%) exhibited significant residual aortic insufficiency, with seven reoperated: two for infectious endocarditis and five for severe aortic insufficiency, maintaining a stable reintervention incidence from the fifth year, reaching 4.1% at 10 and 15 years, with a 15-year reintervention-free rate of 84.3%.

In a multivariable analysis to assess predictors of repair failure, the authors concluded that a suboptimal intraoperative outcome (defined as residual aortic insufficiency ≥ 2+) and leaflet repair (pre-caliper use era) were associated with an increased risk of significant aortic insufficiency development over the follow-up period.

COMMENTARY:

In recent years, aortic valve preservation has gained popularity. Techniques developed over three decades ago have evolved, and thanks to data collection and patient follow-up, analyses confirm excellent short- and long-term results. Recent discussions focus on preserving or simulating the Valsalva sinus region and the sinotubular junction. Although no studies show a clear survival or durability advantage for these patients, imaging and animal studies suggest that preserving the sinotubular junction may benefit leaflet motion and generate more physiological flow throughout the aortic root, potentially impacting repair durability.

This study presents 15-year outcomes of aortic valve reimplantation using the "Valsalva graft," a specially designed Dacron tubular graft to simulate the creation of neo-sinuses of Valsalva. The results are outstanding, with very low operative mortality and long-term cardiovascular mortality limited to five cases, alongside a reintervention rate under 5%

at 15 years. The authors highlight the significance of residual aortic insufficiency ≥ 2+ at the repair's completion. In univariate analysis, statistically significant durability differences appeared between patients with associated connective tissue disease and those with type A dissection. However, the study population includes only 32 patients with connective tissue disorders and 9 with aortic dissection, a limited sample for conclusive findings. Furthermore, no significant differences were observed in the repair rates between bicuspid and tricuspid valves.

There is also no significant difference in survival or repair durability when comparing this study sample to others using techniques that do not preserve the sinotubular junction. One advantage of aortic valve reimplantation using a larger conduit at the sinotubular junction (known as David type V, Stanford modification) is the simplified reimplantation due to added space. However, the Valsalva graft foregoes this benefit but reduces ischemic time and bleeding risk by eliminating an anastomosis.

In conclusion, no conclusive studies demonstrate a definitive correlation or better long-term repair durability or reduced reintervention with sinotubular junction and Valsalva sinus preservation. Current information is primarily based on imaging or flow studies via magnetic resonance. In the absence of significant outcome differences, the choice of aortic valve reimplantation technique should be based on the surgeon's experience and comfort, as all techniques demonstrate excellent results.

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José Manuel Martínez Comendador

Is a Bentall or Wheat Procedure Recommended for Mild-to-Moderate Aortic Root Dilation?

A retrospective analysis by the Mayo Clinic compares long-term outcomes between the Bentall and Wheat procedures in patients with an aortic root diameter of 55 mm or less.

Addressing mild-to-moderate aortic root dilation during concomitant aortic valve and ascending aorta replacement remains controversial. The primary options are composite valve conduit replacement (Bentall procedure) and separate ascending aorta and aortic valve replacement, preserving the root with a prosthetic aortic valve and supracoronary graft (commonly known as the Wheat procedure). The Bentall procedure is more aggressive and may lead to root-related complications, while the Wheat procedure, a seemingly less invasive approach, theoretically increases the risk of aneurysm or dissection in the preserved aortic root. However, no long-term studies to date have validated this risk.

This study by Mayo Clinic offers clarity on this issue through a retrospective analysis of 778 adult nonsyndromic patients with an aortic root diameter ≤55 mm who underwent ascending aorta and aortic valve replacement between January 1994 and June 2017. Patients were divided into two groups according to aortic root management: the Bentall procedure in 406 patients (52%) and separate replacement of the ascending aorta and aortic valve in 372 patients (48%). Propensity score matching was used to balance baseline characteristics, resulting in 188 matched pairs. Analysis revealed a median sinus of Valsalva diameter of 43 mm (39-47 mm). Short- and long-term mortality did not differ significantly between groups: operative mortality was 2% in the Bentall group and 3% in the Wheat group, while long-term mortality rates remained similar after a mean follow-up of 9.6 years (8.4-10.1 years). There were also no significant differences in reoperation rates, with 7% in the Bentall group and 10% in the Wheat group. In the propensity-matched Wheat group, sinus of Valsalva diameter decreased by 2 mm (0-4 mm) after a mean follow-up of 41 months.

In conclusion, for patients with mild-to-moderate aortic root dilation, both the Bentall and Wheat procedures present similar short- and long-term mortality and reoperation risks. The Wheat procedure does not seem associated with subsequent root dilation in midterm echocardiographic follow-up.

COMMENTARY:

Previous posts on this blog have addressed aortic root surgery in the context of aortic dissection, a rare but critical condition. In the study reviewed today, we revisit aortic root surgery, focusing on a much more common clinical scenario. This involves patients who require concurrent aortic valve and ascending aorta surgery, but with mild-to-moderate root dilation (<55 mm). The central question this study raises is whether the Bentall or Wheat procedure is equally, less, or more effective in these cases.

The primary finding from this study, shedding light on this issue after a median follow-up of almost 10 years, is that reintervention rates were low and not significantly different between the two patient groups. While more in-depth analysis is warranted, this outcome supports the notion that either the Bentall or Wheat procedure can be effective and suitable options for this specific patient population.

What does the existing literature say? Thirty years ago, the Stanford group established the Bentall procedure as their preferred intervention for such patients. Shortly after, in

2000, Sundt et al. sought to determine the optimal intervention in patients with bicuspid valves, finding that both the Bentall and Wheat procedures yielded similar long-term outcomes. Subsequent studies supported these findings, with some, like Sioris et al., achieving excellent results by selectively replacing only the dilated noncoronary sinus in the Wheat procedure, effectively avoiding reinterventions. Overall, despite the lack of randomized trials and the reliance on case series, no evidence currently suggests that patients with mild-to-moderate dilation who undergo the Wheat procedure face poor long-term outcomes. The findings of this article, based on an extensive patient series and nearly a decade of follow-up, align with the current body of literature.

A notable aspect of this study is the reduction in sinus of Valsalva diameter by 2-3 mm during a mean echocardiographic follow-up of 41 months. Remarkably, no patient in the Wheat group required reintervention for aortic root dilation over 19 years of clinical follow-up, underscoring the rarity of root dilation to a degree necessitating surgery. Other studies have similarly reported such decreases in size post-Wheat procedure, including reductions of 2-3 mm after 6 years (Vendramin et al.) and up to 9 mm in just 4 years (Nardi et al.). Additionally, some studies suggest that root stabilization may persist for over a decade.

The surgical risk associated with the Bentall procedure is well documented, with recent STS database reviews estimating an increased risk of 2.8%. This risk may be higher for patients with non-significantly dilated roots and low coronary ostia, a scenario common in this study's cohort. Although early mortality did not differ significantly in this Mayo Clinic series compared to the Wheat procedure, characteristic complications, such as coronary revascularization or pseudoaneurysm formation, were observed.

The primary limitation of this study is the inability to ascertain the criteria for selecting Bentall or Wheat procedures for different patients. Propensity score matching was implemented to reduce selection bias, although the matched patient proportion was low. Additionally, the study’s retrospective design led to incomplete follow-up, with sinus of Valsalva measurements missing for some patients, and these measurements were based on echocardiography rather than computed tomography. Lastly, while not a strict limitation, a median follow-up of 10 years may not be sufficient to capture significant differences between procedures, as reoperations often occur 12-20 years post-intervention. Prospective studies with longer follow-ups are thus needed to draw more definitive conclusions.

For aortic roots <55 mm, the choice between a Bentall or Wheat procedure is influenced by a variety of factors, ranging from case-specific variables—such as clinical presentation, patient age, comorbidities, and aortic valve type—to the surgeon’s experience and preferences. Interestingly, both the literature and this study seem to simplify these variables, suggesting that outcomes are similar for both Bentall and Wheat procedures. Nevertheless, in clinical practice, experienced surgeons tailor each case individually. For instance, a young patient with a small body surface area, bicuspid aortic valve, and suboptimal aortic wall tissue quality might prompt many surgeons to perform a root procedure. Conversely, for a 45 mm root in an older patient with a tricuspid valve, a Wheat procedure might be preferable. These nuances are not reflected in these studies, highlighting the essential role of surgeon expertise, potentially the most influential factor in determining prognosis. This is validated by the strong outcomes observed in this study, emphasizing the importance of excellent patient selection for each intervention by the involved surgeons.

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Elio Martín Gutiérrez

New Tools in Aortopathy Clinics for Predicting Diameter Progression in Patients with Chronic Aortopathies Under Surveillance

This document comprises two descriptive studies that suggest biochemical and clinical markers as predictors for adverse outcomes in patients with aortic aneurysms under surveillance.

Outpatient monitoring of patients with chronic aortopathies is a standard responsibility for cardiovascular surgeons. Some centers even establish specialized units dedicated to managing complex aortopathies, particularly those related to collagen disorders. Standard care for these patients focuses on optimal blood pressure control, often using cardioselective beta-blockers and/or ACE inhibitors/ARBs, such as Losartan or Telmisartan, due to their matrix metalloproteinase inhibitory effects, alongside periodic imaging studies. However, there are no reliable clinical parameters to predict aortic diameter progression, and therefore, the increased risk of acute aortic syndromes or the need for additional surgical or interventional procedures. Two recent publications introduce new factors that could help in identifying patients with a higher likelihood of adverse aortic progression.

Ikeno et al. conducted a follow-up of 623 survivors of total aortic arch replacement from 1999 to 2018 (139 acute dissections, 101 chronic dissections, 383 aneurysms), excluding those with collagen disorders or prior descending or thoracoabdominal aortic surgery to maintain sample homogeneity. Among these patients, 232 also underwent some form of elephant trunk procedure, including 183 with aortic dissection (76.2%). Freedom from additional distal aortic dilation procedures was observed in 88.5% at 5 years and 80.2% at 10 years. Overall, freedom from distal aortic events was 81.9% at 5 years and 70.5% at 10 years. Multivariable regression analysis indicated that preoperative descending aortic diameter was a significant risk factor for unfavorable distal aortic events, with this progression more common in patients presenting with acute aortic dissection.

In another study, Dolapoglu et al. evaluated the clinical utility of the C-reactive protein (CRP)/serum albumin ratio for predicting ascending aortic diameter progression in patients with moderate, non-surgical dilation (40–50 mm). CRP, an acute-phase reactant linked to systemic inflammation, is suggested to correlate with elevated matrix metalloproteinase activity and aneurysmal diameter progression. Despite this, a robust clinical correlation remains undemonstrated. A total of 182 patients were included, assessing the annual growth rate of aortic diameter. Multivariable analysis revealed classic clinical factors linked to aortopathy progression, such as hypertension, chronic obstructive pulmonary disease, and positive family history. Notably, a CRP/albumin ratio cutoff of 0.84 (both in mg/dL) also emerged as an independent risk factor, with an ROC area of 0.771 for predicting significant growth in the ascending aorta. This study is pioneering in proposing this analytical parameter, with subanalysis indicating superior performance when compared to isolated CRP values.

COMMENTARY:

The findings from these studies offer insights for the ongoing management of patients with chronic aortopathies. In cases of aortic arch interventions, planning for future procedures must frequently be considered, especially in patients undergoing surgery for acute or chronic dissection, often through elephant trunk techniques. Approximately 20% of patients at 10 years may require secondary procedures. European clinical guidelines currently classify type B dissection patients (primary or residual following type A or non-

A-non-B correction) and those with descending aortic diameters >40 mm as "high risk for late aortic events."

The second study provides a valuable tool in the CRP/albumin ratio. Beyond its predictive capacity for diameter progression in non-surgical ascending aortic dilation, it could aid decision-making in managing patients with ascending aortic dilation and borderline surgical indications (~45 mm), possibly in conjunction with other procedures such as aortic valve replacement.

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Elio Martín Gutiérrez

The Eastern Approach to Intramural Hematoma for Elderly Patients

Comparative study of the short- and mid-term outcomes in patients over 75 years with acute type A intramural hematoma (IMH-A) managed conservatively or treated surgically.

The emergency call for an elderly patient with an acute aortic syndrome type A (AAS-A) at the hospital's door always generates uncertainty regarding the optimal therapeutic approach. On one hand, avoiding a high mortality rate justifies the futility of a substantial surgical effort from the team. However, multiple studies highlight that surgical intervention in selected patients, even octogenarians, may offer survival benefits in the short and mid-term.

The presentation of AAS-A as noncommunicating acute type A aortic dissection (a common term in Asian literature for what we know as ascending aortic intramural hematoma, IMH-A) in elderly patients further supports the potential utility of surgical intervention, as these patients, except for cases of pericardial effusion/tamponade, typically show fewer complications than those with other types of AAS-A. Japanese studies have advocated for conservative management in elderly or high-risk patients with favorable survival outcomes.

This study analyzed short- and mid-term outcomes in 66 patients over 75 years with IMH-A treated at a Japanese center from October 2011 to December 2020: 30 initially assigned to optimal medical management and 36 treated surgically. The surgical intervention performed in most cases involved isolated replacement of the ascending aorta. Three patients (10%) in the medical group showed IMH-A progression to type A aortic dissection, with two undergoing surgery. The groups did not significantly differ in in-hospital or intensive care unit mortality rates or length of stay. During follow-up, four-year survival rates were 78.3% and 71.4% in the surgical and conservative groups, respectively ($p = 0.154$). Seven patients in the medical group experienced late aorta-related events, compared to none in the surgical group ($p = 0.003$), leading to a significantly higher rate of interventions for new aortic events in the conservative management group. However, both groups showed no significant differences in all-cause and aorta-related mortality during the first four years.

The authors concluded that surgical outcomes for IMH-A in elderly patients were favorable. However, this did not translate into significant differences in survival compared to conservative management in either short- or mid-term, when considering all-cause and aortic-related mortality.

COMMENTARY:

The results align with other published findings cited below, supporting this alternative perspective on addressing this aortic pathology. The guidelines from the Japanese Circulation Society (JCS) and the work of Kaji et al., a reference on conservative management of IMH-type AAS, suggest considering IMH as a distinct entity within AAS. IMH is classified into two types: type 1, resulting from bleeding within the tunica media due to rupture of the nourishing vasa vasorum; and type 2, linked to degenerative changes in the aortic wall, such as atherosclerosis, which serve as an entry point for bleeding into the tunica media (e.g., IMH associated with plaque fissure/ulceration).

The "Japanese approach" to IMH leverages these distinct IMH characteristics: a lower compromise of the aortic wall and, therefore, a reduced rupture risk (compared to dissection or penetrating ulcer), along with reduced progression toward the aortic root or

supra-aortic trunks, which lowers risks of malperfusion or aortic insufficiency (relative to dissection). Moreover, type 2 IMH often occurs in older patients with greater atheromatous burden and more comorbidities. This profile suggests that selecting patients for conservative management can yield good outcomes. The Achilles heel of this strategy lies in identifying patients at risk for disease progression, often with transformation to aortic dissection due to communication between the IMH and aortic lumen through media-intimal rupture. Poor prognostic indicators include IMH thickness >11 mm, an aortic diameter >48–50 mm, and the presence of ulcer-like precursor lesions on CT, appearing as small discontinuities in the media-intimal layer. Although conservative management is not routinely practiced in our setting except in patients unfit for surgery, nor is it advocated in our clinical guidelines, we might reconsider IMH-A in stable patients as a non-emergency, akin to an acute coronary syndrome once stabilized: optimal medical treatment, close monitoring including CT scans, and urgent intervention in the following days with a fresh surgical team after optimizing the patient's clinical condition (suspension of antiplatelet/anticoagulant therapy, adequate blood pressure control), etc. This may be a means of improving outcomes, particularly in comorbid or elderly patients where emergent intervention may entail increased morbidity and mortality from inadequate preparation.

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Miguel Ángel Parada Nogueiras

Custodiol in Thoracoabdominal Aneurysm: Does It Really Protect Renal Function?

This study compares renal protection through intraoperative perfusion with Custodiol solution versus Lactated Ringer's solution with methylprednisolone and mannitol in patients undergoing elective thoracoabdominal aortic aneurysm (TAAA) repair.

TAAA, when meeting surgical criteria, has a poor prognosis with a 5-year survival rate of 10-20% if untreated. Open surgery is effective and alters the disease's natural progression, though it remains technically challenging and carries a higher surgical risk, resulting in perioperative complications more frequently than in other cardiovascular surgeries, with high morbidity and mortality rates.

Acute kidney injury (AKI) following cardiac surgery increases the risk of cardiovascular events and mortality. Additionally, TAAA surgery is linked to worse outcomes in terms of postoperative mortality and long-term survival.

This randomized, double-blind, prospective, single-center study (CURITIBA) involved 90 patients with TAAA who underwent elective repair surgery. Each group comprised 45 patients, with no differences observed between groups in terms of key demographic variables, comorbidities, preoperative risk factors, and aneurysm classification per Crawford. The primary goal was to assess postoperative AKI, defined by the KDIGO scale, categorizing patients based on whether renal perfusion was performed with Custodiol solution or Lactated Ringer's solution enriched with methylprednisolone and mannitol. Mortality, survival, and renal function at one year were analyzed. Univariate and multivariate analyses were conducted to identify associations between key variables and the occurrence of AKI. AKI was observed in 62% of patients, with stage 1 (32.9%) prevailing in both groups. In the Custodiol group, 40% of patients developed AKI compared to 60% in the RL group ($p = 0.001$). Any AKI stage was more frequent in the RL group (75% vs. 48.9% with Custodiol, $p = 0.02$), with severe AKI in 35.6% of RL cases versus 24.4% in the Custodiol group, $p=0.36$. The need for renal replacement therapy, either with continuous veno-venous hemofiltration or hemodialysis, was higher in the RL group (13.3% vs. 2.2% with Custodiol), though not statistically significant. No differences were observed in postoperative complications, ICU or hospital stay, or mortality (6 patients in the RL group vs. 4 in the Custodiol group). Univariate analysis indicated that RL solution ($p = 0.01$) and Crawford type II TAAA ($p = 0.05$) were associated with AKI development. Conversely, multivariate analysis identified independent predictors of severe AKI as smoking, COPD, chronic kidney disease, and Crawford type II and III aneurysms, while Custodiol use emerged as an independent protective factor against AKI ($p = 0.003$).

The authors conclude that Custodiol use for intraoperative renal perfusion in open TAAA surgery is safe and significantly reduces AKI incidence compared to perfusion with Lactated Ringer's solution.

COMMENTARY:

Custodiol is a cardioplegic preservation solution, an extracellular crystalloid with low sodium and calcium content, administered in a single dose to induce asystole with a high volume of 1500-2000 mL. It is also used as a preservation solution for cardiac, renal, hepatic, and pancreatic transplants with favorable outcomes. The RL perfusion solution includes 125 mg/L of methylprednisolone and 12.5 g/L of mannitol.

In this study, the renal arteries were cannulated with 9F occlusion-perfusion catheters directly through the ostia intraluminally. Cold solutions at 4°C were administered via a drip perfusion system, averaging 1.5 mL per gram of estimated renal weight, with a mean total of 500 mL for Custodiol and 400 mL for RL ($p = 0.54$), and renal ischemia times of 41 minutes with Custodiol and 36 minutes with RL ($p = 0.46$). Initially, a rapid infusion was applied, followed by drip-controlled dosing based on estimated renal weight. Renal perfusion strategy could be improved, as a drip system does not strictly control parameters like temperature, continuous flow, or perfusion pressure, which could be achieved with auxiliary roller pumps from the extracorporeal circulation machine.

The study has limitations due to its small sample size and single-center nature. Future studies should include larger sample sizes and be multicentric to obtain more consistent evidence. Despite these limitations, this well-designed, randomized study provides robust initial data supporting further investigation into Custodiol as a renal protective solution in this surgery, as it shows no adverse events and better AKI outcomes compared to RL. Nonetheless, despite renal protection strategies, AKI remains high at 62%, indicating room for improvement.

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Elio Martín Gutiérrez

Recovering the Flow: Functional Approach to Aortic Wall Pathophysiology to Predict Risk of Disease Development

Non-systematic review calling for a paradigm shift in the conceptualization of aortic pathology, incorporating functional studies of aortic flow linked to the occurrence of both chronic and acute pathologies.

The extreme compartmentalization applied to cardiovascular pathology often causes a loss of perspective. At times, it can give the impression that the heart's role is merely to pump into a void. Consequently, circulatory pathology is frequently limited to the aortic root, disregarding essential aspects of major vessels, peripheral arteries, pulmonary vessels, microvasculature, lymphatic vessels, and the superficial and deep venous networks, all of which are integral to blood circulation.

This limited perspective has led to the aorta being regarded less as a blood vessel and more as a mere conduit, with its pathology often reduced to simplistic measures of diameter in cross-sectional cuts, much like a sausage. While increasing diameters do correlate with a heightened risk of acute events across all levels of the aorta and major vessels, Salmasi et al. propose a review not aimed at comprehensive updates but as an impetus to generate evidence focused on the functional analysis of aortic pathology.

The authors effectively delineate aortic pathology, wisely interrelating often independently managed concepts. For instance, aortic diameter remains the primary basis for surgical indication and a major predictor of acute aortic events. However, half of all acute aortic events occur in aortas with diameters below the surgical threshold, a fact possibly explained by two additional factors: parietal degeneration and genetic predisposition. In terms of degeneration, the breakdown of medial collagen layers can lead to wall failure, both chronically through inverse remodeling (aneurysmal pathology) and acutely (acute aortic syndrome). For aneurysms, parietal stress is exacerbated by Laplace's overpressure. However, unlike hydrostatic (arterial) pressure, this does not act symmetrically across the vessel due to variations in curvature along a non-cylindrical section. Parietal degeneration may also be genetically predisposed. While various syndromes and implicated genes have been described recently, over 80% of acute aortic events occur sporadically, in patients with no known genetic mutations, which suggests that current knowledge is likely incomplete.

Given this pathophysiological disconnect between the three phenomena, a unifying principle is required. The key lies in flow. Multiple studies of aortic flow have revealed greater medial degeneration in areas with elevated wall stress, leading to weakened zones prone to inverse remodeling (dilation) or structural failure (acute aortic syndrome). Genetics, as currently understood, plays a predisposing role in these degenerative processes, based on the balance between metalloproteinase-mediated resorption and fibroblastic activity for collagen quality and quantity in the aortic wall layers. In other words, aortic pathology shares more similarities with osteoporosis/osteopenia than with other vascular pathologies like atherosclerosis. While atherosclerosis is primarily endothelial, in its advanced stages, it extends into the media layer, becoming intertwined with these degenerative processes of the aortic wall.

From a clinical perspective, two primary methods assess aortic flow: 4D-flow magnetic resonance imaging and angiographic flow simulation, the latter also applied to coronary flow assessment. Despite limited literature on the subject, the authors synthesize valuable insights into aortic physiology, elucidating the mechanisms by which pathology manifests:

1. Wall stress is highest in the descending aorta, followed by the ascending aorta and aortic arch, corresponding to the prevalence and incidence of both chronic and acute aortic pathology. Wall stress also decreases from proximal to distal in the descending aorta, explaining the greater frequency of thoracic than abdominal aortic dissection and the higher incidence of types I and II thoracoabdominal aneurysms, per Crawford's classification.

2. In healthy volunteers, peak wall stress occurs on the anterior aspect of the ascending aorta, with lower-stress regions at the proximal curvature of the lesser curvature and distal curvature of the greater curvature at the arch's entry. This flow pattern correlates with the site of type A aortic dissection flap origin and, in bicuspid aortic valves, with various dilation patterns depending on commissural fusion/orientation.

3. Aneurysms exhibit reduced wall stress compared to healthy aortas. As such, wall stress increases as diameter decreases. However, rather than a protective mechanism against progression, the role of Laplace's overpressure likely becomes more significant as diameter increases.

4. Aneurysmal aortas experience prolonged stress during the cardiac cycle, with a lower systolic-to-diastolic stress ratio due to delayed peak systolic stress, implying prolonged pressurization and reduced diastolic relaxation.

5. In Marfan syndrome patients, flow patterns tend to be particularly eccentric, even in the absence of aneurysmal and/or valvular pathology, due to potential misalignment of the outflow tract associated with the genetic defect. This generates elevated wall stress on the proximal curvature of the lesser curve and distal curvature of the greater curve, which may accelerate parietal degeneration in the aortic arch and sinotubular junction, potentially explaining the increased pathology prevalence in these areas compared to unaffected individuals.

Despite these advances, flow models still treat the aorta as a rigid structure, potentially overestimating wall stress, particularly in the ascending aorta. Emerging models that incorporate fluid-structure interaction offer a more realistic perspective. However, the descending portion still exhibits a stiffer interaction, aligning with a higher prevalence of pathology in that region.

The authors conclude that understanding aortic flow's impact on the wall is critical for identifying cases at risk of adverse events. A multimodal clinical approach—considering predisposing factors, clinical aspects (age, blood pressure control, atherosclerotic load), radiological imaging (including diameters), functional aspects, and biomarkers—will better predict aneurysmal pathology progression and acute syndrome onset. This marks a new frontier in 21st-century aortic pathology, potentially revolutionizing an area still grounded in 19th-century principles.

COMMENTARY:

This article offers an inspirational rather than in-depth review, serving as a non-systematic literature survey on the primary findings from functional aortic flow analysis using non-invasive (4D-flow MRI) and invasive (angiographic flow analysis) tests as a primary prevention strategy for aortic degenerative and/or acute complications. Although pioneering, Evangelista's work over a decade ago emphasized the need for functional flow analysis, particularly using transesophageal echography, for secondary prevention

in patients with residual dissection post type A repair or type B dissections in the descending aorta.

Aortic pathology deserves a shift in approach, likely to be achieved as flow analysis methods improve. Until then, what has sometimes been an uncharted territory has at other times attracted many stakeholders (cardiovascular surgery, vascular surgery, interventional radiology, and even interventional cardiology). It is evident that aortic pathology demands better study, monitoring, and management. It is clear that diameter assessment is obsolete, and cardiovascular surgery should take a leading role in this paradigm shift, both therapeutically (as it offers the full range of therapeutic options suited to aortic pathology anatomy) and diagnostically and in follow-up.

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Section II:

Ischemic heart disease

Elio Martín Gutiérrez

What is better than the internal mammary artery anastomosed to the left anterior descending artery? Multiple arterial grafts.

A comprehensive meta-analysis and review of recent evidence regarding survival outcomes using multiple arterial grafts versus left internal mammary artery plus saphenous vein grafting, including subgroup analyses such as radial artery vs. right internal mammary artery, elderly patients, those with diabetes mellitus, and women.

The selection of grafts for myocardial revascularization has been a recurring topic of debate over recent decades. Buxton's group's experiences with the radial artery, the adverse outcomes of the ART study due to its design, the recent publications of meta-analyses by Gaudino et al. and the long-term RAPCO study, among others, have sustained uncertainty, leading surgeons to cling to their established practices in the absence of definitive evidence, apart from the widely accepted anastomosis of the left internal mammary artery (LIMA) to the left anterior descending artery.

The study under discussion, though seemingly another contribution to this unending debate, aims to further explore the question of the best choice for a second graft in revascularization strategies. The study stands out, without delving into details, due to its meticulous methodology, including an appropriate literature search, careful selection of studies, and comprehensive bias and sensitivity analyses. For the meta-analysis, the authors selected 39 studies comparing outcomes of revascularization using either a single or multiple arterial grafts from 1995 to 2022, comprising a sample of 180459 patients (multiple arterial grafts: 56175 patients; LIMA + saphenous vein: 124284 patients). They analyzed median overall survival and event-free survival, as well as secondary analyses comparing arterial grafts between mammary and radial arteries, and subgroup considerations, including patients over 70 years old, individuals with diabetes mellitus, and women. The multiple arterial graft group demonstrated superior survival (interquartile range = 0.58; $p < 0.0001$) and better event-free survival (interquartile range = 0.82; $p < 0.0001$) compared to isolated LIMA and saphenous vein revascularization. Using the right internal mammary artery as the second arterial conduit was associated with superior survival compared to the radial artery (HR = 0.93; $p = 0.009$). Multiple arterial revascularization showed consistent survival benefits across subgroup analyses in patients over 70 years old, women, and those with diabetes mellitus.

The authors conclude that this meta-analysis indicates that using multiple arterial grafts is associated with better survival outcomes compared to single arterial grafting in patients undergoing isolated myocardial revascularization surgery.

COMMENTARY:

The ongoing shifts in evidence, the flexibility in recommendations, patient heterogeneity, and surgical preferences rooted in each surgeon's or institution's practice contribute to maintaining a spotlight on the diversity of surgical revascularization strategies.

The work of Magouliotis et al. supports the survival benefit of multiple arterial revascularizations, similar to the findings of Gaudino et al. and other review studies. However, this study sheds light on two critical issues:

First, the distinct technical and clinical characteristics of patients undergoing surgical revascularization. Reducing patient heterogeneity to clinical variables and grafts alone is simplistic, but currently, it is the only contribution available from existing evidence. This study is one of the few to conduct independent meta-analyses with subgroups, assessing the benefit of multiple arterial revascularizations in elderly patients, those with diabetes,

and women—all of whom showed benefits. Previous experiences aggregate outcomes into common evidence without addressing the unique characteristics of these three patient groups, where the use of multiple arterial grafts might not have shown benefits given the limited natural survival, potential infectious complications, or differential benefit in women, respectively. Nonetheless, new evidence will continue to be needed in the future. Studies underpinning such research often include patients in whom graft availability and quality of target vessels are, so to speak, unrestricted. This sometimes distances such evidence from real-world scenarios. The elevated risk of mediastinitis in some subgroups (obese diabetic women, particularly insulin-dependent or with poor HbA1c control >7%), peripheral venous insufficiency (treated or untreated), reservation of the saphenous vein graft for peripheral ischemia revascularization, radial artery atheromatosis and/or percutaneous manipulation, or contraindications to using this graft (lesions <90%, especially in the right territory, dialysis candidates, carpal tunnel syndrome, or previous surgeries, vasospastic phenomena…); along with other factors such as ascending aortic calcification, patient age and expected survival, ventricular dysfunction, associated surgical procedures, hemodynamic stability, and potential inotropic and/or vasoconstrictor requirements, etc., make surgical revascularization a truly bespoke strategy for each patient. And, of course, while most surgical practices involve individual grafts with cardiopulmonary bypass (CPB), these studies do not adequately consider other variables, such as off-pump surgery and anastomotic configurations, like sequential or composite grafts.

Second, the advantage of the right internal mammary artery over the radial artery as the second preferred graft. This result may seem to contradict findings from the RAPCO study and Gaudino et al.'s meta-analysis, where the radial artery yielded excellent outcomes. However, it is essential to consider that study design influences results. Gaudino et al.'s work shares apparent similarities with the analyzed study (a meta-analysis comparing single versus multiple arterial grafting and evaluating the radial artery against the right internal mammary artery as a second graft) but has notable differences (it includes 10256 patients from 4 recent randomized studies, but with propensity score resampling, reducing the sample to only 1776 patients). The RAPCO study is a multicenter effort from groups skilled in selecting and using the radial graft appropriately, based on the characteristics mentioned above. Magouliotis et al.'s work spans 27 years, a period when double internal mammary artery use was more widely integrated than radial artery use, which was less accurately selected for target territories. Thus, even while consistently showing the survival benefit of multiple arterial revascularizations, the choice of the second best graft varies according to each study's design characteristics. Perhaps the lesson to be learned is that "one-size-fits-all" revascularization strategies, like systematic double internal mammary use, may be less appropriate than individualized approaches based on patient characteristics. RAPCO's successful outcomes with the radial artery derive from its appropriate selection and use. The right internal mammary artery may indeed be more versatile than the radial artery, yet it remains an arterial graft, occasionally with limited caliber, potentially susceptible to competitive flow in vessels with intermediate lesions, and despite various proximal and distal anastomotic configurations, may not deliver equivalent outcomes in terms of patency and performance for the coronary territory. Moreover, the risk of mediastinitis is significantly higher in some subgroups where the use of the radial artery could maintain multiple arterial revascularizations with a lower complication rate.

Therefore, we can conclude that, in most patients undergoing myocardial revascularization, the use of multiple arterial grafts will provide a survival benefit regardless of clinical characteristics, such as age, diabetes, or sex. The choice of arterial graft(s) accompanying the left internal mammary artery should be tailored as a custom suit, considering both clinical and coronary anatomy characteristics of each patient, to

maximize clinical benefit and minimize the risk of complications (bleeding, mediastinitis, vasospasm…).

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Elio Martín Gutiérrez

Less Heart Attacks, More Survival: Coronary Surgery Proves It Once Again

A meta-analysis of major randomized clinical trials comparing coronary surgery (CABG) versus percutaneous intervention (PCI) that assesses the incidence of new myocardial infarctions during follow-up and their relationship with all-cause mortality.

The benefits of coronary artery bypass grafting (CABG) are indisputable in managing patients with ischemic heart disease. Numerous randomized studies have compared it to its strong competitor, percutaneous coronary intervention (PCI), resulting in piles of papers. For those who support CABG, each graft with optimal flow and pulsatility index—especially if arterial—represents a tangible benefit to the patient, enhancing both life expectancy and quality. However, it is important to remember that any treatment applied once coronary disease is established represents secondary protection, i.e., reducing the risk of future myocardial infarctions and shortening of survival relative to the absence of any therapeutic intervention. In other words, we continue to palliate. And while we may "play to win" with some patients, we may simply aim to "not lose" with others.

The continuous advancement of cardiac intervention and the struggle for shared indications with our specialty is a daily challenge, requiring constant updates and a drive for improvement. Studies like this one aim to strengthen the position of CABG. Recently, the outcomes of ISCHEMIA and REVIVED studies have impacted PCI in the revascularization of stable angina patients compared to optimal medical therapy. It has been suggested that this conclusion could also apply to revascularization with CABG. In fact, stable angina patients represent a large portion of our practice, with those stabilized after an acute coronary syndrome making up nearly the remaining volume. Stable angina indications remain pivotal for determining CABG or PCI assignment according to current clinical guidelines, paralleling stabilized acute coronary syndrome indications to cover most of the clinical spectrum of ischemic heart disease. Therefore, it is inappropriate to generalize PCI outcomes in stable angina treated with medical therapy to CABG, as it offers a treatment alternative with distinct principles and outcomes.

The meta-analysis by Gaudino et al. delves into the outcomes of principal randomized controlled trials (RCTs) published regarding secondary prevention, which is the core expected outcome of revascularization: improved survival and reduced incidence of new myocardial infarctions (MI). They reviewed 20 RCTs, including renowned trials such as BEST, EXCEL, FREEDOM, NOBLE, MASS-II, SYNTAX, PRECOMBAT, ARTS, etc., spanning from 1995 to 2015. Seven of these studies (35%: BEST, CARDia, EXCEL, FREEDOM, MASS-II, NOBLE, and SYNTAX) showed significant mortality reduction for patients undergoing CABG compared to PCI, while no significant differences were found in the remaining studies. Overall, considering all 20 trials, mortality reduction remained in favor of surgery and was independent of included studies according to the sensitivity analysis. In subgroup analysis, a significant association was observed between survival improvement provided by surgery and enhanced protection against new MIs in the surgical arm.

The authors conclude that in RCTs comparing CABG with PCI, the greater reduction in all-cause mortality in the surgical group correlates with CABG's protective effect against new myocardial infarctions.

COMMENTARY:

Although this meta-analysis may not seem to offer new insights, it represents a crucial and benchmark work as the publication date of new myocardial revascularization

indications approaches. First, it counters the results of a previous study by Bangalore et al., which included 14 RCTs (without distinguishing left main coronary artery disease from multivessel disease) and found no significant survival differences. A prior work by Head et al. already contradicted this outcome for multivessel disease. Gaudino et al.'s study confirms this benefit across any revascularization indication. Secondly, it is the first and only study to establish an association between the enhanced all-cause survival of patients undergoing CABG and the reduced incidence of new coronary events. This confirms two aspects: it provides causality to CABG's previously assumed but unconfirmed survival benefit and validates the major flaw in the current trend of considering results in composite events instead of individually, as they are related events and cannot be evaluated together.

Focusing on causality, numerous factors may contribute to the survival benefit demonstrated by CABG in reducing new MIs and improving survival. Firstly, the technique's intrinsic characteristics, as referenced in the editorial accompanying this study. CABG treats vessels with significant lesions in the mid-distal regions, with the anastomosis site selected away from diseased zones (typically progressing from proximal to distal, making it less vulnerable to disease progression), and utilizes one or more “substance-releasing” grafts that counteract endothelial dysfunction in the coronary bed (nitric oxide, neoangiogenic factors). Conversely, stents follow a treatment strategy at the disease site, susceptible to disease progression in the same or proximal areas, and as intravascular foreign bodies, they promote endothelial hyperplasia countered by cytotoxic agents coating the stent, which can flow downstream, impairing endothelial function in the distal bed and associated microcirculation. Secondly, the nature of stents makes them more reliant on patient adherence to dual antiplatelet therapy to reduce the risk of new MIs. CABG usually requires only single antiplatelet therapy, although dual therapy is recommended after an acute coronary syndrome, this recommendation is inconsistently followed in practice and in RCTs. Additionally, Head et al.'s meta-analysis showed that CABG benefits for three-vessel disease were independent of stent type (drug-eluting or metal). Lastly, CABG’s invasiveness has a transformative impact on patient lifestyle. Patients tend to adhere more strictly to healthy diets, physical activity, cessation of smoking, and therapeutic adherence post-surgery compared to PCI, often perceived as less invasive, hence a lesser health concern. Although it is a virtue of CABG that it drives patient behavior change, it remains a human technique performed on humans, where behavior is a major but challenging factor to influence in secondary prevention.

Every critically reviewed work has limitations worth mentioning. This analysis employs a traditional study-level meta-analysis instead of the newer patient-level methodology that aggregates each included study's individual patient outcomes. Secondly, it spans a broad time range (20 years). Despite the minimal impact of stent type on CABG comparison outcomes, as shown in Head et al.'s study, surgical techniques and outcomes have evolved over time. Only in the most recent trials has CABG demonstrated survival benefits, as in older studies, nearly three-quarters of patients received PCI, and only 16% undergoing CABG received it as a primary treatment. Finally, while this meta-analysis includes all revascularization indications, a separate analysis for left main coronary artery disease treatment is needed (as previously done for multivessel disease by Head et al.), despite potentially revealing a technical tie, warranting further critical analysis. The tendency not to publish negative or non-significant results (except for interested non-inferiority designs) does not enhance evidence quality or meta-evidence like this.

In summary, let us continue to proudly defend our coronary surgery, one of the oldest and least varied surgical techniques. Let us practice sound surgical principles and, in

Favaloro's words, “in every medical act, respect for the patient and ethical and moral concepts must be present; then, science and conscience will always be on the same side.” This standard should guide evidence, clinical guidelines, and the beleaguered Heart-Team.

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Elio Martín Gutiérrez

Which Grafts for Which Territories? Still Searching for Direction

A subanalysis of the COMPASS study evaluating one-year patency of various types of coronary grafts through CT angiography, considering technical aspects of revascularization strategy configuration.

The COMPASS study was designed to assess the benefits of antithrombotic therapy in the postoperative period of coronary surgery patients. It included 27395 patients from 83 centers across 22 countries. Three groups were compared: aspirin (ASA) + rivaroxaban, ASA + rivaroxaban placebo, and ASA placebo + rivaroxaban. The study was terminated early after a 23-month follow-up due to demonstrated benefit of dual therapy in reducing primary endpoint events: a composite of all-cause mortality + new stroke + new myocardial infarction (HR = 0.76; $p < 0.01$). However, these results have had limited impact on clinical practice.

The proposed subanalysis aimed to utilize the study protocol with patients randomized between weeks 4 and 14 to assess one-year graft patency via CT angiography. Thus, 1142 patients and 3480 individual grafts were analyzed (with a 20% follow-up loss). Angiographic graft failure was defined as stenosis >75%, string sign, and/or occlusion. With this, an ambitious set of answers was pursued to guide optimal revascularization strategies for multivessel disease, within the range of technical possibilities available. Findings for each graft type were analyzed:

- Left Internal Mammary Artery (LIMA): Results for non-anterior territories or alternative configurations were limited, as 98% were anastomosed to the left anterior descending artery (LAD) and 91% were used in situ. The failure rate was the lowest among all grafts (6.4%), doubling when LAD proximal stenosis was <90% (4.7% vs. 8.2%).

- Radial Artery (RA): The failure rate was the second lowest at 9.9%. The primary limitation was competitive flow, with better patency when anastomosed to territories with >90% lesions (6.8% vs. 13.3%). Outcomes were better in the circumflex artery (Cx) territory compared to the right coronary artery (RCA) territory (6.8% vs. 21.7%), aligning with current revascularization guidelines.

- Saphenous Vein (SV): This was a surprising outcome, consistent with findings from previous studies. The failure rate was 10.4% at one year, independent of the treated vessel's stenosis severity (> or <90%) (10% vs. 11.1%). Although the quality of venous grafts varies among patients, they were unaffected by these results at one year, though marginally influenced by the quality of the target bed (good 10% vs. acceptable-poor 13.1%) and different bypass configurations, i.e., sequential or composite grafts (9.4% vs. 14.8%).

- Right Internal Mammary Artery (RIMA): This graft showed the worst outcomes, with a 26.8% failure rate at one year. As an arterial graft, it was again affected by target vessel stenosis <90% (33% vs. 17%). While adverse outcomes were associated with its use for lateral territories, versus anterior or RCA territories (42% vs. 19% vs. 11.8%, respectively), results were conditional on use. In situ configuration (via transverse sinus) showed worse outcomes than composite configurations to another arterial graft (T or Y from LIMA or RA) or as a free graft from the aorta, which showed the best results (34.1% vs. 22.2% vs. 15.4%).

The authors concluded that results for LIMA and RA were as expected, while SV results exceeded expectations (likely due to one-year follow-up duration), at the expense of RIMA outcomes. Until further analysis identifies the factors impacting RIMA outcomes, findings should guide the use of multiple arterial grafts in multivessel disease.

COMMENTARY:

The COMPASS subanalysis is an ambitious project, with conclusions that are thought-provoking. It has even inspired a commentary by Taggart and a rebuttal from the authors on whether the study, in reference to its name, serves as a compass for guidance or leads surgeons astray regarding graft selection.

Beyond methodological issues that may influence these results, several valuable lessons can be drawn. First, arterial grafts are sensitive to lesions <90% in any territory. This had been assumed only for RA, permitting greater flexibility with LIMA grafts. However, findings indicate that the biology of arterial grafts is similar despite differing properties. Possibly, SV is the preferred graft for intermediate lesions. Second, RIMA as an in situ graft, though attractive for proximal-mid RCA territory and exotic for the left side, is detrimental, and use as a free graft is preferable. Third, sequential versus direct grafting is detrimental for SV grafts, though insufficient data were available for arterial grafts. Despite theoretical hemodynamics (parallel resistances), poor geometry/configuration may underlie these results. However, Y or T composite configurations offer a good alternative for graft length optimization, particularly when LIMA does not reach the proximal ascending aorta. Fourth, the quality of the distal vessel affects SV and RA outcomes, while mammary arteries better tolerate poor run-off.

The study addresses various methodological comments explaining the findings. First, it is a subanalysis of a study not designed for this purpose, with the selected sample potentially introducing biases not accounted for, such as patients' varying antithrombotic regimens and significant follow-up losses. Second, as highlighted by Taggart: despite the multicenter approach, surgeon experience with multiple arterial grafts was limited (8%). Third, although the primary aim was to analyze one-year patency segmented by various factors, these factors interrelate, impacting other results, as seen with in situ RIMA. Fourth, statistical significance may be compromised in small subsamples due to variable atomization.

Nonetheless, this work provides valuable insights into graft configuration in multivessel disease revascularization with multiple arterial grafts. Given the multiple technical variations available for complete coronary artery revascularization using multiple arterial grafts, not all configurations can be equivalent. Findings likely depend on timing and group expertise. Only by applying learned principles, common sense, and case-by-case individualization can the best revascularization strategy be offered for each patient, in each place, and at each time. Radically changing techniques, especially if outcomes are within standards, would lead to unnecessary disorientation.

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Laura Varela Barca

The Radial Artery, the Best Companion for Double Internal Mammary Artery

A systematic review and meta-analysis of observational studies comparing the use of double internal mammary artery (BITA) with saphenous vein (SV) versus BITA with radial artery (RA) in surgical treatment for triple-vessel coronary artery disease. Long-term survival evaluation with follow-up up to 12 years.

Graft selection remains a subject of debate in cardiac surgery. The use of the internal mammary artery (IMA) to revascularize the left anterior descending artery is the reference technique, as it has demonstrated both improved survival and lower complication rates. The application of a second IMA graft, which is recommended by clinical guidelines based on scientific evidence, remains contentious due to the results of recent studies. The only clinical trial on this topic, the ART study, contradicts recent works by Gaudino et al. and Magouliotis et al., likely due to methodological limitations in the former. Nevertheless, we generally accept that the evidence supporting the use of double IMA is robust. The use of a third arterial graft in cases of triple-vessel coronary artery disease represents an additional layer in this debate.

In this context, the meta-analysis by Formica et al. explores this third tier by comparing patients undergoing revascularization with BITA and RA versus BITA and SV. The authors conducted a comprehensive systematic review, focusing solely on articles using propensity score matching. Out of 523 publications, only six observational studies met the criteria, totaling 2500 patients (1250 in each group). Key data were analyzed: baseline patient characteristics, anastomosis configurations, coronary lesion severity, and statistical analysis quality. The primary endpoint was long-term mortality, with immediate postoperative mortality as a secondary outcome.

Results, with a follow-up time of 7.5–12 years, clearly favored complete arterial revascularization. Long-term survival was higher in the RA group ($p = 0.031$). Five-, ten-, and fifteen-year survival rates were also different between the groups, at 96.2%, 88.9%, and 83% in the RA group versus 94.8%, 87.4%, and 77.9% in the SV group. No differences were observed regarding immediate postoperative mortality.

The authors conclude that the use of RA as a third graft in addition to BITA is associated with improved long-term survival without increased immediate postoperative mortality.

COMMENTARY:

Multiple arterial revascularization in patients with coronary artery disease remains a hot topic in cardiac surgery. Despite numerous studies, clinical practice still reflects the preferences of individual surgeons, departments, or hospitals. This is evidenced by the estimated use of double IMA in only 12% of patients in Europe and 7% in the United States.

The RA has both detractors and advocates among cardiac surgeons, leading to heterogeneous usage. It was first used by Carpentier's group in 1974 but was soon abandoned due to vasospasm issues, which were later mitigated by the development of the "pedicled harvesting technique" and the use of vasodilators, such as calcium antagonists. However, its use in severe arterial lesions, especially in the left coronary territory, has demonstrated excellent long-term patency, making it a strong option. The recent RAPCO study supports this theory, showing lower RA occlusion rates compared to SV.

The present meta-analysis by Formica et al. endorses RA use, reporting a significant long-term survival benefit with compelling results. However, certain aspects of this study warrant consideration:

In terms of methodology, the inclusion of observational studies with propensity score matching introduces the inherent limitations of observational studies, along with the exclusion of studies that may have adjusted risk differently. Despite the high quality of the review and meta-analysis, conclusions are based on only six source articles, potentially excluding studies with confounding factor adjustments.

Regarding the patient population analyzed, the mean age was under 70 years, notably younger than our usual practice in Spain. This lower mean age, which the authors acknowledge as a limitation, is also noted in editorials by Tatoulis and the Toronto group. It affects both baseline patient characteristics and comorbidities.

One relevant piece of information is the RA graft location and vessel stenosis. It is known that using the RA in the right coronary artery territory with lesions <80% may not be beneficial, prompting a summary table of RA graft use in the included studies. Unfortunately, only four articles provided information, displaying a heterogeneous configuration challenging to analyze.

A meta-regression study was performed to analyze the influence of risk factors on results, though age could not be analyzed due to data limitations, and no differences were found in other factors.

Even so, the study by Formica et al. is the first meta-analysis to evaluate the use of BITA and RA, concluding that there is no increase in immediate postoperative complications or mortality and that there is a clear long-term survival advantage. According to the raw number of patients in this study, there is an increase of 5 additional survivors per 100 surgeries at 15 years, effectively illustrating the significance of the "small percentage change" in Kaplan-Meier curves.

Therefore, we have further evidence in favor of complete arterial revascularization, adding to the RAPCO study results and prompting a reconsideration of our approach to the third tier of triple-vessel coronary artery disease treatment. It seems reasonable to conclude that the RA should be considered the best companion for double IMA, especially in younger patients.

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Elio Martín Gutiérrez

Consensus on Graft Use in Revascularization Surgery: Crossing Borders

Consensus document from EACTS and STS on indications and surgical management of different graft types in coronary revascularization surgery.

The era of single-strategy revascularization surgery appears to be a thing of the past. Techniques such as the systematic use of double internal mammary artery without combining other grafts, or the exclusive use of the left internal mammary artery with multiple venous grafts, have yielded significant outcomes in revascularization surgery. However, although this is a highly standardized procedure, where systematic repetition is key to achieving consistently reproducible results, pursuing the same strategy without adjusting to different patient profiles seems mistaken today.

Various studies, previously discussed on this blog and led by Gaudino, the first author of this consensus document, have suggested this. However, the significance of this work lies in its nature as an intersocietal consensus document, involving what might be termed the "NATO of cardiac surgery": the EACTS and the STS together. Such works lend consistency and authority to the statements they contain, underscoring the principle that unity strengthens the argument. In a highly competitive field, such unity becomes particularly valuable, especially in the absence of a new update to revascularization guidelines. Additionally, documents like this provide greater depth to the treatment of a topic that, although mentioned in the latest clinical guidelines, is addressed more superficially.

The document comprises a systematic review of studies focused on clinical outcomes and patency of various coronary graft types, each analyzed individually:

Radial Artery: Recent randomized studies have shown excellent patency rates for the radial artery, with a comparison to the saphenous vein yielding an HR = 0.44, $p < 0.001$. In terms of survival, observational studies using the radial artery as a second arterial graft demonstrated a 26% increase in 6-year survival, compared to the same revascularization strategy using the saphenous vein. The radial artery was also associated with an HR = 0.67 and 0.73 at 5 and 10 years, respectively, in the composite event of recurrent myocardial infarction and need for revascularization. In the RAPCO study, radial artery outcomes were superior to those of the right mammary artery as a second arterial graft, showing better patency at 10 years (HR = 0.45) and a lower rate of myocardial infarction and/or revascularization procedures at 15 years (HR = 0.74). It is worth noting that in most studies, the radial artery was anastomosed to the severely diseased circumflex territory, with limited experience in the right territory.

In terms of harvesting technique, it is generally well tolerated in terms of hand function, although performing an Allen test beforehand is recommended, given the variability in test outcomes between operators. Some studies have suggested the benefits of prior echocardiographic assessment to evaluate development, patency, and preexisting calcification before harvesting. In the absence of comparative studies, a common-sense approach prevails, selecting grafts of appropriate quality, with preserved ulnar collateral circulation and without formal contraindications for use (patients with Dupuytren's disease, previous or untreated carpal tunnel syndrome, or any forearm trauma; prior catheterization; potential use for vascular access for dialysis; or vasospastic disorders such as Raynaud's phenomenon). The literature reports a complication rate of approximately 9%, all minor (paresthesias, local pain, less frequently, grip strength loss or distal claudication), although publication bias is likely.

Endoscopic harvesting has been suggested as feasible in expert hands, although it is associated with a higher incidence of endothelial damage, spasm, and challenges in controlling side branches. Given that the radial artery has less collateralization and a more predictable course than the saphenous vein, it may potentially benefit from this technique more than venous grafts. However, solid evidence is scarce and subject to publication biases, so no conclusions are drawn on this aspect.

As for its use, there is insufficient evidence regarding proximal anastomosis. It is typically configured in T or Y anastomosed to the left internal mammary artery, although direct aortic configurations are also common. This strategy may protect the graft from competitive flow but exposes the proximal anastomosis to increased stress. Therefore, using a smaller punch size than that typically employed with the saphenous vein is recommended. The authors do not mention configurations yielding favorable results, such as direct anastomosis immediately over the anastomotic head of a previously anastomosed venous graft, creating a V-configuration. This approach mitigates direct stress on the radial artery and minimizes dependence on the donor vein segment, which might otherwise compromise patency. For distal vessels, it is preferable to use them in vessels with severe proximal stenosis, >70% in the left territory and >90% in the right, to prevent competitive flow. These criteria were established in studies such as RAPS and RAPCO, which included them in their selection criteria. Regarding functional assessment, the IMPAG study set a cutoff of FFR >0.78, although most arterial grafts used were left internal mammary arteries rather than radial arteries, leaving limited data on this specific point. Arguably, a functional study likely suggests intermediate lesions (50-70%) for which this graft might not be advised, regardless of the FFR outcome.

Finally, vasodilator use is recommended for at least one year post-revascularization surgery with dihydropyridine calcium channel blockers (nifedipine, amlodipine). These agents should be carefully titrated for clinical tolerance (20% incidence of headache) and to avoid compromising the use of other pharmacological agents with proven prognostic value in these patients (beta-blockers in the presence of prior infarction, ACE inhibitors/ARBs/ARNI in the presence of ventricular dysfunction).

Right Internal Mammary Artery (RIMA): For many years, RIMA was seen as a promising second arterial graft that could demonstrate benefits over the strategy of a single internal mammary artery graft. A meta-analysis by Benedetto et al., encompassing 9 clinical trials with follow-up periods of more than 4 years, indicated a fourfold increase in patency for RIMA compared to saphenous vein grafts (OR = 0.25). Another meta-analysis by Gaudino et al. found a patency rate of 90.9% for RIMA at over 5 years. Clinically, the ART study showed no difference at 10 years between the use of one or two internal mammary arteries. However, a crossover rate of approximately 20% between groups and the inclusion of patients with additional radial artery grafts in both groups compromised the ability to draw solid conclusions regarding the primary objective.

Despite this, observational evidence has consistently shown the benefits of using RIMA as a second arterial graft in terms of reducing adverse long-term events (>10 years). However, while the rate of early occlusion for RIMA is often lower than that of venous grafts, the increased risk of mediastinitis must be weighed against the patient's survival probability, especially in three specific clinical scenarios:

- Diabetic patients: Female, obese, and diabetic patients present the highest risk of mediastinitis, estimated at around 3%, double that of non-diabetic patients, though this may reflect publication bias.

- Low ejection fraction: Immediate arterial graft performance is not always optimal, which may lead to myocardial hypoperfusion issues in the early postoperative period. Saphenous vein grafts tend to provide better early revascularization performance, making a combined strategy of arterial and venous grafts preferable in these patients rather than pure arterial procedures.

- Advanced age: Given the lack of differential outcomes associated with the use of multiple arterial grafts within periods shorter than 10 years, using RIMA in elderly patients might increase procedural complexity and risk without a clear benefit. Studies have found similar mediastinitis rates in older and younger patients; however, while there is no consensus on an age cutoff, registries suggest diminished survival benefits from multiple arterial graft strategies in patients over 70 years.

Regarding technical utilization, the insights and solutions for RIMA usage are similar to those expressed for the radial artery. It is worth mentioning that T- or Y-composite configurations with proximal anastomoses on the aorta allow for more distal target reach. In contrast, arterial target selection with RIMA offers more flexibility than with the radial artery. Although some studies suggest better tolerance to beds with intermediate lesions, others highlight a performance compromise associated with competitive flow. The IMPAG study set a minimum FFR of >0.78 for considering RIMA implantation. However, despite histological and autoregulatory differences from the radial artery, RIMA grafts benefit from being used in vessels with adequate diameter (>1.93 mm) and severe lesions (>70%).

The authors also explore the technique of crossing RIMA in situ to the left anterior descending artery (LAD), combined with the left internal mammary artery for the rest of the left coronary territory. Limited evidence supports this configuration, with only four studies showing no difference compared to multiple arterial graft strategies while preserving LAD anastomosis with the left internal mammary artery. However, two major limitations are recognized: limited graft length to reach the LAD and potential injury risk crossing the midline during reoperation. With advances in coronary and structural intervention, reoperations may become less frequent in patients with patent grafts. Nonetheless, no recommendations are made regarding these techniques. Other approaches, such as extending RIMA with another graft (saphenous vein or radial artery) to achieve complete revascularization with sequential anastomoses (snake), are not considered.

Lastly, the authors reflect on RIMA harvesting techniques. Although skeletonization has been shown to reduce sternal complication rates, conclusions on its impact on clinical outcomes are limited due to a lack of data. Skeletonization may alter graft vasomotility through increased denervation and manipulation-related damage, though it allows for better graft length and enables exclusion of the distal segment, which tends to be more spastic and less developed. Variability in techniques, including the use of electrocautery versus harmonic scalpels or exclusion methods for collateral branches, limit the authors' ability to reach a conclusive judgment.

Saphenous Vein (SV): While the left internal mammary artery remains the gold standard for revascularization, the saphenous vein remains the benchmark for comparing arterial graft outcomes. Though clearly inferior to the radial artery in optimal territories, SV grafts have shown comparable results to RIMA in a prior meta-analysis by Gaudino, reviewed previously on this blog.

With a patency rate of 82% at 5 years, the SV graft has proven successful, especially given its versatility, which is both its primary strength and limitation, often leading to

indiscriminate target selection. Cautionary measures, similar to those used with the radial artery, have yielded favorable outcomes. However, the comparable outcomes between SV and RIMA may suggest that target vessel characteristics play an equally, if not more, significant role in graft selection, with graft nature only becoming a determinant in the long term.

The authors analyze two aspects of SV graft use: endoscopic and open extraction techniques. Endoscopic harvesting substantially reduces wound complications (the most common complication in revascularization surgery) but may lower patency rates due to endothelial and structural damage, although clinical event translation is yet unclear. More evidence is needed to support endoscopic harvesting, as publication biases likely influence this inconsistency. Current clinical guidelines discourage endoscopic SV extraction. In contrast, randomized studies show better patency with the "no-touch" technique, although clinical events remain unaffected. However, this approach increases wound complication rates, as SV is harvested with surrounding fatty tissue, impacting surgical wounds.

In summary, the authors highlight that revascularization strategy should be "à la carte" rather than a "fixed menu," tailored to each patient's individual needs and characteristics.

COMMENTARY:

This study provides an excellent update and stands as the best consensus on the topic. Some recommendations stemming from a similar analysis, such as conducting surgery with or without extracorporeal circulation support and other technical aspects, are missed. However, it is evident that, after a comprehensive review, this individualized approach will help tailor the procedure to each patient's specific needs. And although revascularization surgery continues to involve grafting vessels beyond proximal lesions, we are transitioning from a single approach to multivessel disease revascularization to over 15 variations of the same intervention. This heterogeneity will need to be incorporated into future research, with registry-based analysis (such as the Spanish Registry of Cardiac Surgery: RECC) and big-data strategies likely offering a path to new scientific evidence. Until then, the left internal mammary artery to the left anterior descending artery remains the gold standard in myocardial revascularization.

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José Manuel Martínez Comendador

Revascularization in Left Main Coronary Artery Disease: A Field Reconquered by Surgery?

Observational study of a large Canadian cohort analyzing long-term clinical outcomes by comparing coronary artery bypass grafting (CABG) with percutaneous coronary intervention (PCI) following propensity score analysis adjustments.

For more than 20 years, it has been known that untreated significant left main coronary artery (LMCA) disease carries a high mortality rate (50% at 5 years), and that coronary artery bypass grafting (CABG) improves survival compared to medical treatment. However, in this context, no randomized clinical trials (RCTs) have compared percutaneous coronary intervention (PCI) with medical treatment, nor are there recent RCTs comparing CABG with medical treatment. Nevertheless, we currently have five high-quality RCTs comparing PCI (mostly using drug-eluting stents) with CABG to clarify which type of revascularization is most appropriate.

The 2018 ESC/EACTS guidelines on coronary revascularization were based on the 3-year results from the EXCEL and NOBLE trials, but the more recent 2021 ACC/AHA/SCAI guidelines considered the 5-year results of EXCEL and updates from two other RCTs with 10-year follow-up, the SYNTAXES and PRECOMBAT studies. The European guidelines granted a class I PCI recommendation for LMCA disease in cases of low-complexity coronary anatomy and a class IIa recommendation if the complexity was intermediate. However, the American guidelines found it reasonable to recommend PCI (class IIa) when it could provide revascularization comparable to CABG. Unlike RCTs, there are no contemporary observational comparative studies of CABG vs. PCI in LMCA disease, and the few previous ones had limited sample sizes.

The aim of this study was to compare the long-term outcomes of these two revascularization strategies in a real-world setting. To do so, clinical and administrative databases from Ontario, Canada, were linked to identify records of all patients treated by CABG or PCI for significant LMCA disease (angiographic evidence of stenosis ≥50%) between 2008 and 2020. Patients who presented with cardiogenic shock, were candidates for emergent revascularization, and/or had STEMI were excluded from the study. Baseline characteristics were compared between groups, and propensity score matching was performed in a 1:1 ratio. Long-term mortality and a composite of major adverse cardiac and cerebrovascular events (MACCE) were compared between the matched groups using a Cox proportional hazards model. After exclusions, 1299 and 21287 patients underwent PCI and CABG, respectively. Before matching, PCI patients were older (75.2 vs. 68 years) and a higher percentage were female (34.6% vs. 20.1%), though they had a lower burden of atherosclerosis. Propensity score matching of 25 covariates yielded 1128 well-matched pairs. There were no differences in early mortality between PCI and CABG (5.5% vs. 3.9%). During 7-year follow-up, all-cause mortality (53.6% vs. 35.2%; HR = 1.63; $p < 0.001$) and MACCE (66.8% vs. 48.6%; HR = 1.77) were significantly higher with PCI compared to CABG.

The authors concluded that CABG was the most common revascularization strategy in this real-world registry. Before propensity score matching, PCI patients were older and at higher risk. After matching, there was no difference in early mortality, but in the long term, CABG provided better survival and greater freedom from MACCE.

COMMENTARY:

This is undoubtedly a particularly relevant study because, for the first time, we have information on clinical outcomes beyond 5 years (7 years) from real-world data of a contemporary cohort of patients with LMCA disease who underwent CABG and PCI. The study's most notable finding, following propensity score analysis, is that CABG provides significantly better long-term survival and freedom from MACCE compared to PCI, including myocardial infarction and repeat revascularization; only the stroke rate was lower with PCI. Secondary conclusions, but highly descriptive of hospital practice, indicate that CABG remains the preferred revascularization technique for LMCA disease at a ratio of 8:1, and PCI is used in older and more comorbid patients.

Despite the existence of six excellent RCTs comparing CABG with PCI in LMCA disease, the management of this pathology remains controversial. One of the most debated aspects when analyzing these RCTs is the definition of periprocedural myocardial infarction (MI). In the EXCEL study, an MI definition based solely on biochemical markers was used instead of the third universal definition of MI; moreover, the decision was made not to include repeat revascularization as part of the MACCE to be analyzed. Conversely, in Tam et al.'s study, a clinical definition of MI was used, and unlike the EXCEL study results, the incidence of periprocedural MI was higher with PCI (2.8%) than with CABG (1.6%). Interestingly, in studies that reanalyzed the EXCEL study—this time using the third universal definition of MI—it was also observed that the MI incidence was higher in the PCI group (3.3%) than in the CABG group.

In the most recent meta-analysis published in *Lancet* in 2021 on LMCA revascularization, four of these RCTs with at least 5 years of follow-up were included. The patients analyzed, in comparison with Tam et al.'s study, were at lower risk, younger, and had a lower incidence of diabetes and ventricular dysfunction. All-cause mortality was similar with CABG and PCI; however, if a Bayesian estimation method was applied, increased mortality with PCI was detected. Additionally, the incidence of MI (using the universal definition), repeat revascularization, and composite events were also significantly higher with PCI. Therefore, while not conclusive, the RCT results suggest that CABG in LMCA disease shows a trend towards greater survival (already detectable even at 5 years) and a lower proportion of MACCE (if the universal MI definition is used and repeat revascularization is included).

In contrast to previous observational studies, the majority were not contemporary, had smaller patient populations, and fewer years of follow-up. Nevertheless, the MAIN-COMPARE registry already demonstrated a higher risk of mortality with PCI (despite patients being younger than those in the current study) and a higher incidence of MACCE at 5 years, as well as repeat revascularization at 10 years. Consequently, once again, observational studies on coronary revascularization—closer to "real-world" scenarios—differ significantly from RCTs in terms of long-term outcomes, clearly favoring CABG as the most appropriate therapeutic strategy in most circumstances.

One of the major limitations of this study is the use of data gathered from clinical report summaries to catalog clinical events such as MI or stroke, which is logically less reliable than definitions used in RCTs. The same is true for the incomplete information available on the coronary anatomical complexity of patients (SYNTAX score) and/or the degree of completeness of coronary revascularization. Lastly, in recent years, there have been significant advancements in PCI, which, when applied currently and in the future, will likely continue to improve outcomes for patients with LMCA disease, which may not yet be fully reflected in the results of this study.

Adding the findings of this study to the existing evidence, it should now be clear that in patients with non-high surgical risk and adequate distal vessels from a surgical technical standpoint, CABG remains the revascularization technique of choice for LMCA disease in stable angina and stabilized acute coronary syndrome. The role of PCI is essential for numerous situations involving LMCA disease encountered in daily practice (proximal LMCA disease in patients with severe comorbidities, LMCA disease in frail patients or those with high surgical risk, primary angioplasty, etc.). This study should be taken into consideration in the development of future revascularization guidelines to position CABG favorably over PCI for LMCA disease in the scenarios mentioned above. Of course, this does not preclude the need for longer-term RCTs to confirm the findings of this study.

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Elio Martín Gutiérrez

Left Main Coronary Artery Disease: Reality Surpasses Clinical Trials

Results from the Swedish registry SWEDENHEART on the comparative outcomes of coronary intervention versus surgical revascularization in left main coronary artery disease and a contrast with findings from major clinical trials.

We are all familiar with the expression "reality surpasses fiction." Often, we find a significant alignment between outcomes in clinical practice and registry data, a consistency that is not always reflected in the findings of clinical trials. Highly restrictive selection criteria, non-inferiority analyses, varied definitions of clinical outcomes, and their interpretation as composite events have been among the methods used to influence results towards predetermined tendencies, often in line with the sponsor's policies. The generation of "fictional evidence" extends even further with successive post-hoc analyses or derived meta-evidence, torturing the data to recount the same alternative reality repeatedly until it becomes dogma.

Revascularization of left main coronary artery disease (LMCA) is not exempt from this controversy. The distortion begins with the consideration of LMCA disease as separate from multi-vessel disease, although it is subsequently classified based on anatomical complexity via the SYNTAX score, which reflects the extent of disease in the remaining coronary tree. This should be considered only when LMCA disease is the sole significant coronary lesion, which represents less than 15% of cases. Consequently, the proportion of LMCA patients with a SYNTAX score indicating surgery as superior to percutaneous coronary intervention (PCI) per current guidelines (>22 points) is over half of cases, around 35% with scores of 22–32 points and approximately 25% with scores >32 points. While considering LMCA disease is relevant for prognosis and the subsequent revascularization recommendation, it should not determine the therapeutic indication unless, as noted, it is the only lesion present.

The SWEDENHEART registry includes patients treated at 28 centers from 2005 to 2015, providing substantial long-term follow-up data. A total of 11337 patients with LMCA disease were included, with 84% undergoing surgical revascularization and 16% receiving PCI. These differences reflect the registry's alignment with guideline-recommended indications, capturing the characteristics of coronary artery disease presentation described above. Patients with prior coronary surgery, presentation as STEMI and/or cardiogenic shock were excluded from the study. Patient characteristics included a mean age of 72.8 years for PCI versus 69.6 years for surgery; a leaner profile compared to our region with a BMI of 26.2 kg/m²; smoking rates >50%; hypertension >60%; and lower rates of diabetes mellitus around 20%, compared to close to 50% in our region. The mode of presentation was in the context of unstable angina or acute coronary syndrome (ACS) in 60-70% of cases, necessitating urgent revascularization during the index admission. Most data, therefore, reflect this urgent context, with only 30% of stable coronary disease cases undergoing elective revascularization. In PCI cases, 1 or 2 stents were used in >60% of cases, nearly 80% if the stent score was 3 or less. For surgery, more than 75% of cases had more than 3 distal anastomoses, though only 2.1% utilized a second internal mammary artery.

After balancing groups for confounding factors and performing Cox regression analysis, PCI in LMCA disease treatment showed higher mortality (HR = 1.5), increased risk of recurrent MI (HR = 6.1), need for repeat revascularization (HR = 14), and major cardiovascular and cerebrovascular events (HR = 2.8). There were no significant differences in the incidence of stroke analyzed independently. Although current clinical guidelines do not influence the preference for surgical over percutaneous treatment in

the presence of diabetes, a favorable interaction in terms of survival was observed, translating into an average 3.6-year increase if patients were treated surgically (p = 0.014). Such favorable interactions for surgery were also observed in subgroup analysis of younger patients <70 years, and as expected, in those with complex LMCA disease involving two or three vessels (compared to >70 years and isolated LMCA disease with/without a single vessel).

The authors concluded that surgical revascularization in patients with LMCA disease is associated with better survival and lower rates of major cardiovascular events compared to PCI.

COMMENTARY:

The SWEDENHEART registry results contribute evidence on the revascularization of LMCA disease, a significant controversy in the treatment of ischemic heart disease.

To date, evidence is based on the four clinical trials NOBLE, EXCEL, PRECOMBAT, and SYNTAX, which randomized mostly stable coronary artery disease patients 1:1 to PCI or surgery. The stents used were drug-eluting, specifically biolimus, everolimus, sirolimus, and paclitaxel, respectively. The real-world context of revascularized patients, mostly undergoing urgent procedures, is poorly represented in these trials since PRECOMBAT excluded patients with an MI in the previous week, NOBLE applied the same criterion in the last 24 hours, and in EXCEL, patients with elevated CK-MB levels post-MI but in decline were excluded. SYNTAX systematically excluded all patients with prior STEMI or NSTEMI prior to revascularization.

A meta-analysis by Gaba et al. contemporaneous with this study explored PCI versus surgery outcomes in LMCA disease revascularization, emphasizing the urgent context following ACS and unstable angina. After pooling patient-level data from the four trials, only 1466 patients were included since the remaining 2927, approximately two-thirds of the sample, had stable coronary artery disease, a population notably different from that of the SWEDENHEART registry. Indeed, stable coronary artery disease was present in 82% and 53% of the NOBLE and EXCEL samples, respectively. The average follow-up was 5 years. In PCI cases, the mean stent score was 2. In surgery cases, although dual mammary artery usage was above 20%, the mean conduit count was only 2. This was due to a significant number of sequential anastomoses for complete revascularization as reflected in the SWEDENHEART registry and lower anatomical complexity of the disease. In NOBLE, complex lesions such as coronary occlusions, bifurcation lesions excluding LMCA, or severely tortuous or calcified vessels were systematically excluded, showing proportions that do not align with the real-world LMCA disease casuistry and single-vessel disease cases. The EXCEL trial, on its part, excluded patients with a SYNTAX score >33 points.

Five-year mortality rates in Gaba et al.'s study were PCI vs. surgery 10.9% vs. 11.5% in ACS patients and 11.3% vs. 9.6% in stable disease patients, all without significant differences. Recurrent MI rates were HR = 1.74 with prior ACS and 3.03 in stable disease; the need for repeat revascularization HR 1.57 with prior ACS and 1.9 in stable disease; all without statistically significant differences. The authors concluded their work with the fallacy of equivalence between the therapeutic options at 5-year outcomes, clearly influenced by the low statistical power and lack of representativeness in the real-world casuistry due to the nature of the analyzed data.

Finally, despite the influence of clinical trial evidence, the SWEDENHEART experience is not unique. Another Canadian registry by Tam et al., using Ontario's administrative database, demonstrated surgical benefits, with a propensity-score-adjusted analysis showing lower mortality (HR = 1.6) and major cardiovascular events (HR = 1.7).

In an era when the EACTS withdrew its endorsement of the current revascularization guidelines in 2018, studies like this are essential. The foundation of the previous consensus document on trials like EXCEL, which introduced a deliberate bias destined to be a milestone in the specialty's history, led to EACTS's stance, without contest or amendment to date by the corresponding cardiology society. Although EXCEL showed better survival with surgery versus PCI, this was obscured by adopting a change in the definition of peri-procedural MI to favor PCI in the composite outcome and justify class I and IIa indications for PCI in SYNTAX scores <22 and 22–32 points, respectively. This imposed fiction should not overshadow rigor and reality, and we hope that with the publication of the new consensus document in the coming months, we will not be "asked to swallow a bitter pill."

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Elio Martín Gutiérrez

Left Main Coronary Artery Revascularization: The Appetizer of New Clinical Guidelines

A joint consensus document by the ESC and EACTS updates the recommendations of the 2018 guidelines regarding revascularization in patients with left main coronary artery disease.

After analyzing the work that we will evaluate in detail below, the conclusions are clear: while prospects look promising, caution is essential. This document, resulting from over a year's work since the 2021 proposal to revise the 2018 revascularization guidelines, culminated in the 2022 version after a meeting between societies, published in 2023 due to the extensive drafting process.

Understanding these types of documents requires analyzing the behind-the-scenes work that, in this case, is published with unprecedented transparency. The work stems from a meeting of six members from each cardiological and surgical society, forming a panel of twelve who signed the document. Among cardiologists, both clinicians and interventionists were represented. All panelists' conflict-of-interest statements were thoroughly reviewed to produce an impartial document, aided by expert statisticians. Statements in the document, presented as a mini-clinical guide, were obtained by a consensus exceeding 75% agreement. Unlike previous documents, such as the 2021 American guidelines, both European societies endorsed the document.

The objective was to establish the optimal treatment for the most debated field in myocardial revascularization, stable or stabilized left main coronary artery disease (LMCA) after an acute event, with suitable complexity for percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), in relation to a low (0-22 points) or intermediate (23-32 points) SYNTAX score and low surgical risk.

The authors offer a retrospective of the statements made in the 2018 guideline and the changes that motivated the 2022 consensus assertions. The retrospective starts with the debate generated by the 3-year results of the EXCEL study and the well-known controversy over the definition of periprocedural acute myocardial infarction (AMI). This study influenced the 2018 guideline, granting a Class I indication to surgery, while PCI maintained a Class I indication for SYNTAX <22 points, IIa for SYNTAX 23-32, and III for SYNTAX >33. The 2018 guideline also referred to peri-procedural risk assessment, crucial in choosing between therapeutic options, acknowledging the STS score over EuroSCORE II for predicting 30-day surgical mortality, but not for PCI. Conversely, the SYNTAX score correlated well with early mortality post-PCI but did not adequately assess surgical risk.

Since 2018, substantial literature justifying this review has emerged, previously highlighted in earlier blog entries. This includes the updated 5-year results of the EXCEL and NOBLE studies, and the 10-year outcomes of SYNTAX and PRECOMBAT. These are the four comparative studies of PCI vs. CABG in LMCA disease, where drug-eluting stents were used in the percutaneous alternative. The authors also reference a meta-analysis by Sabatine et al., combining data from these studies.

Regarding risk assessment, the authors mention the new SYNTAX II system, which emerged after 2018 due to the poor adjustment of the previous system for surgical risk, incorporating clinical variables. However, it still presented notable interobserver variability in assessing coronary anatomy and overestimated risk in the 4-year EXCEL data validation. It was subsequently replaced by the SYNTAX 2020 version, which

demonstrated better adjustment in the validation of cohorts from the FREEDOM, PRECOMBAT, BEST, and a Japanese study for 10-year mortality and 5-year major cardiovascular events. The workgroup, however, does not endorse these systems, considering them underdeveloped. Despite previous calls to discontinue using the SYNTAX score as a decision-making axis, they continue to support its use, viewing it as the best available tool. It remains useful in determining whether coronary anatomy complexity exceeds 32 points—a key threshold in this guide.

Concerning the four analyzed studies, they update the latest follow-up results. Thus, the 5-year NOBLE study reported PCI vs. CABG mortality at 5% vs. 5%, $p>0.05$; new AMI at 8% vs. 3%, $p<0.05$; and revascularization need at 17% vs. 10%, $p<0.05$. In the 5-year EXCEL study, mortality was 13% vs. 9.9%, $p<0.05$; ischemia-driven revascularization 16.9% vs. 10%, $p<0.05$; and AMI, both periprocedural and new-onset according to the fourth international AMI definition, 9.6 vs. 4.7%, $p<0.05$. The 10-year PRECOMBAT study showed mortality at 14.5% vs. 13.8%, $p>0.05$; and new revascularization at 16.1% vs. 8%, $p<0.05$. In the 10-year SYNTAX study, mortality was 27% vs. 28%, $p>0.05$.

Using these data, the authors performed a new patient-level meta-analysis with follow-ups to the latest available dates, enabling results beyond 5 years. Including 4394 patients, 5-year PCI vs. CABG mortality was 11.2% vs. 10.2%, $p=0.33$, and beyond 10 years, 22.4% vs. 20.4%, $p=0.25$. Bayesian analysis favored surgery, albeit with a small margin. Other meta-analysis results included new AMI at 6.2% vs. 2.6%, $p<0.0001$; periprocedural AMI per study protocol (46% of the NOBLE, EXCEL, and complete SYNTAX samples) at 3.2% vs. 4.7%, $p=0.13$; and by the fourth AMI definition, 3.2% vs. 2.3%, $p=0.15$. CABG was superior for revascularization need at 18.3% vs. 10.7%, $p<0.0001$.

The guideline's major conclusion is that in stable or stabilized LMCA disease following an acute event, with complexity according to SYNTAX score <33 and low-risk patients, surgery remains Class I, while PCI is downgraded to IIa (Class III for scores ≥33).

COMMENTARY:

As previously mentioned, maintaining the strength of the surgical indication and downgrading the percutaneous alternative, for a SYNTAX score <22 points to Class IIa, is again a milestone that looks promising for our interests but may not be sufficient in the future.

The authors conduct a parallel analysis of the existing gaps in knowledge in this field and the dependence that still exists on these now illustrious four studies. Among the critical comments made, several methodological warnings stand out, aimed at standardizing the way results are communicated in this and other areas of cardio-surgical controversy, which we list below and have previously referenced in earlier blog posts. First, the mortality considered acceptable is only all-cause mortality, as isolating cardiovascular mortality is misleading. This is because, precisely, some patient deaths from complications in other systems may stem from poor cardiovascular function, which would be artificially analyzed. Second, AMI should be defined based on the criteria of the fourth international definition, as a common framework for defining variables across all studies. Third, composite outcomes should be avoided, especially when one of them disproportionately influences and skews the overall result. This means that the primary outcome of any study cannot be a composite event, and each partial result that would make up the composite should be presented individually. Third, the analysis of stroke incidence is inconsistent across studies and should be the subject of in-depth analysis. This disparity occurs because, logically, the rates post-PCI are initially higher than those

after surgery in the first year. However, during subsequent follow-up, an equalization occurs, the cause of which is poorly understood. Fourth, the analyses conducted in the studies do not consider outcomes that are highly significant in modern healthcare, such as life-years gained and their adjustment by both quality (utility) and value (considering the patient's perception). It remains unknown whether the sequelae of an aggressive approach like surgery could have a negative impact or, conversely, whether the greater frequency of hospitalizations, symptom recurrence, and reinfarctions could burden the percutaneous alternative. This aspect is particularly relevant given the apparent long-term overall survival tie analyzed crudely, as many of the events experienced by patients following index revascularization are mostly non-fatal.

Within the classes of recommendations issued, the authors maintain a call for dialogue and continued teamwork within Heart Teams, with collegial and consensual decision-making involving the patient. They insist on keeping the SYNTAX score as the decision-making axis and weighing different aspects that lead to favoring one therapeutic option over the other. To this effect, they propose a table indicating that surgery will preferably be assigned in patients with: left ventricular ejection fraction <35%, diabetes mellitus, contraindications for dual antiplatelet therapy, failure of previous percutaneous revascularizations, distal or bifurcation LMCA lesions, multivessel disease, predictable incomplete percutaneous revascularization, occluded right coronary artery with graftable distal bed, severe calcification limiting adequate stent expansion, need for concomitant procedures. PCI would be preferable in patients with advanced age and/or low life expectancy, high morbidity, high surgical risk, prior CABG with a patent left internal mammary artery graft to the left anterior descending artery (protected LMCA), ostial or body LMCA lesions, and the classic inherited cases from the TAVI spectrum, such as previous chest radiotherapy, extreme chest deformity, and porcelain ascending aorta (although for the latter, they recognize possible adaptations of surgical technique like no-touch aortic surgery: without CPB and without proximal anastomoses donors in the ascending aorta with various graft configurations).

Lastly, the authors warn of the need to "retire" these four illustrious studies and call for the generation of new evidence, better adapted to our times. There are notable differences from current practice, such as the need to update the morbidity of the populations included in the studies (worse lifestyle habits and aging population), technical and care advances incorporated in both fields (use of multiple arterial grafts, advances in surgical and perfusion techniques, enhanced postoperative recovery protocols, IVUS, functional analysis of coronary lesions, new-generation drug-eluting stents that have left the paclitaxel-coated TAXUS from the SYNTAX study far behind), pharmacological advances (new statins and lipid-lowering therapies, new antiplatelets and oral anticoagulants, and the emergence of SGLT2 inhibitors), and a result analysis more aligned with modern healthcare objectives (efficiency, utility, and value).

With all this, coronary artery bypass surgery continues its steady course. However, after more than half a century of evolution, new milestones will emerge on the long road of revascularization history. This is merely the prelude to future clinical guidelines, long-awaited as they may be, or new studies that will challenge the paradigm we take for granted today.

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José Manuel Martínez Comendador

Myocardial Revascularization Surgery Outcomes in Patients with Moderately Reduced Ejection Fraction

Retrospective analysis of the national Veterans Health Affairs registry database was conducted to assess outcomes and prognosis in stable ischemic heart disease patients undergoing myocardial revascularization surgery based on their ejection fraction classification (preserved, moderately reduced, or severely reduced).

The STICH trial and its 10-year extension highlighted the benefits of coronary artery bypass grafting (CABG) in stable multivessel coronary artery disease for patients with heart failure (HF) and reduced ejection fraction (HFrEF). In 2014, the European Society of Cardiology's heart failure guidelines introduced a new HF phenotype based on ejection fraction, categorizing as midrange ejection fraction (HFmrEF) those with EF between 40-49%. Evidence on CABG outcomes in patients with HFmrEF remains limited. The STICH study included only patients with HFrEF (EF<35%), and previous observational studies did not separately analyze this HFmrEF group.

In this study, a retrospective analysis of the Veterans Health Affairs (VHA) national registry from 2010 to 2019 was conducted to evaluate CABG outcomes in patients with stable ischemic heart disease. Patients were categorized into preserved EF (control group), HFmrEF (EF >40% and <55%), and HFrEF. All-cause mortality and the need for new hospitalization for HF and/or recurrent myocardial infarction were compared between groups using a Cox model and recurrent events analysis, respectively. Among 6533 patients, 1715 (26.3%) had HFmrEF, and 566 (8.6%) had HFrEF; the remaining 4252 (65.1%) with normal EF comprised the control group. Patients with HFrEF were more likely to have diabetes mellitus (59%), insulin therapy (36%), and a history of myocardial infarction (31%). Anemia was significantly more prevalent in HFrEF patients (49%), along with lower serum albumin (mean 3.6 mg/dL). Compared with the control group, a significantly higher mortality risk was observed in the HFmrEF (HR = 1.3) and HFrEF (HR = 1.5) groups. HFmrEF patients were also at higher risk of myocardial infarction (HR = 1.2; $p = 0.04$), and the risk of HF-related hospitalization was significantly higher in HFmrEF (HR = 4.1) and HFrEF patients (HR = 7.2).

The authors conclude that heart failure in patients with moderately reduced ejection fraction has a negative impact on survival after CABG compared with patients with preserved EF. Furthermore, these patients experience higher rates of myocardial infarction and the need for readmission due to HF.

COMMENTARY:

Ischemic heart disease accounts for nearly 70% of all HF cases, and one-third of coronary artery disease patients have HF. From these data alone, the significance of identifying any factor that can alter prognosis in these ischemic heart disease patients with reduced EF is evident. Age, left ventricular EF, the number and type of affected vessels, myocardial viability, associated mitral disease, revascularization quality, and adherence to medical therapy, among other factors, influence CABG outcomes. The STICH trial previously demonstrated that patients with EF <35% assigned to CABG had lower rates of cardiovascular mortality and HF readmissions than those in the medical therapy group, with these results extending over a 10-year follow-up. Separately, there is sufficient literature indicating that CABG offers superior survival outcomes compared with percutaneous intervention (PCI) in patients with HFrEF (LVEF <40%). However, it is worth recalling the disappointing results of PCI compared with medical therapy in the

recent REVIVED study in patients with severe stable coronary artery disease and severe left ventricular dysfunction (LVEF <35%).

This study by Deo et al. provides invaluable, novel insights into this subgroup of HFmrEF patients, confirming a worse prognosis after CABG compared with patients with preserved EF. Until now, there has been limited and conflicting evidence in this relatively new HFmrEF category. Another noteworthy aspect of this study is its analysis of a large, homogeneous cohort (99% male) of CABG patients appropriately categorized into three EF-based groups. This careful classification reduces the heterogeneity found in traditional studies analyzing this HFmrEF subgroup.

Three critical aspects are highlighted in these findings: first, revascularized HFmrEF patients present a higher risk of myocardial infarction, HF-related hospitalizations, and reduced survival compared with those with preserved EF. Five-year survival was 74% in the HFmrEF group, compared with 82% for normal EF patients and 65% for HFrEF patients—figures lower than those reported in previous clinical trials. This discrepancy between “real-world” data and clinical trials’ outcomes persists. Second, nearly 80% of patients received at least three grafts, but only 6% had more than one arterial graft, reflecting an extremely low use of multiple arterial grafts. Third, only 30% of HFmrEF and HFrEF patients were prescribed optimal HF medical therapy at discharge, mainly due to a lack of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or aldosterone antagonists. With new evidence, the inclusion of empagliflozin is now standard in these patients’ pharmacological regimen, though it was not included in this series as it predates 2019.

To conclude, improving clinical outcomes in ischemic heart disease patients with HF requires two priorities: 1) multiple arterial grafting (bilateral internal mammary artery or a combination of internal mammary and radial artery grafts), which benefits long-term results; 2) optimal medical therapy from the start of postoperative care and throughout follow-up, as recommended by major HF management guidelines. There are no excuses; the challenge is not to fulfill duty, but to recognize it.

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Elio Martín Gutiérrez

Surgical Revascularization Guided by Functional Study: From Complete to Adequate

This is a single-center study from a Korean group examining long-term outcomes of complete surgical revascularization without extracorporeal circulation from an anatomic/angiographic or functional perspective.

The concept of complete revascularization in multivessel disease has generated substantial debate among surgical groups. Traditionally, “adequate” revascularization was considered as covering at least one vessel in each heart region. Consequently, surgery involved performing three or four distal anastomoses, largely dependent on the development level of diagonal and posterolateral branches towards the lateral and inferior walls, respectively. The definition of “complete” revascularization originated from the SYNTAX study, where it was defined as “therapeutic coverage (using stent or bypass) of any vessel >1.5 mm with >50% angiographic stenosis.” This concept had a limited impact on surgical practice, requiring only a slight increase in distal anastomoses to achieve the target. However, interventional cardiology soon recognized that attaining complete revascularization demanded excessive therapeutic efforts and overtreatment of lesions with stents, both in number and length, leading to known deleterious results. Thus, the solution to the SYNTAX revascularization criterion emerged with the advent of the pressure guide as a diagnostic tool, allowing assessment of the hemodynamic significance of lesions beyond the angiographic criterion. FFR, iFR, and other techniques became part of our vocabulary, with the FAME study validating the approach, showing better outcomes for intervention guided by functional studies compared to traditional angiography in treating multivessel disease. Meanwhile, other forms of functional ischemia assessment, such as MIBI scintigraphy or SPECT, focused on the benefits of revascularization in patients with ventricular dysfunction, though with limited success.

For a time, the percutaneous approach regained ground lost after the SYNTAX study, as certain “three-vessel” cases were managed as “two-vessel” cases until the recent FAME III study publication. This study made a significant challenge by comparing the optimized results of intervention, guided by functional analysis, against surgery guided by conventional angiography. The results, unexpectedly, showed the superiority of the surgical approach, supported by medium- and long-term follow-up from classic clinical trials (SYNTAXES, EXCEL, NOBLE, BEST, FREEDOM, PRECOMBAT). All of this ultimately reinforced coronary bypass as the excellent treatment option it is for multivessel disease, particularly in diabetic patients.

Nevertheless, the concept of revascularization in multivessel disease from a functional rather than anatomical perspective remains valid. After all, coronary lesions develop over time (metachronous) within the vascular tree, allowing for collateral circulation development between territories to compensate, even for occluded vessels. Consequently, vessel-to-territory correspondence becomes blurred, moving beyond strictly anatomical criteria. Moreover, if we consider that ischemic territories would be those fed by vessels with significant lesions, that angiographic assessment of intermediate stenoses (50-75%) is deficient, and that treating territories (percutaneous or surgical) without ischemia or significant lesion in their supplying vessel is harmful, then functional study-guided revascularization is justified.

Thus, if functional analysis can improve percutaneous revascularization outcomes, why wouldn’t it do so in surgical cases? In this regard, Sohn et al. designed this study to capture their center’s experience between 2006 and 2017 with 1162 patients undergoing coronary artery bypass surgery without extracorporeal circulation. In 1014 cases

(87.3%), anatomical revascularization met the criteria, differing from the SYNTAX criterion, with coverage of any vessel with >70% lesion instead of >50%. In 1077 cases (92.7%), complete functional revascularization was achieved, covering all territories with ischemia demonstrated by preoperative SPECT. Following the center's protocol, graft patency was checked on the first postoperative day using angiography to identify early graft failures. Follow-up was subsequently conducted at 5- and 10-year intervals, focusing on survival.

At early angiographic control, 98.8% of grafts remained patent, including arterial grafts from both mammary arteries, the gastroepiploic artery, and saphenous vein. The technique without extracorporeal circulation involved creating a Y-composite graft with the left internal mammary artery anastomosed to the left anterior descending artery, along with a second graft, primarily using the saphenous vein, followed by the gastroepiploic artery, and finally the right mammary artery. Coverage of the lateral and postero-inferior walls was achieved through multiple sequential anastomoses. Early mortality was seven patients. Of the remaining 1155 patients, late mortality accounted for 322 deaths, with 5- and 10-year survival rates of 84.3% and 66.7%, respectively. Univariate analysis showed that complete revascularization from a functional perspective significantly correlated with improved survival (p = 0.038), which was not observed for complete anatomical revascularization (p = 0.859). Likewise, multivariate analysis confirmed that complete revascularization from a functional perspective was an independent factor for better survival (HR = 1.54; 95% CI 1.08-2.22; p = 0.019).

The authors conclude that complete functional revascularization, assessed through ischemia analysis by SPECT rather than anatomic evaluation based on angiographic criteria, positively impacts long-term survival in patients undergoing coronary artery bypass surgery without extracorporeal circulation.

COMMENTARY:

The work by Sohn et al. introduces a new approach to functional revascularization strategy, using ischemia analysis by SPECT rather than pressure-guided angiographic support. While this method is uncommon in our setting, it is a reasonable approach given the physiopathology of multivessel disease. Knowing which territories exhibit ischemia might be more critical than determining if the lesions in their supplying vessels are truly significant, as vessel-to-territory correspondence is not as precise in this disease. However, significant lesions require covering affected vessels, regardless of whether they exhibit ischemia in their territory, as a preventive measure against future coronary events or if they supply ischemic territory, which can sometimes be challenging to link, especially when a major branch is occluded. This explains why only a 5.4% difference existed in meeting one or the other revascularization criterion with the performed surgery, despite the perceived differences in functional and anatomical approaches. Had the anatomical revascularization criterion been set at >50% instead of >70%, these differences would likely have increased.

A second critique is that, if revascularization is considered from a functional standpoint, it would also be logical to verify revascularization effectiveness using a functional test, not solely an anatomical test like angiography, by repeating SPECT to demonstrate ischemia reversal after revascularization.

Other inherent aspects, such as early postoperative angiographic patency check, graft selection, and some notably low comorbidities (ventricular dysfunction with LVEF <35% in 14.5% of patients, COPD in 2.5%, and chronic renal failure with creatinine clearance <60 mL/kg/m2 in 13.9%), differentiate this population and practice from those at our centers.

Finally, the authors argue that there is insufficient evidence to support a revascularization strategy based on FFR analysis. Although there is limited research on the subject and no significant differences in survival, need for revascularization, or myocardial infarction between anatomical and functional approaches in most studies (e.g., GRAFFITI, FARGO, IMPAG), studies like Fournier et al. showed survival benefits, while Botman et al., Toth et al., and the FARGO and IMPAG studies showed better coronary graft patency with FFR-guided target selection compared to conventional angiography. Authors like Taggart and Fournier suggest that performing more grafts for intermediate lesion coverage only increases the use of venous grafts, which are more likely to fail in follow-up, increase perioperative morbidity, and promote atherosclerotic changes in the native coronary bed due to more turbulent flow hemodynamics that encourages endothelial dysfunction.

While more research in this area is needed, as mentioned previously, revascularization strategy is highly personalized. Functional data complement anatomical information and allow improved target vessel and graft selection, in type and number, adhering to each one's properties and indications, thereby avoiding morbidity from unnecessary graft extractions or limited-use anastomoses. This way, the achieved revascularization may be termed anatomically or functionally complete, but it will almost certainly be "adequate."

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Elio Martín Gutiérrez

Coronary artery bypass grafting for patent stented vessels: Preventive Strategy or Futile Gesture?

Comparative study of mid-to-long-term experience in a single center on grafting patent stented vessels versus leaving them ungrafted in patients undergoing surgical revascularization

Approaching revascularization in a patient who previously underwent percutaneous coronary intervention (PCI) always involves a level of complexity when determining the optimal revascularization strategy. The technology for percutaneous coronary interventions has evolved significantly in recent decades, much more than surgical techniques. Although surgery has undergone refinements to improve both the safety and quality of revascularization, it is likely that many cardiac surgeons are not fully familiar with the implications of percutaneous coronary revascularization.

Briefly, once the lesion to be treated is crossed, either through simple guidewire passage or via complex procedures for highly calcified or tortuous occlusive lesions (such as subadventitial dissection or rotational atherectomy), the goal is to remodel the vascular lumen to restore patency. Balloon angioplasty was the preferred procedure for non-occlusive coronary lesions for many years. However, the advent of stents improved angiographic outcomes by reducing acute/subacute vessel occlusions and restenosis. This is because stents significantly reduce early elastic recoil and prevent dissection, thereby ensuring an excellent immediate outcome and mitigating late elastic recoil.

Any intraluminal injury results in neointimal proliferation, leading to lumen reduction. This phenomenon occurred with balloon angioplasty but is even more pronounced with the mechanical injury caused by the stent against the vessel wall, which paradoxically may counteract the effect of maintaining the coronary lumen over the long term. In this context, drug-eluting stents (DES) represented a significant advancement, as the uncoated stent mesh (bare-metal stent, BMS) is covered by a polymer that carries an antiproliferative drug, released gradually over time. These new devices reduced neointimal hyperplasia, showing significantly better angiographic and clinical outcomes compared to their predecessors.

However, the initial enthusiasm surrounding DES was somewhat dampened by findings that they did not reduce thrombosis risk. According to Moussa et al.'s 2020 study, thrombosis occurred in about 10% of cases, even with DES, especially beyond the first year after implantation. This risk was partly attributed to delayed stent endothelialization due to the antiproliferative agents. Despite being an infrequent complication, its clinical implications were substantial, as 25% of these patients experienced severe myocardial infarction. Thus, efforts shifted toward the parallel development of potent antiplatelet therapies. First, P2Y12 receptor inhibitors such as clopidogrel were introduced, followed by prasugrel and ticagrelor, and eventually, cangrelor, a parenteral agent with an ultra-short half-life, replaced IIb/IIIa glycoprotein inhibitors (abciximab, tirofiban, and eptifibatide).

Subsequent modifications to DES led to numerous clinical trials with each new product, primarily involving changes to the drug agent (from paclitaxel to sirolimus and more recently to everolimus, zotarolimus, or biolimus) and the stent mesh, with cobalt-chromium and platinum-chromium alloys providing greater radial strength and more adaptable, thinner, and flexible structures. Recently, the pursuit of a balance between

intimal hyperplasia control and mechanical remodeling led to the development of bioresorbable stents and those without permanent polymers. The former use polylactic acid mesh that dissolves after two years, aiming to restore vascular function without permanent foreign materials; however, they have not met the desired clinical outcomes. Stents without permanent polymers, on the other hand, have found a more promising clinical niche and are directly applicable to surgical revascularization. Their rapid bioabsorption or absence of a permanent polymer reduces the impact on elective or deferred urgent revascularization scheduling. These stents can carry an antiproliferative drug on a short-duration biodegradable polymer, limiting the initial hyperplasia response while enabling faster endothelialization, which in turn allows for reduced intensity of antiplatelet therapy and fewer thrombotic events.

Given all these considerations, the presence of previous stents in coronary arteries should influence the surgical approach in three main aspects:

1. **Nature of the Stents**: As previously indicated, the type of stent—either DES or BMS—has crucial implications for clinical outcomes, which will be discussed in the study analyzed below.

2. **Time Elapsed Since Implantation**: This is particularly important concerning the minimum duration of dual antiplatelet therapy, assessing the risk-benefit balance of suspending such treatment, the need for bridging therapy with cangrelor (discontinued between 1 and 12 hours before surgery), and the continuation of therapy postoperatively. These decisions should be made jointly by cardiologists and surgeons within a Heart Team setting.

3. **Angiographic Study**: Proper identification of the distal territory supplied by the stented vessel, as well as its location, is essential. Evaluating the quality of the distal vessel for grafting is also important. Some authors have described techniques involving anastomosis by removing previously implanted stent segments. We believe this approach yields poor outcomes, and it is preferable to select territories involving native vessels, even if it means grafting more distally. Careful handling of the heart during surgery is also crucial to prevent distortion, which could result in new lesions, particularly in vessels not intended for treatment. Evaluation of in-stent restenosis (ISR) should be exhaustive, and if there is any doubt, intermediate lesions should be assessed using intravascular imaging (IVUS or OCT). Lastly, the presence of polymer within the arterial lumen could cause late endothelial toxicity, chronic inflammation, fibrin deposits, or even neoatherosclerosis, all of which could negatively impact the distal vascular bed.

The study at hand stands out for its originality as it aims to challenge a previously widely accepted paradigm. This is a comparative study with a control group, where patients undergoing surgical revascularization are evaluated regarding the grafting of previously stented vessels with nonsignificant stenosis (equal to or less than 49%). Historically, a fundamental principle of coronary artery bypass grafting (CABG) was the requirement of significant stenosis for grafts to function effectively and have adequate durability, both in the short term and during follow-up. This was due to the phenomenon of competitive flow, in which the absence of significant pressure drop across lesions without significant stenosis could result in inadequate graft flow due to a lack of a sufficient gradient between proximal and distal portions, ultimately leading to graft failure—manifesting differently depending on whether the graft was venous (thrombosis) or arterial (string sign).

The study selected 52 patients who had undergone prior percutaneous revascularization with a stent placed in the right coronary artery (RCA) or circumflex artery. Of these, 24 patients received bypass grafting to the previously stented vessels, using saphenous vein grafts, despite the vessels being patent. In the remaining 28 patients, no bypass grafting was performed distal to the stented segments. Patients with additional concomitant surgeries other than revascularization (due to potential graft distortion from greater cardiac manipulation) and those with two or more stents in different vessels were excluded. However, patients with multiple stents in the same vessel were included. Dual antiplatelet therapy was discontinued in 20 patients—16 with BMS after six weeks (implanted for recent acute coronary syndrome) and four with DES after one year of treatment. All patients received bridging with low molecular weight heparin (LMWH), and aspirin (ASA) was continued in every case. Postoperative bridging with LMWH was provided, and dual antiplatelet therapy was gradually reinitiated for at least one year.

Angiographic assessment of stent and graft patency was performed primarily through CT coronary angiography, with a median follow-up of 49 months for patients without bypass and 53.5 months for those with bypass. In 18 patients, a repeat catheterization was required due to recurrent angina or new acute coronary syndrome (ACS), and the opportunity was taken to assess the patency of both stents and bypass grafts instead of utilizing CT coronary angiography.

The study groups were comparable. No perioperative mortality occurred in either group, with a single case of late death due to a brain malignancy. In the group without bypass, 71.4% of non-grafted vessels remained patent in the native bed, whereas in the group with bypass grafting, 95.8% of the vessels remained patent distally (considering the native bed/stent and/or graft), with a statistically significant difference of $p = .02$. Although there was no significant mortality, morbidity was greater in the non-bypassed group, affecting 42.8% of patients compared to 25% of those who received bypass grafting. Morbidity was primarily related to the need for additional revascularization procedures.

Furthermore, differences were found in the analysis of patency between stents and bypass grafts in vessels with patent stents. For stents alone, 71.4% remained patent without grafting compared to 66.7% with bypass grafting. Occlusions primarily occurred in BMS (43.75%), which only occurred in 10% of DES. For bypass grafts, 91.6% remained patent, unaffected by the supposed phenomenon of competitive flow. The interaction between bypass grafts and stents was notable: the occlusion rate for different stent types was significantly influenced by whether they were bypassed or not—75% occlusion for non-bypassed BMS versus 30% for those bypassed; for DES, no occlusions occurred in non-bypassed stents, while 50% of the bypassed stents (2 out of 4) were occluded.

Although the study has several limitations that will be addressed later, the authors conclude that in patients with patent stents undergoing surgical revascularization, the strategy of leaving stented vessels ungrafted appears acceptable for DES but may not be safe for BMS.

COMMENTARY:

The analyzed study likely raises more questions than it answers, representing one of those original works that inspire not only further research in the field but also a reflection that might explain its findings. The results obtained seem to contradict the principles of surgical revascularization. However, they may be influenced by different factors that could even be considered biases within the study design.

Aside from the fact that the study uses a small sample size with limited statistical power, the first point that stands out is the low volume of DES implanted—accounting for less than half of all implanted stents—despite the study covering the period between 2015 and 2020. Secondly, there was also an imbalance in the distribution of BMS and DES between the two groups: only 4 out of 20 DES were bypassed compared to 20 out of 32 BMS. The study was non-randomized, and patients for whom bypassing patent stents was selected were mostly those with BMS. It is well-known that BMS outcomes are significantly inferior to those of DES, which could explain the favorable patency results for the distal vessel and lower rates of repeat revascularization when stents were covered by grafts.

Thirdly, a bias could have been introduced in assessing preoperative stenosis severity, as only simple angiography was used. Given the number of BMS, the extent of ISR might have been underestimated, particularly since ISR is more common in BMS than in DES. Thus, patients selected for bypass may have had significant ISR, while others were left uncovered and likely contributed to the postoperative coronary events. Indeed, in terms of patency, DES outcomes were noteworthy, with the majority remaining patent without bypass grafting. Hence, more than expanding the grafting of BMS, the takeaway is the need for a diagnostic study that leaves no room for doubt, using IVUS or OCT for any ISR of uncertain significance. This measure would effectively reduce future morbidity and mortality associated with new ACS.

Regardless, the surgical revascularization of patients who previously underwent percutaneous coronary interventions remains a therapeutic challenge, with ongoing uncertainty about the best management strategy. The outcomes for these patients are notably poorer compared to those without prior stent implantation. This is because, even considering that revascularization decisions may have been made outside current guidelines, these patients typically have more complex coronary artery disease, a longer disease progression, and likely have already experienced an acute coronary syndrome (ACS) that led to the percutaneous revascularization. In terms of surgical revascularization, factors such as the loss of proximal vascular territory or the distal bed disease resulting from drug release from the permanent polymer of DES may be major obstacles to successful surgical intervention. In this respect, stents without permanent polymers fit perfectly into a context of sequential revascularization following ACS.

Once again, studies like this remind us that the treatment we offer our patients is the product of a collaborative effort between cardiologists and surgeons, utilizing two therapeutic options that each have their indication and timing within the natural history of coronary heart disease—in this case, ischemic heart disease. Interference is inevitable, but above all, an adequate study and discussion of the best therapeutic management typically leads to the best outcomes. To that end, joint assessment of angiographic findings, completion of the study with functional or intravascular diagnostics in case of doubt, and optimal antiplatelet therapy strategies are all critical aspects. Thus, the simplistic message that might be drawn from this study—grafting all previous BMS regardless of their patency—could be seen as negligent and unacceptable within modern, responsible clinical practice.

In this way, this study, while providing evidence that grafting patent stented vessels (especially BMS) might be beneficial, also highlights the nuanced decision-making required in each case. Particularly, it emphasizes the importance of individualized patient care based on thorough assessment, advanced diagnostic tools, and, whenever possible, the collaborative decision-making process of a Heart Team to tailor the strategy to each patient's unique condition.

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Elio Martín Gutiérrez

Do We Need to Revascularize a Chronically Occluded Right Coronary Artery?

A single-center Japanese study analyzing the outcomes of revascularization, specifically regarding clinical results and graft patency, in chronically occluded right coronary arteries during coronary artery bypass graft surgery.

In cases of multivessel disease, particularly with coronary occlusions, blood flow paths deviate from typical topographic routes, becoming collateral. These collateral vessels provide supplementary blood flow to regions initially served by other branches. Moreover, they sustain the epicardial vessels by retrograde filling from capillary networks, which discharge into both the venous area and the previously closed epicardial vessel due to a loss of coronary autoregulation, where the pre-capillary sphincters of the occluded vessel remain permanently open.

This collateral flow, whether homocoronary or heterocoronary, may stay compensated (chronic coronary syndrome or stable angina) or decompensate, leading to the clinical spectrum of ischemic heart disease. In compensated situations, conservative management strategies may be considered, especially in light of the ISCHEMIA study findings, except in cases such as single-vessel patency, left main coronary artery disease, or ventricular dysfunction where revascularization provides a prognostic advantage. However, misinterpretations of this study have influenced the surgical revascularization indications in American guidelines, as previously discussed in prior blog entries.

In exacerbated disease (unstable angina and acute coronary syndrome), revascularization becomes essential when the balance between perfusion and myocardial demand is insufficient for one or more ventricular segments. Identifying the culprit vessel, assessing whether the occluded vessel contributes to the acute ischemic scenario, and selecting the optimal revascularization strategy based on coronary anatomy, technical options, clinical presentation, and surgical risk are vital.

For treating occlusive coronary lesions in multivessel disease, a debate exists: does revascularization of the remaining coronary tree sufficiently resolve ischemia by covering other regions and leveraging collateral circulation for the occluded vessel's territory? This study examines this issue specifically for the right coronary artery territory. The controversy arises between two opposing arguments:

- Against: Coronary grafts with native flow competition, as seen with collateral supply, may impair graft patency. Additionally, it adds morbidity due to graft harvesting and may accelerate atherosclerosis in the native bed. Often, these beds are hard to evaluate as epicardial vessels appear hypoperfused or belong to regions with transmural infarcts. Thus, without viability studies, bypass may be deemed a futile effort.

- In favor: If a preserved epicardial vessel exists, bypass grafting could logically support the myocardial territory, as achieving a nearly anatomical complete revascularization is among the best predictors of improved survival and favorable outcomes in multivessel disease revascularization.

To address this question, the outcomes of 200 patients treated from 2015 to 2022 with multivessel disease were retrospectively analyzed, including 76 with occluded right coronary arteries and 124 with significant but non-occlusive lesions. Cases involving reoperations, sequential anastomoses between the circumflex and right coronary artery,

and grafts using the gastroepiploic artery were excluded to ensure series homogeneity. In most cases, independent grafts were used, primarily saphenous vein grafts for the right coronary artery, and intraoperative flow verification and postoperative dual antiplatelet therapy were administered.

No major differences were found between the groups. Patients with occluded right coronary arteries had a higher incidence of prior myocardial infarction ($p = 0.015$) and fewer distal anastomoses (4.0 ±0.8 vs. 4.3 ± 0.9; $p = 0.036$). Intraoperative flow measurements showed no significant differences (30 cc/min vs. 25 cc/min; $p = 0.114$), nor did pulsatility (2.1 vs. 2.4; $p = 0.079$) or diastolic filling indices (65% vs. 64%; $p = 0.844$) between the groups. Patency checks a week post-surgery revealed no significant differences between grafts in occluded and non-occluded right coronary arteries (94.7% vs. 96%; $p = 0.733$). When grading occlusion severity according to Rentrop classification (grade 0-1: low collateral, 32 patients; grade 2: moderate collateral, 26 patients; grade 3: high collateral, 18 patients), saphenous graft patency worsened with increased competitive flow: 96.9%, 96.2%, and 88.9% for grades 0-1, 2, and 3, respectively, though differences were not statistically significant.

The authors conclude that right coronary artery occlusions do not compromise coronary graft patency in multivessel revascularization.

COMMENTARY:

This Japanese study, despite its limitations as a single-center, non-randomized, statistically limited study, seems adequate to address the previously discussed controversy: effective revascularization of multivessel disease requires anatomical completeness, including territories supplied by vessels with significant lesions, such as right coronary artery occlusions.

Therefore, the strategies commonly used in off-pump revascularization surgery, where the length of the mammary artery grafts may be insufficient to cover both lateral-posterior and inferior territories, may not be entirely appropriate. When a preserved epicardial coronary vessel is present, whether the posterior descending, posterolateral trunks, or the right coronary artery itself, bypass yields similar outcomes to vessels with non-occlusive significant lesions. Additional grafts, usually saphenous vein grafts, may be required; however, with a favorable distal bed, a radial artery may be considered for lesions >90% in the right territory. This approach may challenge the "no-touch aorta" strategy in off-pump surgery, as proximal anastomoses on the aorta may be needed. However, the authors report no stroke penalty (<2%) by following a "touch the aorta well" strategy using epiaortic ultrasonography, thus preserving revascularization outcomes.

A notable outcome is the 12% graft occlusion rate in cases with substantial collateral supply. Although speculative, based on personal experience, leaving right coronary artery occlusions untreated may be suitable in limited graft availability and preserved ventricular function cases with Rentrop 3 collateral supply and epicardial vessel diameter below 1.5 mm, formally meeting the SYNTAX criterion.

In summary, this study reinforces that, except in rare cases, "doing less is indeed the enemy of good." Achieving perfect revascularization across all territories is key to successful multivessel disease revascularization, regardless of occlusive lesion collateral supply or myocardial viability study findings.

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Elio Martín Gutiérrez

Design-based evidence: Discrepancies in Clinical Characteristics Between Myocardial Revascularization Registries and Clinical Trials

This review article compares discrepancies in pre-procedural variables between patients in clinical trials and registries, both for coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI).

Clinical trials have formed the cornerstone of Evidence-Based Medicine development over the last decades. Conducted in controlled research settings, they minimize bias through randomization and multicentricity, estimating the potential benefit of a new therapeutic strategy over a conventional one. While these designs provide excellent internal validity, their applicability to everyday practice can be limited. This limitation is primarily attributed to selection bias, a significant factor in study design. Excessive or overly strict exclusion criteria detach the study sample from the target population, resulting in conclusions that reflect laboratory findings rather than clinical research.

In contrast, registries offer evidence with characteristics opposite to those of clinical trials. Retrospective by design, data in registries are typically collected after patient clinical outcomes have occurred. With minimal selection criteria, registries include consecutive patients with few restrictions, resulting in large case volumes and multicentricity that minimize bias, thereby ensuring strong external validity. However, the reliance on strict data collection, which is not as flawless as in clinical trials, and the influence of each country's healthcare idiosyncrasies hinder the exploitation and relevance of registries in scientific evidence (clinical guidelines).

Various experts have highlighted the need to reevaluate reference sources in Evidence-Based Medicine. A study evaluating 52 clinical trials in Cardiology, Mental Health, and Oncology revealed that 70% of them (37 of 52) did not represent the target population for which their conclusions would be applied. For this reason, the authors conducted an extensive review, analyzing 14 primary clinical trials comparing CABG and PCI, as well as 10 major national registries (4 for CABG and 6 for PCI). They examined 16 pre-procedural variables to define patient characteristics and compared samples from trials and registries for each treatment type, CABG and PCI. This review included 2252257 patients, with 11824 from trials (50% CABG, 50% PCI) and 2238623 from registries (423843 CABG, 1814780 PCI). Patients in trials and registries demonstrated notable differences. For CABG, 5 out of 16 variables showed statistically significant differences between registries and trials. Trial patients displayed lower morbidity: reduced smoking rates, better ventricular function, lower prior MI rates, and more single-vessel disease. Early mortality was better in trials (2%) compared to registries (3%), $p = 0.005$. For PCI, 9 out of 16 variables showed significant differences, indicating lower morbidity among trial participants: they were younger, had lower smoking rates, and better ventricular function. Trials had more anatomical cases characteristic of surgery, LMD and/or three-vessel disease, compared to registries. Early mortality in trials was also better than in registries, 1% vs. 2%, $p = 0.003$.

The authors emphasized the observed differences and the limited external validity of the clinical trials supporting current clinical guidelines.

COMMENTARY:

Evidence-Based Medicine is currently facing significant scrutiny. The scientific progress achieved over the past decades through clinical trials has been unprecedented across all fields of Medicine. However, the involvement of the pharmaceutical industry with necessary funding, and the demonstrated polarization of results through pre-intervention patient selection or post-procedural variable redefinition, has weakened the credibility and real-world applicability of these studies.

The results identified by the authors confirm that similar trends occur in the evidence base for daily practice. Recommendations for stable coronary artery disease management between PCI and CABG remain controversial, and the new myocardial revascularization guidelines from the ESC/EACTS are expected in the coming months. Although limited validity has been detected in clinical trials within this field, the authors acknowledge that it is less significant than in other pathologies, such as valvular surgery and structural interventionism. A solution must be sought in the coming years. Emerging computational systems and the development of significant national registries, like our RECC, open the door to Big Data as a new evidence source. This potentially more realistic approach may introduce new limitations and biases, which we will need to navigate to identify the best therapeutic strategies for our patients. Until then, multidisciplinary collaboration and common sense should prevail.

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Elio Martín Gutiérrez

Hybrid Revascularization: A Possible Alternative with Favorable Outcomes

This retrospective study adjusted by propensity score analysis compares mid- to long-term revascularization outcomes in multivessel disease patients treated with conventional off-pump coronary artery bypass grafting (OPCAB), percutaneous coronary intervention (PCI), and hybrid revascularization.

We live in a constantly evolving environment, where the tailored alignment of therapeutic alternatives with patient characteristics enhances the care we offer. The treatment of structural heart disease exemplifies this phenomenon. However, coronary revascularization remains polarized between surgery (CABG) and percutaneous intervention (PCI). Hybrid revascularization has gained limited popularity, as the drawbacks of each revascularization strategy (CABG: invasiveness, bleeding, postoperative recovery, surgical wound; PCI: restenosis, progression of proximal native disease, dual antiplatelet therapy, vascular access complications) often outweigh its advantages (CABG: patency of arterial graft(s), avoidance of cardiopulmonary bypass (CPB), reduced stent use; PCI: minimally invasive percutaneous treatment, reduced morbidity from graft harvest, angiographic verification of surgical results, complete revascularization supported by the internal mammary artery graft to the left anterior descending artery).

Experience with hybrid revascularization has been limited both in quantity and in the follow-up duration of studies. It remains a minority approach; authors report it represents only 0.48% of CABG procedures in the United States. Thus, we analyze a study that gathered multivessel disease patients treated between 2007 and 2018, including 585 who underwent hybrid revascularization, 15,118 OPCAB, and 54,502 PCI. After propensity score matching, three homogeneous groups of 540 patients each were obtained. Two key factors influencing the results were the method used for hybrid therapy and coronary anatomy characteristics. Firstly, hybrid revascularization was performed using minimally invasive off-pump techniques (MIDCAB) with the left internal mammary artery anastomosed to the left anterior descending artery through a left anterior small thoracotomy (LAST) by experienced surgeons. Sequentially, but in the same procedure, complete revascularization of remaining coronary disease was performed, minimizing any period of protection loss between procedures. The percutaneous procedure reevaluated the surgical outcome angiographically, enabling embolization of dominant collateral branches causing steal, especially in left main coronary artery disease. Secondly, patients had real-world characteristics, with higher SYNTAX scores (mean 27) compared to previous studies (15–23) and higher left main disease (37% vs. 7–17%) and three-vessel disease (62% vs. 34–40%) prevalence. After a median follow-up of more than 8 years, the rate of major adverse cardiac and cerebrovascular events (MACCE) was comparable between hybrid revascularization and OPCAB (28.7% and 23.9%, respectively) and significantly higher in PCI (45.3%; $p < 0.001$). Mortality did not differ significantly across the three options (OPCAB 9.7%, hybrid 12.7%, and PCI 15.6%; $p > 0.05$). For MACCE stratified by EuroSCORE II (low <0.9%, medium 0.9–1.5%, high >1.5%), similar outcomes were seen for low- and medium-risk groups, but in the high-risk category, MACCE was lower for hybrid revascularization than OPCAB or PCI (31.9% vs. 47% vs. 53.7%; $p = 0.014$). For individual MACCE events, the need for repeat revascularization affected stent-based approaches, with rates of 9.8%, 17.3%, and 34.8% for OPCAB, hybrid revascularization, and PCI, respectively; $p < 0.001$. These differences were non-significant for low-complexity coronary anatomy (SYNTAX score <22). Cost-utility (quality of life) and cost-value analysis revealed similar scores for

physical capacity, treatment satisfaction, and quality of life across OPCAB, hybrid revascularization, and PCI, with minimal differences.

The authors conclude that, compared to traditional revascularization strategies, hybrid revascularization offers satisfactory MACCE and functional capacity outcomes for multivessel coronary disease patients.

COMMENTARY:

This study represents the largest and longest follow-up analysis focused on hybrid revascularization outcomes compared to traditional multivessel disease approaches. It optimizes minimally invasive principles, avoids operator bias with highly experienced surgeons, and provides real-world data, positioning hybrid revascularization as an attractive alternative for select patient subgroups.

CABG, with or without CPB, remains the treatment standard for multivessel disease. Regardless of technical variations (grafts, on- or off-pump, aortic manipulation, or proximal anastomoses), CABG principles involve covering the myocardial territories affected by multivessel disease, where tributary coronary artery correspondence may be less defined, especially with artery occlusion. In multivessel disease, “the blood's pathways may be as intricate as God’s, with collaterals.” Revascularization should apply at least one arterial graft, which, despite other associated graft failures or disease, especially if venous or inadequately used arterial grafts, maintains patency and can supply large myocardial areas. Therefore, the use of multiple arterial grafts can still extend this benefit. Hybrid revascularization assimilates this concept, using stents' minimal invasiveness while preserving the long-term benefit of the left internal mammary artery graft to the left anterior descending artery.

These results suggest that hybrid revascularization may find its niche in multivessel disease subgroups, specifically non-diabetic, frail patients (limited mobility, comorbidities, high surgical bleeding risk, etc.) and/or those with intermediate surgical risk (EuroSCORE II >1.5, differing significantly from the thresholds used for TAVI), with coronary anatomy complexity suitable for PCI (SYNTAX score <22, currently class I indication for PCI and CABG in non-diabetic patients). The reduction in MACCE, alongside similar survival and revascularization rates relative to OPCAB, positions hybrid revascularization as a tailored alternative for certain patients. Once again, the hybrid nature, not only of the treatments but of the specialists involved, stands out. This combination enhances benefits and overcomes the limitations of two techniques traditionally seen as incompatible.

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Carlota Hernández Díez

Results of Percutaneous or Surgical Revascularization by SYNTAX Score Stratification: The Beginning of the End?

This meta-analysis, encompassing 6 clinical trials, compares percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in cases of left main coronary artery disease or multivessel disease, presenting results stratified according to the SYNTAX score.

Scoring systems are designed to assist clinical decision-making. Among them, the SYNTAX score, based on the eponymous clinical trial, quantifies disease severity by assessing the complexity of coronary artery lesions and categorizes cases into three tertiles: low risk (score 0-22), intermediate risk (23-32 points), and high risk (>33 points), being one of the most widely used scores in Cardiology. Its calculation is recommended in the latest European coronary revascularization guidelines of 2018 (Class I, Level of Evidence B) for patients with left main coronary artery disease (LMCA) or multivessel disease.

In clinical practice, the SYNTAX score is commonly applied to choose the revascularization approach (PCI versus CABG) for these patients, with low-risk cases often selected for PCI and high-risk cases for surgical treatment. However, the score was not initially designed for this purpose and has not been prospectively validated.

Gaudino et al. conducted a meta-analysis examining the association between SYNTAX score tertiles and long-term outcomes for major adverse cardiac and cerebrovascular events (MACCE) and all-cause mortality. This analysis included 6 randomized clinical trials evaluating PCI versus CABG in patients with multivessel or LMCA disease, covering a study period from 2004 to 2015 and incorporating data from 8269 patients (4134 in the PCI group, 4135 in the CABG group). Patient samples were consistent across trials and study groups, except for the percentage of diabetic patients, which reached 100% in one study (the FREEDOM trial). The clinical context included patients with stable angina and acute coronary syndrome/unstable angina, with a mean follow-up of 6.2 years. Due to the time frame of these studies, the use of drug-eluting stents and dual antiplatelet therapy (including newer agents such as ticagrelor) was common. In addition, IVUS was utilized in 4 of the trials as a supportive intracoronary diagnostic technique. As for the surgical revascularization techniques, left internal mammary artery grafts were used in 80-90% of cases, with an average of 3 grafts per patient.

For analysis, the incidence rate ratios (IRRs) method was employed as a risk estimator and to generate interaction effects, both in overall estimates and by SYNTAX score subgroups. Various sub-analyses were also conducted for trials involving patients with LMCA and multivessel disease. Overall, PCI was associated with a significant increase in MACCE (IRR 1.39; 95% confidence interval (CI): 1.27-1.51) and a non-significant increase in all-cause mortality (IRR 1.17; CI: 0.98-1.40). In the low-risk SYNTAX score group, these findings were confirmed, with a significant increase in MACCE (IRR 1.25; CI: 1.02-1.54) and a non-significant increase in all-cause mortality (IRR 1.07; CI: 0.76-1.5). In the intermediate-risk group, PCI significantly increased both MACCE (IRR 1.48; CI: 1.30-1.69) and all-cause mortality (IRR 1.38; CI: 1.07-1.77). In the high-risk group, PCI again significantly increased MACCE incidence (IRR 1.39; CI: 1.18-1.63) and non-significantly increased all-cause mortality (IRR 1.03; CI: 0.70-1.52). Tests for treatment effect heterogeneity by SYNTAX score, for both MACCE and mortality, showed no significant results (*p*-interaction 0.4 and 0.34, respectively). The results were consistent for both LMCA and multivessel disease patients (MACCE: *p*-interaction 0.85 for LMCA and 0.78 for multivessel; all-cause mortality: *p*-interaction 0.12 for LMCA and 0.34 for

multivessel). Similarly, analysis comparing risk tertiles showed no significant differences.

Given that CABG is associated with better outcomes than PCI for multivessel and LMCA disease regardless of anatomical complexity, the authors conclude that, due to the lack of association between SYNTAX score and clinical outcomes in trials comparing PCI and CABG, the score should be abandoned in favor of multidimensional scores when choosing the revascularization strategy.

COMMENTARY:

This meta-analysis includes 6 significant studies (SYNTAX, EXCEL, NOBLE, BEST, FREEDOM, and PRECOMBAT) assessing PCI versus CABG for LMCA and multivessel disease, with outcomes reported based on pre-treatment SYNTAX scores. Despite possible methodological limitations, this meta-analysis confirms the lack of correlation between SYNTAX score and clinical outcomes, with surgical revascularization proving more favorable across all score levels. Notably, the increased MACCE and mortality rates with PCI, even in lower scores, highlight that PCI is usually chosen for these lower-risk patients as recommended in the latest myocardial revascularization guidelines. It is important to consider that the SYNTAX score is purely angiographic, with considerable interobserver variability. In this type of patient, it seems reasonable to use scores that include clinical parameters when choosing the revascularization strategy, as multiple factors can impact treatment outcomes. Perhaps, in patients not eligible for surgery, the SYNTAX score might help assess PCI viability and technical success. Considering this meta-analysis' findings, where CABG reduces events and mortality across all score tertiles, it is advisable to discontinue using SYNTAX as the primary tool for revascularization selection, a shift that should be reflected in future clinical guidelines and in our practice.

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Elio Martín Gutiérrez

Coronary Artery Bypass Grafting vs. Percutaneous Intervention in Patients with NSTE-ACS: No News, Good News

Comparative meta-analysis of prospective studies on urgent revascularization in patients with multivessel disease presenting specifically as Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS), via coronary artery bypass grafting or percutaneous intervention.

The evidence favoring surgical treatment of multivessel coronary disease is currently undeniable, especially for diabetic patients or those with intermediate-to-high anatomical complexity as measured by the SYNTAX score. Multiple studies support this, though these recommendations have been primarily established for stable angina presentation. In an urgent setting, where the patient presents with NSTE-ACS requiring in-hospital revascularization, specific recommendations are absent. Current guidelines suggest following the indications for stable angina, as once the patient's clinical condition stabilizes, it may be assimilated into this context due to a lack of specific evidence on this topic. Additionally, most evidence supporting the benefit of surgery over intervention (e.g., SYNTAXES, NOBLE, FREEDOM, PRECOMBAT) also depends on revascularization indications in settings other than acute coronary syndrome.

In response to this, a Dutch group conducted a systematic review of comparative revascularization studies in the NSTE-ACS context, identifying four prospective studies that included 1542 patients in the surgical arm and 1630 in the interventional arm. The number of treated vessels ranged from 2.55 to 2.8, with no significant difference between the two approaches, and follow-up durations varied: one year in two studies, two years in one, and five years in the fourth. There were no significant differences in one-year outcomes in terms of mortality (OR = 1.05; 95% CI 0.66-1.66), new myocardial infarction (OR = 0.78; 95% CI 0.40-1.51), or periprocedural stroke (OR = 1.54; 95% CI 0.55-4.35). However, the need for repeat revascularization over follow-ups of one to two years was one-fifth in the surgical group compared to the interventional group (OR = 0.21; 95% CI 0.13-0.34).

The authors concluded that in patients with NSTE-ACS and multivessel coronary disease, urgent surgical revascularization offers comparable outcomes to intervention in terms of periprocedural complications, with added benefits in terms of future revascularization requirements, whose impact on survival should be evaluated with extended follow-up.

COMMENTARY:

Although limited in size, this is the first meta-analysis aggregating comparative evidence between percutaneous intervention and surgery in the urgent revascularization of NSTE-ACS patients.

While survival outcomes are not significant, this is likely due to the insufficient follow-up period. Nevertheless, incomplete revascularization and the need for repeated procedures have been shown to negatively impact survival in patients with multivessel disease. Indeed, coronary occlusion is one of the main independent predictors of incomplete revascularization according to the SYNTAX score, particularly affecting the percutaneous option.

Additionally, it is essential to highlight the importance of focusing on NSTE-ACS. Although treatment assumptions are based on stable angina guidelines, NSTE-ACS has distinct characteristics. It represents an acute condition marked by an imbalance in

perfusion across territories, with insufficient time for collateral development. Complete revascularization may, therefore, be even more critical in this presentation than in stable angina patients, where compensatory supply is better balanced. Furthermore, in the FAME III study, although intervention was guided by functional analysis, angiography-based surgical revascularization resulted in improved cardio-cerebrovascular event outcomes at one year.

In conclusion, no news is good news. The assumptions made regarding revascularization indications by clinical guidelines and the lack of specific randomized evidence are supported by this meta-analysis, reinforcing current clinical practice. Remember that among the clinical presentations of ischemic heart disease with multivessel involvement, half of the cases are NSTE-ACS, meaning many of our patients have received extrapolated indications without direct evidence. From now on, this not-so-small meta-analysis provides evidence to fill a knowledge gap before any future "changes" arise. While change can be good, in this case, no change is also a positive outcome.

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José Manuel Martínez Comendador

Does a good state of physical and mental health impact mortality when comparing surgical and percutaneous revascularization?

This SYNTAXES substudy investigates the relationship between preprocedural physical and mental health and 10-year mortality in patients who have undergone coronary revascularization, either surgically or percutaneously.

The ongoing debate regarding the optimal revascularization strategy for patients with complex coronary disease, such as left main coronary artery disease (LMCAD) or three-vessel disease, persists. Clinical and anatomical factors—including age, diabetes, and anatomical complexity as measured by the SYNTAX score—are key in deciding between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). However, a patient's general health, reflecting physical and mental resilience, could significantly impact outcomes for these treatments. Assessing preprocedural physical and mental health enables a comprehensive understanding of the patient's tolerance to invasive procedures and subsequent treatments, including rehabilitation. Previous studies have shown that physical limitations or mental health decline correlate with poorer outcomes in coronary artery disease (CAD) patients, including those undergoing PCI or CABG. Nevertheless, data describing the effect of preprocedural physical or mental health on long-term outcomes between CABG and PCI remain scarce.

The aim of this SYNTAXES substudy (SYNTAX Extended Survival) was to evaluate the association between patient-reported preprocedural physical and mental health and 10-year all-cause mortality following PCI or CABG in patients with LMCAD or three-vessel disease, assessing the interaction between preprocedural physical and mental health and treatment effects of PCI versus CABG. Patients were stratified by terciles of preprocedural Physical Component Summary (PCS) or Mental Component Summary (MCS) scores derived from the validated 36-Item Short Form Health Survey (SF-36), where higher PCS and MCS scores indicate better physical and mental health, respectively. The primary outcome was 10-year all-cause mortality.

A total of 1656 patients with available SF-36 data were included in this study. Both higher PCS and MCS scores independently associated with lower 10-year mortality (10-point increase in PCS, adjusted hazard ratio [HR] 0.84, $p = 0.021$; 10-point increase in MCS, HR 0.85, $p = 0.005$). A significant survival advantage with CABG over PCI was observed in the highest PCS (>45.5) and MCS (>52.3) terciles, with significant treatment-by-subgroup interactions (PCS p-interaction = 0.033; MCS p-interaction = 0.015). Among patients with high PCS (>45.5) and MCS (>52.3), 10-year mortality was significantly greater with PCI than CABG (30.5% vs. 12.2%; HR 2.87, $p = 0.001$), whereas for those with low PCS (≤45.5) or MCS (≤52.3), there were no significant mortality differences between PCI and CABG at 10 years, leading to a significant treatment-by-subgroup interaction (p-interaction = 0.002).

The authors concluded that, among patients with LMCAD or three-vessel disease, patient-reported preprocedural physical and mental health strongly correlates with long-term mortality and modifies the relative treatment effects of PCI versus CABG. Patients with optimal physical and mental health demonstrated better 10-year survival with CABG compared to PCI. Assessing patient-reported physical and mental health is crucial in selecting the optimal revascularization strategy.

COMMENTARY:

In 2005, the SYNTAX trial was conducted across 17 European and American countries, randomizing 1800 patients with three-vessel or LMCAD to undergo either CABG or PCI using paclitaxel-eluting stents. A subsequent report in 2019 presented 10-year survival outcomes for the majority of these patients (93% for PCI and 95% for CABG). The SYNTAX trial incorporated quality-of-life assessments, both pre- and post-procedure, using the SF-36 Health Survey, enabling the current study.

This study highlighted that CABG's advantages over PCI were most pronounced in patients with higher physical and mental health scores at baseline, particularly those in the top tercile of each. A notable survival advantage at 10 years was observed in CABG patients with high scores in both domains, with nearly three times the survival rate compared to PCI.

Most remarkably, this survival benefit of CABG in patients with good physical and mental health operates independently of the SYNTAX score, suggesting CABG as the preferred option even when severe three-vessel disease is not present. These findings propose that preprocedural physical and mental health evaluations might serve as a valuable tool in personalizing myocardial revascularization approaches, a consideration previously unexplored at this scale.

Given today's focus on personalized medicine, it's striking that this data was not previously accessible despite being available. CABG is known to be an invasive procedure, requiring patient resilience for a successful recovery. Generally, CABG is not recommended for patients with less than five years of life expectancy, due to the delayed survival benefits which become apparent two to three years post-procedure for three-vessel disease cases. CABG's invasiveness may demand nearly a year for complete recovery.

These findings provide a fresh and practical insight into myocardial revascularization, challenging previous assumptions. It suggests that younger or active patients with multivessel or LMCAD may not benefit most from PCI, as once assumed, since CABG appears more advantageous for those with good health scores. Conversely, CABG should not be considered for patients with low physical or mental health scores, especially when PCI or optimal medical therapy are viable alternatives.

The SYNTAXES study has notable limitations. First, patients in the CABG group received guideline-directed medical therapy less frequently (e.g., over 25% were not on statins). Second, there's no information on patients who transitioned from PCI to CABG over time, which could have influenced results. Additionally, significant patient attrition occurred during follow-up, representing 7% of the PCI group and 5% of the CABG group, potentially introducing bias. Overall, 13% of SYNTAX patients did not contribute data to the current study, limiting generalizability. Lastly, information on late causes of death or major adverse cardiac events, which could provide further context, is missing.

Technological advances in PCI and CABG may also affect the applicability of these results. Modern PCI technology may offer improved outcomes compared to those available at SYNTAX's inception, while recent CABG studies report nearly half the adverse events found in early trials like SYNTAX and FREEDOM.

A crucial question raised by this study is whether objective tools to measure physical and mental performance at baseline are needed, or if high-functioning patients who might benefit more from CABG can be identified more simply through clinical assessment.

In summary, this article provides a novel and practical perspective on myocardial revascularization, supporting personalized medicine in coronary surgery. For patients

with a good pre-revascularization health status, CABG has strong support, independent of SYNTAX severity. Conversely, PCI or medical therapy options may be preferable for those with deteriorated physical and mental functioning.

Ultimately, this study invites a closer examination of the comprehensive health status of patients when making revascularization decisions, fostering a more personalized approach in treating coronary artery disease.

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Elio Martín Gutiérrez

Ventricular Dysfunction, Viability, and Revascularization: The Never-Ending Story

This literature review addresses the role of viability studies in the indication for revascularization and the prognosis of patients with ischemic dilated cardiomyopathy, proposing a new decision algorithm for managing this clinical scenario.

Ischemic heart disease affects 1.7% of the global population and is the leading cause of death in many national statistics across genders, accounting for 9 million deaths annually worldwide. Among its diverse presentations, we focus here on ischemic dilated cardiomyopathy. This condition entails a reduction in the left ventricular ejection fraction (EF) alongside a process of myocardial remodeling that underlies ventricular dysfunction, predisposition to ventricular arrhythmias, and functional mitral valve impairment.

Ventricular remodeling has been described as an ongoing histological phenomenon occurring asynchronously across various myocardial territories. This process, underpinned by ischemia as an imbalance between metabolic demands of viable myocardium and the oxygen and nutrient supply from coronary circulation, leads to degenerative changes. Myocardial oxygen extraction from coronary blood flow is nearly maximal, so the primary means of adjusting supply to meet stress-related demands is through increased coronary blood flow, largely mediated by epicardial vessel vasodilation (nitric oxide-mediated) and precapillary coronary sphincter dilation. When these compensatory mechanisms are insufficient, ischemia occurs. Although microvascular pathology coexists with atherosclerotic disease and endothelial dysfunction, significant epicardial vessel lesions primarily drive the resistance to blood flow and decrease perfusion to specific myocardial territories.

Ischemia's effects manifest both chronically and as abrupt events known as acute coronary syndromes. Acute ischemia is well-known for its ECG sequence of ischemia-injury-necrosis, resulting in myocardial damage over a short period. Necrotic zones are replaced with electrically and mechanically dysfunctional fibrous tissue. Chronic ischemia leads to a gradual, microscopic process of sarcomere unit loss, similarly replaced by fibrous tissue. However, an intermediate, potentially recoverable state also exists, comprising stunned and hibernating myocardium. Stunned myocardium often occurs in the surrounding “penumbral” area around infarcted zones—a term borrowed from stroke terminology—where necrosis may extend unless revascularization, typically through primary angioplasty of the culprit lesion, is achieved. Once necrosis is contained, a surrounding stunned area may remain, potentially recoverable over time with restored circulation from the tributary vessel or collateral supply from adjacent territories. It is worth noting that coronary circulation is terminal, offering little cross-supply between territories upon acute occlusion. However, collateral circulation often develops when ischemic episodes evolve gradually.

Chronic presentation of potentially recoverable myocardium relates to hibernation, a cellular metabolic adaptation reducing contractile activity to balance requirements with a blood supply sufficient only to maintain viability. In the context of these simultaneous phenomena, the feedback effect of functional mitral regurgitation and volume overload, which increase ventricular diameters, must also be integrated. Neurohormonal responses, such as sympathetic tone increase and upregulation of beta-receptor expression and the renin-angiotensin-aldosterone axis, aim for short-term hemodynamic compensation but contribute to further myocardial degeneration over time. Indeed, the so-called “eccentric hypertrophy” of the left ventricle adapts to reduced EF, maintaining the same volume per minute through tachycardia and ejection from an enlarged ventricular cavity, despite each beat’s ejected percentage being lower than in a

functionally normal heart. This enlarged heart, with increased blood volume, elevates ventricular pressures during diastolic filling (end-diastole), which may compromise myocardial perfusion and aggravate ventricular dysfunction and dilation. Tension forces (tenting) on the mitral valve during ventricular contraction may exacerbate mitral regurgitation. This process of hemodynamic deterioration continues in a steady decline, even without acute decompensation or ischemic events, which would only worsen the situation further. Mention should be made of the role of natriuretic peptides, which have long-term beneficial effects and represent therapeutic targets, such as sacubitril and SGLT-2 inhibitors, two major protagonists in modern pharmacotherapy.

Viability assessment has evolved through the proposal of four complementary studies, each providing unique perspectives on the same phenomenon; likely, a multimodal approach offers a closer approximation than any single test alone. Dobutamine stress echocardiography assesses contractile reserve, identifying viable zones (thick and contractile), non-viable zones (thin akinetic scars), and, to some extent, potentially recoverable zones (thick, hypocontractile or akinetic). Additionally, it can induce ischemia to complete the functional analysis. Another ischemia-inducing technique is PET, assessing myocardial metabolic function. However, discrepancies arise, as metabolic activity may suggest viability but not necessarily contractile improvement with dobutamine testing. The remaining two studies do not induce ischemia but instead provide better tissue resolution. SPECT evaluates cellular membrane integrity, disrupted in fibrotic zones, while MRI, the gold standard for ventricular function assessment, is especially valuable with gadolinium, enhancing myocardial perfusion and highlighting fibrotic, non-viable areas. Discrepancies can occur in potentially recoverable zones, where the crux of ventricular dysfunction-viability-revascularization resides.

Within this sea of ideas, various studies—discussed below—have shaped the classical paradigm in this patient subset. When viable myocardium is present, indicated by 4 or more ventricular segments (of 17), revascularization plus optimized medical therapy improves left ventricular function, prevents acute events (heart failure decompensation and ischemia), and enhances patient functional capacity and survival.

COMMENTARY:

Several observational studies have focused on myocardial viability's role as a guide in therapeutic strategies, especially regarding coronary revascularization. Although outcomes varied, data aggregation in some meta-analyses indicated that viable myocardium correlates with a nearly 80% reduction in annual mortality post-revascularization. However, these studies often introduced biases due to retrospective design, protocol heterogeneity, and selective revascularization in patients with better viability. Confounding factors were not always adjusted for, and treatment options at the time of these studies were more limited than today.

Clinical trials began in 2000 and have continued into the current decade. The PARR-2 trial (2000–2004) enrolled 430 patients with EF <35%, assessing viability through PET. The HEART study (2002–2004) aimed for 800 patients but only enrolled 138 before premature termination, all with EF <35% and varied viability protocols. Both compared surgical revascularization with optimal medical therapy, showing no survival or major cardiac event benefits for revascularization guided by viability assessment.

The STICH trial (2002–2007) included 1212 patients with EF <35% and provided 10-year follow-up data. Revascularization reduced mortality compared to optimal medical therapy (58.9% vs. 66.1%; $p = 0.02$). This trial generated numerous sub-analyses, including one evaluating viability's role in treatment allocation among 601 patients who underwent SPECT or dobutamine stress echocardiography, with no significant interaction observed.

The trial coined the “4 of 17 segments” criterion for sufficient viability, which applied to nearly all patients analyzed. Additional STICH post-hoc analyses offered varying conclusions:

Patients with and without inducible ischemia on dobutamine stress echocardiography showed no survival differences at 5 and 10 years. Similarly, ischemia presence or extent did not affect cardiac events with surgical revascularization versus conservative management. EF improvement at 4 years was associated with viable myocardium, achievable with medical therapy rather than surgical revascularization. Increased remodeling, with worse EF and larger ventricular diameters, did not correlate with more frequent infarcts, though clinically, tolerance was lower in such cases due to reduced functional reserve. Revascularization reduced fatal infarcts and sudden death.

Following the STICH study’s initial impact (favoring surgical revascularization but not viability studies), new questions arose due to poorly designed post-hoc interpretations. These studies had limited statistical power, with inconsistent viability thresholds and imaging protocols. New pharmacologic therapies eventually rendered these studies obsolete until the Revived-BICS2 study (2013–2020). This trial randomized 700 patients with EF <35% to percutaneous revascularization versus optimal medical therapy, using modern agents. Viability assessment used dobutamine stress echocardiography or MRI, again requiring >4 viable segments for revascularization. However, with a median follow-up of 41 months, interventionism showed no survival benefit over medical therapy, nor did viability analysis significantly interact with treatment choice.

Thus, the authors question the classic paradigm, suggesting a new approach where viable territories and revascularization feasibility of tributary vessels must align. Only then might revascularization yield benefits for left ventricular function, cardiac events, and survival. However, this assertion remains speculative, as no study to date supports it. A new STICH study using current medical therapy would be invaluable, yet even the Revived-BICS2 study provides no interventional support. We argue that this view oversimplifies surgical revascularization and underestimates the potential for myocardial recovery previously discussed. Surgical revascularization promotes collateral formation and offers the best option for suitable patients, particularly those needing additional procedures (mitral valve repair/replacement) and/or with diabetes. Indeed, this new paradigm seems based on two flawed assumptions:

The Revived-BICS2 study focused on interventionism, where vessel viability mismatch may occur, as closed vessels might prevent complete revascularization. However, this limitation does not apply to coronary bypass surgery. The SYNTAX study established the concept of complete revascularization, showing that clinical benefit requires comprehensive revascularization. The ISCHEMIA trial, previously discussed in the blog, had inappropriate conclusions extrapolating medical versus interventional results to all revascularization, disregarding surgery’s unique advantages, which were underrepresented in the invasive cohort.

Ultimately, we still lack clarity on viability studies’ role and surgical revascularization’s advantage over optimal medical therapy. Until new evidence emerges, a win-win strategy—complete revascularization plus advanced medical therapy—appears to offer the best prognosis for these patients.

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Elio Martín Gutiérrez

Optimal Therapeutic Management of Patients with Stable Coronary Disease: Success Lies Within Our Reach

Summary of American societies' clinical guidelines for the clinical and therapeutic management of patients with stable coronary disease.

American societies associated with the clinical and therapeutic management of ischemic heart disease (American Heart Association [AHA], American College of Cardiology [ACC], American College of Clinical Pharmacy [ACCP], American Society for Preventive Cardiology [ASPC], National Lipid Association [NLA], and Preventive Cardiovascular Nurses Association [PCNA]) have released an updated version of the previous clinical guidelines from 2012 and 2014. Interestingly, earlier versions included endorsements from the Society of Thoracic Surgeons (STS) and the Society for Cardiovascular Angiography and Interventions (SCAI). However, in the 2023 edition, representatives of invasive therapies are not directly involved, with the SCAI merely endorsing the guidelines without mention of surgical society support.

These guidelines, developed by these societies, present a distinctly clinical focus in an extensive document spanning 111 pages, addressing various aspects such as epidemiology, early detection, diagnosis, lifestyle modifications, pharmacologic and non-pharmacologic treatments. Particularly, the latter covers patient assignment to interventional or surgical therapy, a topic that has generated considerable discussion on social networks (and likely contributed to the absence of STS endorsement). Although commentaries in cardiothoracic journals have yet to appear, given the recent publication date, such discussions are expected imminently. Nonetheless, this extensive work provides numerous recommendations and insights applicable to our patients. It is within our control to either disengage from or actively participate as integral members of the care team managing this condition. Personally, I believe that the latter path affirms our role as surgeons, that is, physicians who operate—not merely technicians performing coronary bypasses.

COMMENTARY:

As previously mentioned, the document is comprehensive, but we will attempt to summarize the most relevant recommendations that can be directly applied to our surgical practice:

Epidemiology: In a globalized world, coronary disease prevalence exhibits notable regional differences, likely due to variations in dietary habits, lifestyle factors (such as smoking), demographics, and healthcare access. In descending order of prevalence, the regions affected include: the Maghreb, the Middle East; Russia and its neighboring states, Mongolia, and the Indian subcontinent; China, Indonesia, and Central America; the rest of Africa, South America, and Oceania, with the lowest prevalence found in most of Europe, Japan, and North America.

Diagnosis and Risk Stratification: Various recommendations are provided regarding additional studies to be performed when there is a change in symptom profile despite maximum medical treatment. However, our role in determining diagnostic testing is limited in this context. More importantly, a list of clinical characteristics and complementary findings that negatively impact prognosis is available. This information can guide decision-making in patient management. Key factors include demographic aspects (e.g., age, male sex, limited social support, and lower socioeconomic status); comorbidities (e.g., obesity, previous myocardial infarction or revascularization, heart failure, atrial fibrillation or flutter, diabetes mellitus, dyslipidemia, chronic kidney disease,

active smoking, peripheral artery disease, depressive disorders, and poor medication adherence); cardiologic test results (e.g., inability to perform exercise testing, reduced functional capacity or left ventricular deterioration during stress testing, pharmacologically induced angina, ventricular hypertrophy or left bundle branch block on ECG, reduced ejection fraction or ventricular hypertrophy on echocardiography, high coronary calcium levels on cardiac CT angiography, poor ventricular function, particularly with hypertrophy or scars on MRI); and analytical findings (e.g., persistently elevated troponin and/or natriuretic peptide levels).

Therapeutic Management:

As mentioned earlier, optimal medical therapy is essential in managing these patients. The lack of symptom control or the occurrence of acute events often leads to additional studies aimed at recommending revascularization procedures, such as coronary artery bypass grafting (CABG). Surgery presents a valuable opportunity to update pharmacologic treatment and promote lifestyle changes that can improve patient outcomes. It is in our hands to be one of the initial links to catalyze this clinical change.

Throughout the clinical course, adherence to therapeutic prescriptions should be emphasized (class I).

In therapeutic decision-making, the guidelines highlight two aspects that steer our practice away from medical paternalism and the restrictions inherent in specialty silos:

1. Team-Based Care within a continuum that extends beyond cardiologists and surgeons. This includes the involvement of nurses, rehabilitation specialists, physiotherapists, pharmacists, dietitians, social workers, primary care physicians, and occupational health physicians (class I). This collaborative team aims to maximize patient understanding of disease progression, symptom awareness, adherence to therapeutic prescriptions and healthy lifestyle choices, self-care, and reintegration into an active life (class I).

2. Shared Decision-Making with Patients: This includes exploring treatment options, assessing associated risks and benefits, understanding patient preferences and attitudes toward each option, assessing cardiovascular risk and the impact on life expectancy and quality, and evaluating the symptom burden and current quality of life (class I). We must take responsibility—alongside cardiologists—for the information provided to the patient and the decisions made with them.

Dietary Aspects and Nutritional Supplements: We should recommend a diet rich in vegetables, fruits, legumes, whole grains, nuts, and lean protein (class I). Fats should be minimized, particularly saturated fats (<6% of total caloric intake), which should be replaced with monounsaturated and polyunsaturated fats (class 2a). Sodium intake should be limited to <1.5 g per day (class 2a). Highly processed foods, refined sugars, and sugary drinks should be minimized (class 2a), and trans fats should be avoided entirely (class 3). Omega-3 fatty acid supplements, as well as vitamins C, D, and F, beta-carotene, and calcium, have not shown a proven benefit and are therefore not recommended (class 3).

Mental Health: Mental health considerations must be actively addressed (class 2a) to identify the need for pharmacologic or non-pharmacologic support. Adequate patient information and education help reduce stress, improve self-management, and prevent complications. In terms of smoking cessation, repeated encouragement to quit smoking

should be given at each patient evaluation, with both pharmacologic and non-pharmacologic options offered (class 1). For pharmacologic support, varenicline may be preferable to bupropion (class 2b), and the replacement of cigarettes with electronic alternatives or similar products is not recommended as a smoking cessation strategy, as they pose similar risks. Regarding alcohol consumption, it is advised to systematically assess alcohol intake during anamnesis and recommend abstinence (class 1); if the patient already consumes alcohol, it should be limited to one serving for women and two for men of wine or beer (class 2a). No form of alcohol consumption, including wine, should be recommended to reduce cardiovascular risk (class 3). Finally, regarding sexual activity, it should be adjusted to the patient's exercise capacity both pre- and postoperatively (class 2a). In patients enrolled in cardiac rehabilitation programs involving regular exercise, sexual activity is recommended as a measure to reduce cardiovascular risk (class 2a). The use of phosphodiesterase type 5 inhibitors should be avoided in patients treated with nitrates due to the risk of severe hypotension (class 3).

Physical Exercise, Rehabilitation, and Vaccination: All patients with stable clinical conditions, whether or not they have undergone previous revascularization, should be encouraged to participate in cardiac rehabilitation programs and to establish a routine of physical activity (class I). This includes 150 minutes per week of moderate-intensity aerobic activity or 75 minutes per week of high-intensity aerobic activity. For patients without contraindications, muscle-strengthening exercises (low load, high repetitions) twice a week are also recommended. These activities are preferable to merely incorporating more active lifestyle habits, such as walking for transportation or reducing sedentary behavior (class 2a). Routine vaccination against influenza (class I), SARS-CoV-2 (class I), and pneumococcus (class 2a) is recommended.

Pharmacologic Treatment: The guidelines provide recommendations for the various pharmacologic groups in the therapeutic spectrum of ischemic heart disease:

- Antiplatelet Therapy: Recommendations suggest a less aggressive approach to antiplatelet therapy, including shortening the duration of dual antiplatelet therapy even in cases with drug-eluting stents (a maximum of six months, class I). For patients requiring concomitant oral anticoagulation, this dual therapy is limited to one month, after which a single antiplatelet agent, preferably clopidogrel, should continue (class I). Notably, in stable cases, once one year has passed since the last acute event, adding a second antiplatelet agent does not prevent major ischemic events and may lead to hemorrhagic complications (class 3). Regarding coronary surgery, dual antiplatelet therapy for 3–6 months is recognized as class 2b to reduce the incidence of saphenous vein graft thrombosis.

- Beta-Blockers: Their indication has been narrowed to patients with left ventricular dysfunction (<40%) to improve survival (class I) and for one year following a myocardial infarction (class I). Outside these indications, they offer no clinical benefit (class 2b). Recommended agents include metoprolol, atenolol, and carvedilol, with other beta-blockers less favored (class I).

- Renin-Angiotensin-Aldosterone System Inhibitors (RAASi): ACE inhibitors or ARBs are recommended for patients with hypertension, diabetes, chronic kidney disease, and/or left ventricular dysfunction (<40%) (class I). Outside these situations, they provide no clinical benefit (class 2b).

- Lipid-Lowering Agents: Statins remain the cornerstone of lipid management (class I), with the goal of reducing LDL levels by at least 50%.

The highest tolerated dose should be used, and for more aggressive LDL targets (<70 mg/dL), ezetimibe is recommended as an adjunct therapy (class 2a). In cases where these targets are not met, particularly in familial hypercholesterolemia, PCSK9 inhibitors are considered (class 2a/2b). New agents like bempedoic acid and inclisiran lack clear recommendations (class 2b), and niacin, fibrates, or omega-3 supplements are not advised alongside statins. The most potent agents are atorvastatin and rosuvastatin, followed by simvastatin, lovastatin, and pitavastatin; all are lipophilic with dose-dependent effects, as well as corresponding tolerability and side effect profiles. The hydrophilic statins pravastatin and rosuvastatin, while less potent, are generally better tolerated.

- SGLT2 Inhibitors (-gliflozins) and GLP-1 Receptor Agonists (-glutides): These are new additions to heart failure pharmacotherapy, now integral to ischemic heart disease management. Both are recommended for diabetic patients (class I). In patients with left ventricular dysfunction (<40%), SGLT2 inhibitors are indicated even in the absence of diabetes (class I).

- Hormone Replacement Therapy in Postmenopausal Women with Coronary Disease is not recommended due to increased thromboembolic risk and lack of clinical benefit (class 3).

Revascularization Therapy: This is the most controversial aspect. The recommendations adhere to the 2021 revascularization guidelines from American societies, with a simplified approach to coronary anatomy indications and a focus on the SYNTAX score, where only a score of >33 remains a decisive point. Key indications are summarized into three categories:

1. Intermediate-Low Surgical Risk Non-Diabetic Patients: Surgery is class I recommended for left main coronary artery disease. A notable point is that CABG remains superior for SYNTAX scores >33 (class 2a), though intermediate and low scores are not explicitly addressed.

2. High Surgical Risk Patients: Percutaneous intervention is class 2a recommended to improve symptoms and outcomes in patients deemed unsuitable for surgery.

3. Diabetic Patients: Revascularization for multivessel disease is a class I indication. For left main coronary disease, percutaneous intervention is class 2b recommended for SYNTAX scores <33, while intermediate and low scores are not mentioned.

These guidelines provide an update on optimal therapeutic management of patients with stable ischemic heart disease. Their application is especially relevant in the postoperative setting, following revascularization surgery, as they allow for the appropriate prescription of both medications and lifestyle changes to enhance patient survival and quality of life from the time of hospital discharge.

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Elio Martín Gutiérrez

Coronary Disease Revascularization in Stable Patients: Repeating Past Mistakes

Position Statement and Commentary by STS and AATS on the 2023 ACC/AHA Chronic Coronary Syndrome Revascularization Guidelines.

The human tendency to repeat mistakes is again evident in the latest chronic coronary disease revascularization guidelines, with the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) study at the core of the issue.

In contrast to the seemingly settled European perspective on left main coronary artery (LMCA) revascularization guidelines, previously discussed on this blog, the American counterpart differs markedly. Representatives from STS and AATS issued a position document critiquing the missed opportunity to correct errors from the 2021 ACC/AHA/SCAI revascularization guidelines, which drew widespread disapproval from surgical societies globally. Key areas of critique in the 2021 guidelines included:

- Downgrading the indication for surgery in multivessel disease with moderate-to-severe left ventricular dysfunction from Class I to IIa.

- Downgrading the indication for surgery in multivessel disease with preserved left ventricular function from Class I to IIb.

These conclusions led to the resignation of the sole surgical representative from the guidelines committee, followed by the withdrawal of two surgeons from the 2023 committee after extensive attempts to amend the inaccuracies.

Beyond the ISCHEMIA study, data on surgical revascularization compared to medical treatment are limited, although there are ample studies on percutaneous myocardial revascularization vs. medical therapy. Logically, where surgery outperforms interventional procedures in cases of moderate surgical risk, it should also do so against medical therapy. However, misinterpretation of the ISCHEMIA methodology has led to conclusions that defy logic.

In ISCHEMIA, patients were randomized to either initial medical treatment or revascularization strategy, with angiographic evaluation post-randomization determining the invasive approach. Thus, conclusions from medical vs. surgical comparisons remain observational due to inherent selection bias—patients with more severe disease were likelier to receive surgery, while those randomized to medical treatment typically had less extensive disease, thereby skewing outcomes.

As with many current trials, the ISCHEMIA population, highly selected, does not reflect the typical surgical cohort. Diabetic prevalence was low, and peripheral/cerebrovascular disease rates were notably lower than in the STS registry. LMCA disease was underrepresented at just over a third, compared to nearly half in surgical registries.

Moreover, ISCHEMIA's high crossover rate, with 20% of patients initially managed conservatively crossing to revascularization within three years due to poor symptom control or acute events, underscores the limitations of medical therapy alone. While advances in non-invasive diagnostics, such as coronary CTA, allow for better management without immediate revascularization, the ISCHEMIA study's findings on the initial conservative approach have not been adequately incorporated into the 2023 guidelines. The downgraded revascularization indications from 2021 remain, potentially jeopardizing some patients by delaying prognostically beneficial revascularization.

The broader implications of ISCHEMIA extend beyond its direct findings. Several meta-analyses supporting the 2023 recommendations incorporate this study and suffer from substantial errors. For instance, a major meta-analysis by Bangalore et al. included only 16% of patients undergoing surgical revascularization, with half of the trials omitting surgery as an invasive strategy, thereby leading to erroneous extrapolations in the guidelines. Additionally, only a minority had coronary anatomy indicating surgery, undermining the rationale behind the downgraded recommendations.

The authors argue that the publication of the 2023 guidelines was another missed opportunity to rectify the 2021 errors, further solidifying the STS and AATS opposition to this consensus document.

COMMENTARY:

While regrettable, such documents remain essential. Surgical groups once again demonstrate critical thinking, transparency, scientific integrity, and unity. STS and AATS members joined guideline committees, presented well-reasoned arguments, and ultimately, faced with systematic dismissal, opposed principles that contravene both common sense and good practice. Unfortunately, patients bear the brunt of this conflict, fostering tension among societies and impeding clinical fluidity, which can lead to biased, evidence-deficient decision-making in patient management. This may result in unnecessary risks, delayed elective revascularization, and avoidable acute events, worsening outcomes. Nonetheless, the authors emphasize that consensus is still achievable by amending the guidelines. Meanwhile, across the Atlantic, the recent EACTS/ESC consensus remains a benchmark.

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José Manuel Martínez Comendador

Current Management of Post-Infarction VSD: An Established Paradigm Shift?

This article examines the findings from a survey conducted across 39 European centers regarding current clinical practices in the management of post-acute myocardial infarction (AMI) ventricular septal defect (VSD).

The incidence of VSD following AMI has decreased from 2% to around 0.2% due to myocardial revascularization strategies, including thrombolysis and percutaneous coronary intervention (PCI). Without surgical intervention, the outcome remains fatal, with in-hospital mortality ranging from 20 to 65%, showing limited improvement over the past two decades.

Given its high mortality and low incidence, the accumulated evidence on this condition is sparse, mainly limited to small registries and single-center experiences. These works underpin current, albeit weak and controversial, clinical recommendations. Despite the recent CAUTION study (Mechanical Complications of Acute Myocardial Infarction: An International Multicenter Cohort), which represents the most extensive analysis to date with a significant patient sample and has enriched our understanding of VSD surgical outcomes, it has yet to provide the clarity required to establish standardized clinical protocols. Nor has it defined the current role of pre- or postoperative mechanical circulatory support (MCS) devices, such as extracorporeal membrane oxygenation (ECMO) and percutaneous closure devices, which are not yet included in clinical guidelines.

The present study aimed to investigate, through a survey of multiple European centers, the actual practice of surgeons in addressing this pathology. To collect information on all aspects of VSD treatment, a digital questionnaire comprising 38 questions was completed in 39 centers across eight European countries from April to October 2022. Most centers handle between 1 and 5 VSD cases per year, with surgery remaining the preferred treatment over percutaneous closure (71.8% vs. 28.2%). Delayed surgical repair is the favored strategy (87.2%), with the patient's hemodynamic status influencing the approach in most centers. Although most centers seek to stabilize patients and delay surgery, even in cases of cardiogenic shock, 33.3% do not perform coronary angiography in unstable patients, and a considerable proportion does not pursue revascularization. When performed, revascularization timing and type vary significantly across hospitals. Most centers use MCS, particularly veno-arterial ECMO, primarily as a preoperative measure to stabilize patients and defer surgical repair.

The authors conclude that, in European clinical practice, delayed surgery is the preferred strategy for managing VSD, irrespective of hemodynamic conditions. Moreover, ECMO is emerging as the most widely adopted MCS as a bridge to surgery.

COMMENTARY:

The results of this survey conducted in European centers provide an accurate view of current clinical practices in the management of VSD in Europe, reflecting reality in Spain, as half of the surveyed centers were Spanish. A key takeaway is the significant shift in the management of this condition in recent years, characterized by a delayed surgical approach supported by some form of MCS, particularly veno-arterial ECMO (with or without intra-aortic balloon pump or Impella). ECMO, once considered an alternative and reserved for patients on the brink of multiorgan failure, has become an essential component in treating this complication, allowing for surgery with a prudent delay and in a more stable clinical condition.

Examining survey responses reveals that most centers prefer delayed rather than early treatment. For stable patients, 90% favor delayed intervention, with most opting for initial ECMO use, reserving it only when needed. In other words, in 90% of stable cases, ECMO is considered to enable delayed intervention (minimum of 5 days). For unstable patients, nearly 70% also prefer delayed surgery following stabilization with ECMO, while the remaining centers would consider emergent surgery with prior ECMO implantation. In summary, ECMO use is considered in nearly all cases, both stable and unstable, with delayed surgery representing over 90% for stable and approximately three-quarters for unstable patients.

This represents a drastic departure from the findings of the CAUTION study, which analyzed 475 patients across 26 centers over 20 years and serves as a benchmark in post-AMI VSD studies. In CAUTION, ECMO was employed as an adjunct in a minority of cases, even in the most recent years, with increased mortality associated with ECMO use, likely due to patients' poorer hemodynamic conditions. Furthermore, nearly half of the patients underwent urgent surgery in CAUTION, correlating with higher mortality compared to those treated with delayed surgery, generally reserved for more stable patients. In short, VSD management, from 2000 to 2021, was fundamentally different from the current approach.

Moreover, current clinical guidelines do not yet support the widespread preoperative use of ECMO observed in this survey. In cases of cardiogenic shock, guidelines recommend intra-aortic balloon pump with a class IIa indication, while ECMO and other MCS devices are not addressed. The accumulating evidence from recent studies demonstrates the central, beneficial role of MCS in stabilizing these patients to prevent clinical deterioration, bolstering surgeons' confidence in these devices. This justifies, at least partially, their use and calls for reconsidering and updating clinical guidelines.

Regarding the optimal timing for surgery, there is no consensus across guidelines. While American guidelines advocate immediate surgery for all VSD patients, European guidelines suggest postponing it in cases where patients respond to aggressive therapy. This discrepancy contributes to the confusion over the best strategy. The notion that delayed surgery results in better outcomes is not new and is based on years of experience, favoring stable patients who reach surgery after several days. Factors contributing to the improved prognosis of delayed cases include potential partial myocardial recovery after revascularization and the transformation of friable, necrotic tissue into firmer, fibrous tissue, allowing for a more secure and successful repair. Additionally, MCS device advancements and their reliability in this context have enabled patients who previously would not have reached delayed surgery to now arrive in better conditions. These advances have led to surgeons adopting MCS as a natural approach to treating this disease.

Conversely, the survey shows that only a minority of centers systematically employ post-surgical ECMO, despite most in-hospital deaths resulting from low cardiac output syndrome.

An emerging trend is the increasing acceptance of percutaneous closure, not only for inoperable patients but also as a first choice in cases where VSD closure is technically feasible. A recent British national registry demonstrated comparable outcomes to surgery in selected cases. However, overall evidence remains insufficient to draw definitive conclusions on this matter. According to this survey, approximately 30% of centers would consider percutaneous closure if technically feasible or if the patient is deemed inoperable. Notably, no information is available on whether percutaneous closure is actually accessible in these centers.

The formation of a shock treatment team is considered in less than 50% of centers, possibly due to the low annual case volume.

Interestingly, approximately one-third of centers do not perform coronary angiography unless the patient is hemodynamically stable, affecting revascularization opportunities. Additionally, revascularization methods, when pursued, vary widely, reflecting a lack of consensus in this area. The CAUTION study indicated that about one-third of patients underwent revascularization before surgery, correlating with higher mortality, possibly due to increased hemorrhagic risk. Additionally, only half of the patients received concomitant surgical revascularization, which showed no association with increased mortality, aligning with other studies.

The survey lacks questions on posterior VSD, associated with higher mortality according to the CAUTION study and various meta-analyses, due to its impact on right ventricular dysfunction and surgical complexity.

The primary limitation of this study is its retrospective nature, relying solely on the information reported by each center, which may not accurately reflect actual procedures. Nonetheless, the study realistically depicts the paradigm shift in post-AMI VSD management. Currently, Spanish cardiac surgeons favor preoperative ECMO stabilization and delayed surgery in almost all cases.

Future prospective studies are needed to enhance our understanding of optimal disease management. Given that we are often one step ahead of clinical guidelines, the adoption of advanced technologies could start to shift the course of this deadly complication.

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Section III:

Congenital heart disease

Bunty Ramchandani

Partial heart transplantation: a solution to valve growth challenges?

Review article discussing the necessity, clinical feasibility, and initial experiences with partial heart transplantation.

Heart valves represent the pinnacle of design and durability. They open and close approximately 70 times per minute, 100,000 times per day, and about 3 billion times during a lifetime. Given their extensive usage, it is remarkable how rarely they fail. Valvular disease affects approximately 75 million people worldwide, leading to around 280,000 valve replacements annually. The exceptional performance of these cardiac components lies in their ability to repair daily wear and tear, a quality that surpasses any human-designed biological prosthesis. Moreover, their capacity for growth alongside the individual prompts some centers to consider using living cardiac components as substitutes for prosthetic alternatives.

The lack of growth in prostheses and homografts poses a persistent challenge for most pediatric cardiac surgeons. Consequently, they often prioritize valve repair and re-repair, even at the cost of prolonged ischemia times. A suboptimal repair is frequently deemed preferable to valve replacement in pediatric patients. When repair is not feasible, various solutions exist, yet none are entirely satisfactory. Mechanical or biological prostheses, each with distinct advantages and disadvantages, are available. Homografts—either homovital (procured directly from untreated cadavers) or cryopreserved (stored at –135°C for logistical distribution reasons)—serve as structural components in surgery without preserving cellular viability. However, homografts lack growth capacity, necessitating multiple reoperations in pediatric patients to replace them with larger grafts. Furthermore, the implantation of homografts is not without risks. Neonatal or infant aortic valve surgery using homografts carries a mortality rate of 40%, escalating to 49% in truncal valve surgeries and followed by a yearly mortality rate of 15%. Costs are another concern, with a homograft priced around $25,000 in the United States.

Developing bioprostheses capable of growth is the ultimate goal in pediatric cardiac surgery. Technological limitations currently hinder the creation of living biological prostheses, as cellular growth and differentiation must be programmed. Efforts to achieve this milestone have occasionally resulted in major biomedical research scandals, such as the Paolo Macchiarini case involving artificial trachea transplants. Conversely, the Ross procedure, which autotransplants the pulmonary root, has demonstrated that such grafts grow with the patient. While the valve leaflets exhibit good durability, the primary challenge is long-term neo-root dilation due to the exposure of pulmonary tissue to systemic pressure. The Ross procedure has two major drawbacks: it sacrifices the right side of the heart, requiring multiple interventions to address outflow tract obstruction using prostheses or homografts, and it is a highly complex surgery with neonatal mortality exceeding 25%.

An alternative solution involves transplanting a heart that grows with the patient, despite the need for immunosuppressive treatment. This approach is also limited by organ scarcity in this age group, resulting in long waiting lists, as well as the added morbidity associated with immunosuppressive therapy. Although the mortality rate for transplantation is lower than that of the Ross procedure at less than 5%, it rises to approximately 35–50% at 20 years due to coronary allograft vasculopathy, ultimately leading to ventricular dysfunction.

The advantages and challenges of the Ross procedure and cardiac transplantation have given rise to the concept of partial heart transplantation. This technique seeks to combine the benefits of both approaches while minimizing their disadvantages. Partial heart transplantation, also referred to as a living homograft, retains the growth and repair properties of these tissues. Similar to the Ross procedure, these tissues are devascularized and re-implanted without compromising biological viability. However, only the aortic homograft is transplanted, avoiding the drawbacks associated with pulmonary valve involvement and providing a true systemic-pressure aortic root. Unlike conventional transplantation, partial heart transplants would require less stringent immunosuppression and would not experience coronary vasculopathy since only valves, not vascularized myocardium, are transplanted. If immunosuppression were discontinued, the transplanted valves would revert to functioning as standard homografts. Consequently, partial heart transplantation could mitigate some long-term complications of orthotopic heart transplantation, such as the 12% incidence of Epstein-Barr virus-related lymphoproliferative disease and 6% incidence of severe renal dysfunction caused by calcineurin inhibitors within 10 years.

The availability of donors for partial heart transplantation exceeds initial expectations. Any orthotopic cardiac transplant donor could also serve as a partial transplant donor. Moreover, approximately one-third of pediatric patients undergoing heart transplantation have dilated cardiomyopathy, where ventricular failure rather than valvular dysfunction is the issue. The hearts explanted from these patients could be utilized for partial transplants. Each donor heart could potentially benefit multiple recipients, amplifying the domino effect of such transplants. Nevertheless, implementing this technique requires complex logistics. Conducting several domino transplants simultaneously, as demonstrated by hospitals such as Morgan Stanley and Duke Children's, involves coordinating multiple teams across different hospitals, often necessitating air transport.

Significant questions remain regarding partial heart transplantation. Regulatory aspects must address whether these materials should be classified as biological products or organs. Coding systems for clinical and accounting purposes need to be established. Immunosuppressive regimens and acceptable ischemia times for these components must be defined. Ideal candidates for this type of surgery need to be identified. Additionally, the feasibility of using this technique for atrioventricular valve lesions and managing subvalvular apparatus in such cases remains to be explored.

COMMENTARY:

Dr. Rajab's review article eloquently argues the need to incorporate partial heart transplantation into our therapeutic arsenal. By tracing the necessity for these tissues from experimental surgeries in the laboratory to initial clinical experiences, it highlights a field ripe for exploration. With growing heart transplant waitlists, innovative strategies to salvage organs or organ parts are imperative. Fortunately, Spain's centralized National Transplant Organization (ONT) has vast experience coordinating simultaneous transplants. Integrating partial heart transplantation into ONT's operations seems logistically feasible.

Who knows? In the future, xenotransplant-derived components might serve similar purposes. Until then, maximizing organ utilization, even through unconventional maneuvers like domino transplants—orthotopic transplantation in a dilated cardiomyopathy patient and using the dilated heart's valves for another recipient—is essential.

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Diana Salas Mera

The size matters: assessment of different methods for evaluating donor-recipient mismatch and their prognostic significance in pediatric heart transplantation

This retrospective study, based on data from the international Pediatric Heart Transplant Society registry, evaluates donor-recipient size mismatch using different parameters and its impact on 1- and 5-year graft survival and post-transplant morbidity.

The adequacy of graft size is one of the most critical factors when considering a cardiac offer, with weight being the most commonly used metric for donor-recipient adjustment. However, studies assessing the impact of weight mismatch on survival have yielded inconsistent results, likely due to the erroneous assumption of a linear correlation with heart size, neglecting other factors. While virtual adjustment using imaging would be ideal, it is rarely feasible in clinical practice due to limited donor imaging availability and the time constraints for accepting offers. To address these limitations, predictive models based on cardiac MRI and/or CT imaging of healthy subjects have been developed in recent years. These models estimate heart size in terms of mass (Predicted Heart Mass, PHM) or volume (Total Cardiac Volume, TCV), incorporating variables such as sex, age, weight, and height. This commentary reviews an article comparing various methods for assessing donor-recipient size mismatch, including these predictive models, in pediatric populations.

This retrospective study uses data from the Pediatric Heart Transplant Society international registry, encompassing over 50 pediatric transplant centers. It includes all pediatric heart transplants (recipient age <18 years) performed between January 1993 and December 2021. Donor and recipient variables were collected to assess mismatch based on weight, height, BMI, body surface area (BSA), PHM, and TCV; the latter two parameters were calculated using published formulas. Cox regression analysis was employed to determine whether mismatch, calculated by each metric, was an independent risk factor for graft loss (death/retransplantation) at 1 and 5 years, adjusting for other risk factors identified in the literature. For significant variables, post-transplant morbidity was assessed by analyzing freedom from rejection and hemodynamically significant rejection at 1 year and graft vasculopathy at 1 and 5 years using the Kaplan-Meier method.

A total of 7,715 donor-recipient pairs were analyzed. Adequate matching (donor/recipient ratio between –20% and +20%) was achieved in 36% of pairs based on weight, 39% on PHM, 50% on BSA, 57% on BMI, 71% on height, and 93% on TCV. Violin plots showed that TCV exhibited greater symmetry and fewer outliers compared to other metrics. Among all mismatch metrics, only height and TCV were independent predictors of graft survival in the adjusted analysis. Both undersized and oversized donors by height were associated with increased graft loss at 1 and 5 years, with a greater effect observed in undersized donors. For TCV, minimally undersized donors (donor/recipient ratio up to –20%) were associated with reduced graft loss, whereas oversized donors up to 25% had no impact on survival. Post-transplant morbidity analysis revealed that recipients of moderately undersized donors by height (donor/recipient ratio <–30%) experienced higher rates of early rejection ($p < .0001$), with no significant differences observed for hemodynamically significant rejection or graft vasculopathy. No significant differences were found in post-transplant morbidity based on TCV mismatch for any evaluated events.

COMMENTARY:

The current shortage of organs for transplantation, especially pronounced in the pediatric population, drives the need for strategies to maximize donor utilization. Identifying a parameter for assessing donor-recipient mismatch that has prognostic implications and avoids discarding potentially suitable hearts based solely on weight mismatch is particularly appealing. This is the main interest of the reviewed article, which is the first to compare different metrics, including TCV and PHM, in children.

A notable finding of the study is the variability in adequate donor-recipient matching percentages depending on the method used, with marked differences such as 93% for TCV versus only 36% for weight. This supports growing evidence that weight, as an isolated measure, likely overestimates mismatch.

Since height and TCV were the only metrics impacting survival, the authors concluded that TCV appears to be the best donor-recipient adjustment measure, citing its symmetrical distribution in violin plots and its direct representation of heart size. However, the model used to calculate TCV was developed by Plasencia et al. in a single-center study of 90 patients, warranting caution until the model or alternatives are validated in larger populations.

Interestingly, PHM mismatch did not independently predict graft loss, as shown in adult studies. This may be due, as the authors acknowledge, to the pediatric PHM model being developed with only 50 subjects (compared to 5,098 for left ventricular mass and 4,204 for right ventricular mass in adult models), making it less robust. Another limitation is the lack of adjusted analysis in post-transplant morbidity evaluation, which showed higher rejection rates in moderately undersized donors by height, likely influenced by other factors such as less frequent induction immunosuppression in this group. Additionally, morbidity outcomes chosen for the study were not primarily related to heart size, whereas primary graft dysfunction—known to correlate with undersized donors in adults—was not analyzed.

Overall, this article underscores the need for a better parameter than weight to assess donor-recipient mismatch in pediatric heart transplantation, to standardize practices across centers and maximize organ utilization. Future directions may involve more direct measures of heart size, either by improving access to donor imaging and streamlining virtual adjustment processes or by refining predictive models for TCV or PHM. In the interim, based on the present study's findings, height could at least be considered as an additional mismatch measure, especially avoiding undersized donors due to their greater impact on survival.

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Blanca Torres Maestro

Ventricular assist devices as a bridge to transplantation: challenging the established order

This retrospective single-center study evaluates the impact of pre-transplant ventricular assist device (VAD) support on pediatric patients and/or those with congenital heart disease undergoing heart transplantation, compared to patients who did not require such support before transplantation.

We are currently witnessing a period in which, similar to the adult population, the number of pediatric patients requiring heart transplantation is increasing, while the number of donors remains limited. This has made the development of long-term assist devices imperative, primarily aimed at serving as a "bridge to transplantation."

The article under discussion today addresses the impact on the post-transplant period of using long-term ventricular assist devices as a bridge to transplantation in pediatric patients and/or those with congenital heart disease, compared to those who did not require such devices. Although this is a single-center study, it is quite comprehensive and provides encouraging data for this complex patient group.

The study includes a total of 181 pediatric and/or congenital heart disease patients who underwent 186 transplants over an 11-year period, from January 2011 to January 2022. Among these, 28.5% (53/186) had pre-transplant VAD support: 50 were paracorporeal (Berlin EXCOR®), and 3 were continuous-flow devices (HeartWare HVAD®). Specifically, biventricular assist devices were implanted in 53% of the patients (and in the majority of single-ventricle physiology cases). The authors clearly favor pulsatile-flow devices due to their more physiological performance and more intuitive management compared to continuous-flow devices. Furthermore, they highlight an institutional preference for biventricular over univentricular assist devices, especially in neonates and infants with biventricular physiology, owing to the difficulty in predicting subsequent right ventricular failure in patients supported solely with univentricular devices.

Patients with long-term VAD support were observed to be younger than those without it (4.8 years vs. 12.1 years; $p = .0001$), had undergone more cardiac surgeries (3 vs. 1.8; $p = .0003$), and were more likely to receive ABO-incompatible transplants (18.9% vs. 6.8%; $p = .028$).

In univariate analysis, the following factors were associated with decreased long-term survival: prior cardiac surgery (HR = 6; $p = .015$), single-ventricle physiology (HR = 2.4; $p = .038$), congenital vs. acquired heart disease (HR = 5.7; $p = .005$), and pre-transplant renal failure (HR = 3.4; $p = .003$). However, multivariate analysis, adjusting for these factors, did not reveal a clear impact of pre-transplant VAD support on long-term survival.

Kaplan-Meier survival curves also showed no significant differences in 5- and 10-year post-transplant survival between patients with and without pre-transplant VAD support.

The authors note a significant statistical limitation due to sample size but emphasize the importance of multicenter studies to confirm and support such promising results for this patient population.

COMMENTARY:

Traditionally, ECMO (Extra-Corporeal Membrane Oxygenation) has been the primary alternative in pediatric populations with refractory heart failure, including as a bridge to transplantation. However, in recent years, long-term ventricular assist devices (VADs) increasingly tailored to pediatric patients have largely displaced ECMO in this role. Moreover, technological advancements in these devices and their management have improved outcomes for more complex patients, such as younger children and those with congenital heart disease, who present unique challenges due to their weight, anatomy, and more complex pathophysiology.

Numerous studies have aimed to evaluate the impact of pre-transplant long-term VAD support on post-transplant outcomes and long-term survival compared to patients who did not require it. Clearly, the former represents a higher-risk group, often in poorer clinical condition and with more negative survival risk factors, some of which can be categorized as "modifiable risk factors" (renal dysfunction, respiratory insufficiency, hepatic failure, critical illness polyneuropathy, etc.). These modifiable risk factors can be effectively mitigated or even improved significantly with VAD support, allowing the patient's baseline condition to improve over time. VADs have enabled patients who would otherwise not survive on the waiting list to undergo transplantation, often in better condition than when initially listed.

This is likely one of the main reasons why there appear to be no clear differences in post-transplant survival between the two patient cohorts: VAD support allows patients to improve to the point where surgical risk at transplantation is comparable to that of those who did not require prior assistance.

Unlike other studies, such as the Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs) report, which indicated that pulsatile biventricular VADs were less frequently used and had worse outcomes compared to continuous-flow devices, our authors preferred the former for the reasons previously explained and achieved very promising results. Both the Pedimacs registry findings and our country's experience were analyzed in previous blog entries. This underscores that patient management strategies are not uniform, and institutional protocols vary—each potentially valid, as corroborated by these results.

These findings suggest that, with these data in hand, we should consider developing registries and multicenter studies to help standardize the management of these children. This will enable us to continue improving and challenging the natural history of many congenital heart diseases, ultimately shedding light on what would otherwise be a grim prognosis for these patients.

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María Luz Polo López

Pediatric ventricular assist in Spain: 15 years of experience

This study presents the Spanish experience with durable ventricular assist devices (VAD) in children from 2006 to 2020. The overall results are summarized, and risk factors for mortality in this pediatric population are analyzed.

This is a multicenter retrospective study conducted in the six Spanish hospitals performing pediatric heart transplants. Data were collected from patients under 18 years of age who underwent durable VAD implantation between 2006 and 2020.

Most patients were young children with a body surface area (BSA) below 0.7 m^2, accounting for 63% of the cohort. The predominant initial diagnoses were cardiomyopathy (63.6%, mostly dilated), congenital heart disease (24.6%), myocarditis (9.3%), and early cardiac failure post-heart transplantation (2.5%). Nearly half of the patients were in INTERMACS 2 pre-implantation; 90% required intravenous inotropic support, 72% were on mechanical ventilation, 32% had experienced cardiac arrest, 38% were on extracorporeal membrane oxygenation (ECMO), 28% had renal failure, and 16.5% exhibited hepatic dysfunction (bilirubin >34 µmol/L).

The primary indications for VAD implantation were bridge-to-transplantation (85.6%), bridge-to-decision (9.3%), and bridge-to-recovery (5.1%). Paracorporeal VADs were implanted in 118 children, with the majority being pulsatile-flow (Berlin Heart EXCOR®, 63.3%), followed by continuous-flow (Levitronix®, 30.5%), and a minority using both types (5.9%). Most devices were univentricular and left-sided (64.4%), with biventricular support in 33.9%. Right ventricular support was rarely employed. The median support duration was 30 days, during which 62% of children were weaned off mechanical ventilation.

Common complications included non-cerebral bleeding (39%), stroke (38%), and pump exchange due to device-related issues (34%). Complications were more frequent in continuous-flow devices compared to pulsatile-flow. Despite this, outcomes were favorable, with 70% of patients either transplanted, recovered, or remaining on support at the study's end. VAD explantation was primarily due to transplantation (62%), with a smaller percentage due to recovery (5%). Hospital discharge survival was achieved in 65% of cases, while in-hospital mortality was 29%, primarily due to multiorgan failure (42.5%) or stroke (27.5%).

Factors associated with higher in-hospital mortality included body weight <5 kg, congenital heart disease, pre-implantation bilirubin >34 µmol/L, and bridge-to-decision strategy. These factors were also inversely related to late survival. INTERMACS category and prior cardiac arrest were linked to reduced long-term survival. However, no significant increase in mortality was observed in children with pre-implantation renal failure or those requiring ECMO before VAD implantation.

In conclusion, VAD implantation in children allows 67% to reach transplantation or recovery. Pre-implantation factors associated with higher mortality were weight <5 kg, congenital heart disease diagnosis, cholestatic liver dysfunction, bridge-to-decision strategy, INTERMACS category, and prior cardiac arrest. Neither renal failure nor pre-implant ECMO use was linked to increased mortality.

COMMENTARY:

This report represents the first collective experience in Spain of medium- and long-term VAD implantation in the pediatric population. The primary indication for these devices in children has been as a bridge-to-transplantation. VAD implantation in children reduces waiting list mortality and increases the likelihood of reaching transplantation. Similar to adult populations, the use of VADs has steadily increased over time, with over 40% of transplanted children now receiving VAD support.

Advancements in anticoagulation protocols and perioperative hemostasis management, including the use of bivalirudin, bedside aggregometry in intensive care units, and meticulous surgical techniques, have reduced VAD-associated complications.

The Berlin Heart EXCOR®, a paracorporeal, pulsatile-flow VAD, supports patients across a range of body sizes, from neonates to adults. In pediatric cases, definitive VAD cannulas are occasionally connected to a centrifugal continuous-flow pump (Levitronix®) to stabilize postoperative inflammatory phases and optimize anticoagulation before transitioning to a Berlin Heart EXCOR® pump. Intracorporeal continuous-flow devices and total artificial hearts, commonly used in adults, are limited to larger children (BSA >0.7 m^2) and cannot be used in smaller children.

These Spanish outcomes compare favorably with European and American registries, particularly considering the higher prevalence of small children (BSA <0.7 m^2), critical pre-implantation conditions, and the predominance of congenital heart disease compared to cardiomyopathy in this cohort. Durable pediatric VADs provide time to achieve transplantation or recovery in 67% of cases. The main complications are bleeding and thrombosis due to the anticoagulation and antiplatelet therapies required by these devices.

Mortality risk factors in this study align with international data and include low body weight (<5 kg), congenital heart disease, unstable clinical conditions, hepatic dysfunction, and bridge-to-decision indication. However, renal failure and pre-implantation ECMO use were not associated with increased risk. These findings underscore the importance of optimizing the timing of VAD implantation to balance risks of premature exposure against the progression of end-organ dysfunction.

Judicious ECMO use for patient stabilization and organ recovery may enhance outcomes in bridge-to-decision cases. Identifying modifiable factors, such as timing and stabilization strategies, remains critical for improving pediatric VAD outcomes in Spain.

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Bunty Ramchandani

Current status of ventricular assist devices in the pediatric population.

Sixth annual report of the Pedimacs registry (2012–2021), evaluating 1,355 devices in 1,109 patients under 19 years of age

Ventricular assist devices (VADs) are a crucial therapeutic tool for managing patients with decompensated congestive heart failure. Unlike the adult population, experience in children is limited. However, this has not prevented a "boom" in their utilization over the past two decades. For instance, in 2005, only 10% of heart transplant recipients had a VAD prior to transplantation, whereas this figure is now approximately one-third.

The Pediatric Interagency Registry for Mechanical Support (Pedimacs), under the STS, has recently published its sixth annual report on VAD use in the pediatric population. This report includes data spanning nine years (2012–2021) covering 1,355 devices implanted in 1,109 patients (<19 years) across 42 U.S. hospitals. Key findings are as follows:

- Most common indications: cardiomyopathy (58%), congenital heart disease (26%), and myocarditis (9%).
- Most popular devices: implantable continuous-flow (40%), paracorporeal pulsatile (28%), and paracorporeal continuous-flow (27%).
- Device selection influenced by patient characteristics: Patients supported with paracorporeal continuous-flow VADs tended to be younger, had more complex congenital heart defects, and were in worse clinical condition.
- Outcomes at six months: >80% of patients were well, whether transplanted, recovered, or alive with a VAD. For the subgroup with implantable continuous-flow devices, this figure exceeded 90%.

The first two weeks post-implantation presented the highest risk for adverse events, primarily bleeding and neurological complications, which negatively impacted long-term survival.

COMMENTARY:

This report attempts to capture the current landscape of pediatric VAD use, highlighting the challenges of a heterogeneous pediatric population. The registry includes children with congenital heart defects (univentricular physiology accounts for two-thirds of congenital cases), biventricular physiology, primary cardiomyopathies, and acquired heart conditions. Primary diagnosis significantly influences baseline condition, age, type of device implanted, and, consequently, survival outcomes. Added to this is the variability in clinical management, such as timing of VAD indication, particularly in high-risk groups (e.g., single ventricles, cardiogenic shock, restrictive or hypertrophic cardiomyopathies).

When interpreting data from implantable continuous-flow VADs, it is essential to consider that most experience was with the HeartWare device, which was withdrawn by the FDA in 2021. The approval of HeartMate 3 for pediatric use is a recent milestone achieved in

December 2020. Positive outcomes associated with these devices are partly attributable to their use in older, less complex, and less critically ill children.

In conclusion, Pedimacs data cannot be entirely extrapolated to other contexts due to inherent biases in a voluntary registry and significant differences between healthcare systems in the U.S. and Spain. However, Pedimacs does illustrate the growing trend of VAD use in the pediatric population—a trend that is already being observed in our country.

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Bunty Ramchandani

Transposition of the great arteries with intact septum: the british experience

Survival outcomes, reintervention, and hospital resource utilization in transposition of the great arteries with intact septum in the United Kingdom

Transposition of the great arteries (TGA) occurs when there is a ventriculo-arterial discordance, leading to the origin of the aorta from the right ventricle and the pulmonary artery from the left ventricle. The prevalence of TGA is approximately 5 cases per 10,000 live births, accounting for 3% of all congenital heart diseases and 20% of cyanotic lesions. The dextro-looped form (d-TGA) describes the positioning of the right ventricle to the right of the left ventricle, with the aorta positioned anteriorly and to the right of the pulmonary artery. The term "dextro" refers to the looping of the ventricles during cardiac morphogenesis, specifying the spatial relation of the right ventricle to the left. It is distinct from levo-TGA (l-TGA), also known as congenitally corrected TGA, a rarer condition characterized by both atrioventricular and ventriculo-arterial discordance. Cyanosis in l-TGA is uncommon unless associated lesions are present.

In d-TGA, the systemic and pulmonary circulations are arranged in parallel, a condition incompatible with life unless blood mixing occurs between these circuits. This mixing can happen intracardially via a patent foramen ovale, atrial or ventricular septal defects, or extracardially through a patent ductus arteriosus or bronchopulmonary collateral vessels. Postnatal management aims to optimize this mixing, which is most efficient at the atrial level due to low-pressure bidirectional flows across the septum.

Despite significant advances in the management of TGA, many questions remain unanswered. What is the ideal timing for surgery? Who benefits most from balloon atrial septostomy (Rashkind procedure)? Post-discharge, what care do these patients require? What long-term issues may arise? How do neonatal decisions influence outcomes? Most studies comprise case series or single-center experiences with limited follow-up.

Today's study provides insights into the national experience of TGA with intact septum (TGA-IS) treated with arterial switch surgery in the United Kingdom from 2000 to 2017. The study explores survival, reintervention rates, and healthcare resource utilization using data from the mandatory National Congenital Heart Disease Audit, encompassing all centers treating these patients. Complex TGA cases, alternative procedures, or deaths before surgery were excluded.

A total of 1,772 patients were identified, with a median age at surgery of 9.5 days. Ten-year mortality and reintervention rates were 3.2% and 10.7%, respectively. The median length of hospital stay after surgery was 19 days. In the first year post-surgery, patients required 7 hospital days on average, decreasing to 1 day/year after the fifth year, primarily for outpatient visits. Neither the age at surgery nor the need for balloon atrial septostomy were associated with increased mortality or reintervention rates. However, low birth weight, circulatory support, renal failure requiring therapy, and associated comorbidities were significant risk factors for mortality and reintervention. Comparisons between patients undergoing septostomy and those proceeding directly to surgery revealed no statistically significant differences.

The authors concluded that while mortality and healthcare resource utilization for this condition were low, reintervention was frequent. Early surgery was advocated, with individualized decisions regarding atrial septostomy based on patient risk factors.

COMMENTARY:

In many parts of the world, such registries are voluntary, involving selected institutions whose results may not be generalizable. The comprehensiveness of this registry is enviable, encompassing over 1,700 TGA-IS patients. The British data demonstrate exceptional survival rates exceeding 97%, reflecting the reproducibility of arterial switch surgery across centers, comparable to leading congenital heart centers globally.

However, many questions posed at the outset remain unresolved. No cases involved surgery beyond three weeks of life, suggesting that late presentations in developed settings are rare. Operating in the first week of life does not appear to offer additional benefits, aligning with recent studies advocating early surgery. The role of atrial septostomy also remains unclear due to variability in pre-existing atrial septal communication and clinical practices across centers.

One limitation of this registry is the absence of coronary anatomy data. Complex coronary patterns, such as intramural coronaries or single ostium, significantly influence hospital mortality and future reinterventions. Similarly, the relationships of great vessels and commissural alignment, which affect right ventricular outflow tract obstruction and valvular function, are not documented.

As Dr. Barron notes in his editorial, reinterventions in TGA occur at different stages. In the first year, they are predominantly coronary-related. From the second to the fifth year, they involve pulmonary branches or right ventricular outflow obstruction. A third phase, requiring over 17 years of follow-up, involves neoaortic dilation, as the neoaorta, originally pulmonary tissue, endures systemic pressure.

In conclusion, TGA will remain a topic of discussion for decades. Like tetralogy of Fallot, we must address the sequelae of our predecessors' successes.

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Blanca Torres Maestro

David versus Goliath: how to tackle coronary anomalies in D-TGA

A retrospective observational study analyzing outcomes following arterial switch surgery with coronary translocation using the modified Yacoub pouch technique in 14 neonates with D-transposition of the great arteries (D-TGA) and anomalous coronary patterns (single coronary ostium and intramural course).

D-transposition of the great arteries (D-TGA) is among the most common cyanotic congenital heart defects, accounting for one-fifth of this subgroup and with an incidence of approximately 3-5% of all cardiac malformations. It involves ventriculo-arterial discordance due to a failure in the rotation of the conotruncal septum during embryonic development. It is typically 2-3 times more frequent in males. According to published series, coronary pattern anomalies may occur in up to one-third of cases and significantly influence the complexity of surgical repair. The arterial switch operation, or Jatene procedure, is the standard corrective technique, with the transfer of coronary buttons being the most critical step, directly affecting the postoperative course and prognosis. Certain series have shown that specific coronary anomalies are associated with a higher risk of coronary events in the postoperative period, as well as the need for ECMO and early mortality.

To understand normal coronary patterns in D-TGA, we rely on the Leiden Convention system. This approach imagines the observer viewing the pulmonary artery from the aorta at the non-coronary sinus. The adjacent sinus to the right of the pulmonary artery is labeled sinus 1, and the sinus to the left is sinus 2. The normal and most frequent pattern involves the left anterior descending and circumflex arteries originating from sinus 1, and the right coronary artery from sinus 2. Any deviation from this pattern is considered abnormal.

There is a wide range of coronary anomalies. Patterns associated with higher surgical risk include those with an intramural course of a coronary artery and those with multiple arteries originating from the same sinus, regardless of whether they arise from a single ostium or multiple ostia. In cases of coronary anomalies, alternative techniques exist to facilitate coronary translocation, reducing the risk of kinking, stenosis, or over-stretching.

Earlier this year, the Leiden group published an article on an alternative technique for single coronary ostium cases in D-TGA. This involves a modification of the traditional Yacoub aortocoronary pouch technique, adding a pericardial patch as a "roof" to the coronary button, creating a pouch that promotes better coronary flow and reduces the risk of external compression. The study is a single-center retrospective analysis of short- and mid-term outcomes of this technique in patients with D-TGA and a single coronary ostium with an intramural course.

The study includes 14 cases performed using this technique among 516 patients undergoing arterial switch surgery for TGA between January 1977 and April 2022. The two most frequent anomalous patterns were both coronary arteries arising from sinus 2 with an intramural course of the left trunk (11 patients) and, in 2 cases, both coronary arteries also originating from sinus 2 but with the right coronary artery being intramural. Seven patients had an intact ventricular septum (50%), five had intact septum (35.7%), and two had Taussig-Bing anomaly (14.3%).

Mortality was observed in 21.4% (3 patients), all related to intraoperative or immediate postoperative infarctions, with failure to recover adequate ventricular function or electrical activity. The remaining patients are alive at follow-up (9.1 years) without ischemic, arrhythmic, or clinical events (e.g., exercise intolerance), nor have they required surgical intervention for coronary ischemic events. All exhibit preserved ventricular function, and no stenosis or compression of the coronary arteries has been observed in follow-up scans.

Despite being a retrospective single-center study with a heterogeneous patient population and data collected over different eras (thus not always having access to newer surgical techniques discussed below), the authors conclude that the modified Yacoub pouch technique appears to be a useful option for arterial switch cases in patients with D-TGA and a single coronary ostium with an intramural course, with acceptable short- and mid-term outcomes.

COMMENTARY:

Traditional techniques for coronary transfer during arterial switch surgery are primarily the coronary button and the trap-door technique (a "J"-shaped incision in the neo-aorta and apposition of the coronary button at this level). However, these are not always suitable for anomalous coronary patterns, especially intramural coronaries, multiple ostia in the same sinus, juxtacommissural ostia, etc. Below, we describe some coronary translocation techniques for these complex cases, which, although requiring experienced hands, have significantly improved the prognosis of these children:

- Yacoub pouch: Anastomosis of the upper edge of the coronary button to the lower edge of the transected neo-aorta.
- Coronary unroofing followed by translocation using the button technique.
- Expanded trap-door with pericardial patches.
- In situ translocation: Creation of an aortopulmonary window, completing the anastomosis with a portion of the distal aorta.

In summary, coronary ischemic events in neonates are among the most feared complications, and for good reason: it is extremely challenging to revascularize a coronary artery in such small patients. The consequences are often devastating and frequently lead to the patient's death. In arterial switch surgery, where coronary manipulation is significant, the surgeon’s precision and experience are critical, especially in the case of coronary anomalies. These anomalies not only are less frequent but also carry a higher risk of complications (kinking, torsion, stenosis, etc.) once transferred.

As shown, these patterns are often associated with worse prognoses and postoperative outcomes in most series. Indeed, in our own series at La Paz Hospital, anomalous coronary patterns were significantly associated with increased hospital morbidity and the need for ECMO in the immediate postoperative period. However, unlike other series, we did not find a significant association with increased hospital mortality. The technique used at our center for anomalous coronary patterns, in addition to the trap-door and coronary button, was the Yacoub aortocoronary pouch in 3 of our 46 patients with coronary anomalies (intramural coronary artery).

The existence of so many techniques for coronary translocation in anomalous patterns reflects the importance of this step in arterial switch surgery. This underscores the value of different groups sharing their experiences with the surgical community to minimize ischemic events in these patients as much as possible. Although these techniques seem to help these patients achieve good short- and mid-term outcomes, multicenter and long-term studies are necessary to better understand the evolution of these patients.

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Bunty Ramchandani

Congenital Aortic Root Malformations: How Should They Be Named?

Consensus document on the anatomy, imaging, and nomenclature of congenital aortic root malformations.

Congenital malformations of the aortic valve are characterized by their considerable heterogeneity. It is not surprising that numerous classifications have been proposed in the past 15 years. For bicuspid aortic valves alone, up to 12 different classifications have been published. The most recent international nomenclature document for bicuspid aortic valves marked a significant step toward unifying criteria. Today's article aims to take it further by attempting to encompass all phenotypic expressions of the aortic root using a very similar classification. With minor nuances, the classification system can be considered nearly identical. It is based on simplifying the classification and distinguishing different types of aortic valves by the number of sinuses, the number of leaflets, commissural orientation, and the morphology of the subcommissural triangles.

COMMENTARY:

The aortic root is a complex three-dimensional structure separating the left ventricle from the tubular portion of the aorta. It comprises three semilunar leaflets, each supported by its corresponding sinus. These sinuses are separated by triangular spaces known as subcommissural triangles. The leaflets are anchored distally at the sinotubular junction, while proximally, their nadirs may join, forming a virtual ring. This ring should not be confused with the ventriculo-arterial junction, which is a muscular-arterial interface located within the sinuses from which the coronary arteries originate. The noncoronary leaflet, in contrast, is supported by the central fibrous body, composed of the membranous septum and the fibrous trigones.

Globally, the framework of the aortic root can be divided into three zones: the sinotubular junction, the surgical annulus, and the virtual ring. The latter is the "aortic annulus" typically measured by echocardiography. Regarding the semilunar valves, their middle portion, between commissures, features the nodule of Arantius. The apposition surfaces on both sides of this nodule are called lunules. The non-coapting bellies of the semilunar leaflets extend to the arterial wall, forming the hemodynamic interface of the ventriculo-arterial junction during diastole.

The nomenclature proposed by Tretter et al. simplifies prior frameworks by first assessing the number of sinuses. Most often, malformed roots present three sinuses, occasionally two, and rarely four. This is the first distinction from the international nomenclature proposed by Michelena et al., which focuses on describing bicuspid aortic valves.

Aortic valves with three sinuses but bicuspid opening are classified as functionally bicuspid. In the international nomenclature, they are categorized as "fused bicuspid aortic valve." These congenital malformations account for more than 90% of cases, reflecting the fusion of two leaflets during development, resulting in a raphe. The resulting subcommissural triangle is hypoplastic and therefore does not extend distally to the sinotubular junction. The raphe may vary in extent or even be absent, necessitating the identification of subcommissural triangle hypoplasia when in doubt. Tretter et al. classify

incomplete raphes as "forme fruste" bicuspid aortic valves, aligning with the international nomenclature's separate category for this variant.

The next step after identifying this type of aortic valve with fused leaflets is to determine the degree of asymmetry to evaluate repairability and durability. In symmetrical forms, the two commissures are positioned at 160–180°. When commissures are positioned between 120–139°, the valve is highly asymmetrical, resembling a tricuspid valve configuration but with two fused leaflets. Depending on the repair strategy used, commissural orientation and repositioning have been shown to improve functionality and durability.

Ten percent of malformed roots present two sinuses. This architecture is more frequently associated with syndromes such as Turner syndrome. Roots with two sinuses and two leaflets will have only two subcommissural triangles. Each triangle will be of normal height, resulting in two normal commissures. This configuration produces an orifice parallel to the normal plane of the sinotubular junction and may explain why these roots dilate less than the fused forms. This group can be further subclassified based on leaflet orientation: anteroposterior or laterolateral.

Unicuspid valves often have three sinuses and are exceedingly rare in the adult population. They are the most common variant in critical neonatal aortic stenosis, where the apposition zones of the noncoronary and left coronary leaflets often fuse. This typically results in two zones of fusion, each with its corresponding raphe and hypoplastic subcommissural triangle. In infants and neonates, the leaflets are frequently thickened, further limiting valve opening.

The quadricuspid valve is the unicorn of variants, with an incidence of less than 0.005% among adults undergoing cardiac imaging. It features four sinuses with four leaflets; fusion of one or more leaflets can occur, complicating diagnosis.

The classification proposed by Tretter et al. closely resembles that of Michelena et al. However, it introduces subtle differences, such as avoiding the term cusp, including forme fruste bicuspid valves under fused forms, and referring to fused forms as functionally bicuspid. More importantly, it seeks to encompass all possible variants of aortic roots. This nomenclature represents a significant advance over prior alphanumeric systems, enhancing comprehension and clinical applicability. This classification could also be applied to describe truncal valves in repair surgery for truncus arteriosus.

The article highlights the limitations of the continuity equation in 2D echocardiography for oval annuli and emphasizes the use of magnetic resonance imaging or computed tomography for adequate structural assessment. It underscores the lack of evidence regarding different measurement methods, both geometric and across the cardiac cycle, leaving substantial room for improvement in the near future.

In conclusion, the articles by Tretter et al. and Michelena et al. are essential reading for anyone managing aortic valves—not only for their proposed classification but also for their educational value and exquisite iconography.

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Bunty Ramchandani

Aortic valve replacement in children: a difficult situation, an uncertain future

A meta-analysis and microsimulation study aimed to review and estimate the outcomes of different aortic valve replacement strategies in the pediatric population.

Valve repair is the gold standard in aortic valve disease, particularly in pediatrics, as it allows for somatic tissue growth and avoids lifelong anticoagulation. However, there are instances where a valve can no longer be repaired, leaving replacement as the only option. Selecting the optimal substitute for the aortic valve in children is a complex issue that requires evaluating short- and long-term risk-benefit ratios, with scientific evidence on this subject being notably scarce. Presently, it is extremely challenging to inform parents about their child's life expectancy following valve replacement, the number of reinterventions required, anticoagulation needs, thrombotic or bleeding risks, or how these risks may evolve over time.

The therapeutic arsenal includes several options for aortic valve replacement: mechanical or biological prostheses, homografts, the Ross procedure (pulmonary autograft), and since 2007, the Ozaki technique, which replaces aortic leaflets with autologous or heterologous pericardium, allowing annular growth.

This article aims to review the literature on aortic valve replacement in children and perform a microsimulation to estimate mid- and long-term outcomes of different substitutes. To this end, a systematic review of literature on aortic valve replacement in patients under 18 years of age from 1990 to 2021 was conducted. Studies on pediatric Ross procedure, mechanical valve replacement, biological valve replacement, and homografts were included. Early events were defined as those occurring within 30 days, and late events as those occurring beyond 30 days. Time-to-event data were collected, and a microsimulation model was applied.

A total of 68 studies were evaluated, of which only one was prospective and another exclusively evaluated the outcomes of bioprostheses. A total of 5259 patients were studied, with an average follow-up of 5.9 years and 37,435 patient-years. The mean age of patients undergoing the Ross procedure, mechanical valve replacement, and homograft was 9.2 years, 13 years, and 8.4 years, respectively. Early mortality for the Ross procedure, mechanical valve replacement, and homograft was 3.7%, 7%, and 10.6%, respectively, while late mortality was .5%/year, 1%/year, and 1.4%/year, respectively. Microsimulation at 20 years estimated a survival of 18.9 years for the Ross procedure and 17 years for mechanical valve replacement. The estimated reintervention rate on the aortic valve at 20 years was 42% for the Ross procedure and 17.8% for mechanical valves.

The authors concluded that the outcomes of aortic valve replacement in the pediatric population are suboptimal, with high mortality, particularly in younger patients, and a significant reintervention rate. In this context, they advocate for the Ross procedure, as it appears to offer a survival advantage over mechanical valve replacement.

COMMENTARY:

There is no perfect substitute, as this study's results clearly illustrate. The Ross procedure, described by Donald Ross in 1967, replaces the aortic valve with living tissue that can accommodate somatic growth. However, it is a technically complex procedure

that “burdens” the right side of the heart to replace the left side. In other words, it transforms a single-valve disease into a two-valve disease. The procedure involves implanting a pulmonary autograft in the aortic position, a tissue designed to withstand relatively low pressures, as its medial layer is structurally thinner than aortic tissue. Over time, patients have shown a risk of annular dilation requiring reintervention, either with prosthetic replacement or, in some cases, a David procedure if the leaflets are unaffected. This is in addition to the multiple right-sided reinterventions patients will require.

Replacement with a prosthesis condemns the annular growth. Biological prostheses are rarely used due to their poor durability; the only published study on this included 24 patients for whom a Ross procedure was not feasible, with a follow-up period of just 46 months. Homografts do not last much longer and exhibited the highest rates of mortality and reintervention in this study. The drawbacks of homografts include their limited availability, erratic deterioration depending on the patient’s age and growth rate, immune response, and blood group incompatibilities. For most surgeons, this substitute is considered a last resort. Mechanical prostheses, while the most common alternative, are not without risks, with a thromboembolic event and stroke rate of .4%/year each. Ensuring effective anticoagulation management in children is challenging, causing significant concerns for patients, families, and healthcare providers.

Based on the presented data, extrapolating adult outcomes to pediatric substitutes would be a mistake. Even within the pediatric population, we cannot generalize outcomes, as a Ross procedure in an infant with mortality rates around 16.3% is not comparable to the 3.7% in older children. Similarly, a Ross-Konno procedure, necessary in cases of severe left ventricular outflow tract obstruction, differs from a standard Ross procedure. A mechanical valve implanted at 7 years of age carries a higher risk of reintervention and prosthesis-related adverse events than one implanted at 17 years. This explains the high annular enlargement rate recorded in the study. Substitutes should not be evaluated in isolation but tailored to patient profiles. Mortality, reintervention, and thromboembolic events should not be the sole considerations. Quality of life offered to patients must also be considered, including the lifelong need for anticoagulation with mechanical prostheses and the estimated 42% reintervention rate on the aortic valve at 20 years with the Ross procedure, alongside multiple right ventricular outflow tract reinterventions.

As for the study’s limitations, it should be noted that this is a meta-analysis of highly heterogeneous retrospective studies, lacking a control group. Studies with fewer than 20 patients were excluded. The microsimulation was based on linear event rates, so caution is required when interpreting these values. Lastly, the Ozaki technique was not mentioned as a potential comparator. This technique replaces the aortic leaflets while preserving the annulus, thus allowing annular growth similar to the Ross procedure. It does not involve manipulation of the right heart. Although it is not a definitive solution for aortic valve disease, it serves as a bridge to complete the patient’s somatic development before implanting a larger prosthesis.

What is the best substitute for the aortic valve? Perhaps no technique is inherently superior. The choice of surgical technique should depend on the patient’s profile. As surgeons, we must not focus solely on the short term but reflect on the quality of life we can offer our patients in the long term.

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Elsa Carolina Ríos Rosado

Aortic valve preservation: is it the same in children as in adults?

A retrospective study from the Royal Children's Hospital (Melbourne, Australia) analyzing long-term outcomes of aortic root surgery with valve preservation.

Nearly 35 years have passed since Tirone David described the replacement of the aortic root and ascending aorta with preservation (reimplantation) of the aortic valve. Today, this procedure, known as the David procedure, is the gold standard for adults with aneurysms of the aorta involving the sinuses of Valsalva. Due to its excellent surgical outcomes and the benefit of preserving the native aortic valve, the procedure was quickly extended to the pediatric population.

Initially, the surgical indication was aortic root aneurysm in children with Marfan or Loeys-Dietz syndrome. It gradually expanded to treat patients with cono-truncal congenital anomalies such as tetralogy of Fallot and transposition of the great arteries. However, the outcomes in this patient group have been inconsistent: some studies report discouraging results, while others describe survival and freedom from aortic valve reoperation comparable to that seen in adults.

In this article, the authors retrospectively reviewed 17 pediatric patients who underwent the David procedure at the Royal Children's Hospital between April 2006 and April 2016. Clinical and imaging data were retrieved from electronic medical records. Echocardiographic evaluation included aortic root diameters (with Z-scores) and the degree of valvular regurgitation before and after surgery. Kaplan-Meier estimates were used for survival analysis.

Among the cases reviewed, the most common etiological diagnosis was transposition of the great arteries following an arterial switch operation, followed by Loeys-Dietz syndrome and Marfan syndrome. Eleven of the 17 patients had detailed surgical reports, showing that 63.6% required central plication to achieve adequate valvular coaptation. One patient underwent subcommissural annuloplasty, and two required cusp resection and extension. No mortality was reported during follow-up. However, five patients (29.4%) underwent reoperations, and four (23.5%) required aortic valve replacement. Freedom from reoperation for aortic valve replacement at 1, 5, and 10 years was 93.8%, 93.8%, and 68.2%, respectively. The indication for aortic valve reoperation was recurrent severe valvular regurgitation. One patient operated on at the age of 3 underwent reoperation 3 months later for proximal anastomosis dehiscence. A patient with Loeys-Dietz syndrome required ascending aorta and arch replacement a decade after the reparative surgery.

The authors concluded that while aortic valve-sparing surgery can be successfully performed in pediatric patients, it demands a highly skilled and experienced surgeon due to the frequently dysplastic nature of the aortic valves in this population.

COMMENTARY:

Not long ago, valve-sparing surgery revolutionized aortic root interventions, establishing itself as the optimal treatment for sinus aorta dilation with secondary valvular insufficiency. However, it is important to recognize that children represent a distinct subgroup of patients with unique considerations regarding indications, techniques, and

surgical outcomes. As a reference, in the adult population, David et al. reported an accumulated reintervention rate of 2.1% at 10 years and 6% at 20 years of follow-up. Similarly, our group at the Puerta de Hierro Hospital reported freedom from aortic valve reoperation at 10 and 15 years of 96% and 87%, respectively. In contrast, this Australian team reports a 10-year freedom from valve replacement of 68.2% in children. What is different about children?

It is crucial to emphasize the peculiarities of pediatric aortic valves. While in adults the repaired leaflets are typically morphologically normal, pediatric valves are often markedly dysplastic, necessitating more extensive interventions, particularly in bicuspid valves and those following arterial switch operations, where the neo-aortic root is histologically and morphologically pulmonary.

Adolescents with bicuspid aortic valves form a noteworthy subgroup. The authors highlight a higher failure rate of repairs in these patients due to inadequate stabilization of the annulus. Given their experience and the increased frequency of leaflet abnormalities, a shift toward Ross procedures with the inclusion technique appears highly valid. This approach has shown greater valve longevity, minimal coronary distortion risk, and a right ventricle-to-pulmonary artery conduit lifespan exceeding initial expectations.

Another discussion point is surgical indication. While in adults the recommendation is based on an established aortic diameter linked to increased morbidity and mortality, pediatric teams interpret arterial dimensions using Z-scores, complicating a realistic estimation of aortic dilation severity. Since children are known to have a very low risk of aortic dissection and rupture, the authors emphasize delaying surgery until the aorto-ventricular junction measures at least 21 mm, allowing for the placement of a minimum 24-mm Dacron graft that can accommodate the patient into adulthood without requiring replacement.

Finally, at the technical level, beyond the challenge of valvular dysplasia, the left ventricular outflow tract is more deeply embedded within the right ventricle in tetralogy of Fallot, complicating the dissection of the aortic root. In these cases, it may be necessary to position the proximal suture line slightly higher within the subcommissural triangle between the cusps.

In conclusion, children and their pathologies are distinct, and surgical success parameters often differ significantly from adults. To ensure favorable outcomes from aortic valve-sparing surgery in the pediatric population, these interventions must be performed at specialized centers by surgeons with extensive valve repair experience, especially when addressing leaflet abnormalities.

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Bunty Ramchandani

Future of the aortic valve following isolated repair of ventricular septal defect

This American single-center study evaluates the development of aortic regurgitation (AR) during follow-up after isolated repair of ventricular septal defects (VSDs) to identify predictive factors.

Ventricular septal defect (VSD) is a common congenital heart defect, with an incidence of 1.5-6 cases per 1000 live births. Certain VSDs are associated with AR due to prolapse of the noncoronary and right coronary leaflets. The prolapse of an aortic valve leaflet associated with a VSD is termed Laubry-Pezzi syndrome. This phenomenon is caused by the Venturi effect, which reduces the left-to-right shunt but distorts the aortic valve leaflets, leading to AR due to impaired leaflet coaptation. The development of AR, even if trivial, in the context of a VSD is an indication for patch closure surgery regardless of hemodynamic impact.

The article under review, conducted at Children's National Hospital in Washington, DC, is a single-center, retrospective study analyzing patients who underwent VSD closure without concomitant aortic valve intervention. The study reviewed cases from April 2007 to March 2016, excluding patients with non-perimembranous or non-subpulmonary VSDs (juxta-arterial in Van Praagh's terminology), those without AR at the time of surgery, or those with less than 6 months of follow-up.

A total of 37 patients were identified, half of whom were male. The mean age at surgery was 2.7 years, with a mean weight of 13.4 kg. Preoperative echocardiograms showed mild or greater AR in 17 patients. The study reported no mortality, surgical reinterventions, or percutaneous procedures. At a median follow-up of 4.3 years, only five patients presented with mild or greater AR, while 76% (28 patients) had no degree of AR. Multivariable logistic regression identified left ventricular ejection fraction (LVEF) as a predictor of AR persistence during follow-up ($p = .002$).

The authors concluded that VSD closure, even in cases with mild AR, can yield excellent outcomes without requiring aortic valve intervention. When AR is trivial or mild at the time of surgery, it generally improves during follow-up. Reduced LVEF is a predictor of AR persistence post-surgery.

COMMENTARY:

Risk factors for the development of AR after VSD closure include preoperative AR, large VSDs, structural abnormalities of the aortic leaflets, sinus of Valsalva aneurysm, among others. Aortic valve intervention is usually indicated when AR exceeds a mild grade. However, AR can progress during follow-up even in patients with trivial preoperative AR. Few studies have tracked these patients to determine the progression of AR.

Subpulmonary VSDs rarely close spontaneously, and in the case of perimembranous VSDs, spontaneous closure beyond 1-2 years of life is infrequent. Both entities can be associated with right coronary sinus herniation, with or without AR. The Venturi effect causes leaflet deformation, and AR often manifests between 5 and 8 years of age. Therefore, trivial AR or a subpulmonary VSD are indications for surgical VSD closure, regardless of shunt volume. Other mechanisms contributing to AR in these patients include inadequate leaflet support on the adjacent side of the VSD, abnormal

commissural suspension, lack of apposition force, and discontinuity between the aortic medial layer and the annulus.

The main limitation of this study is its retrospective nature, small sample size, and short follow-up duration. As a strength, it is the first study to identify reduced LVEF as a predictor of persistent or worsening AR.

In conclusion, surgical VSD closure provides excellent short- and long-term outcomes. It prevents the onset or worsening of aortic valve disease by eliminating the deleterious effects of the Venturi effect on the aortic leaflets. Therefore, waiting for spontaneous closure in this patient subset is counterproductive.

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Bunty Ramchandani

What Happens with the Neoaorta in Truncus?

A single-center, retrospective study from Boston Children's Hospital reports 35 years of experience with truncal root dilatation.

Truncus arteriosus, also known as common arterial trunk, is characterized by a single ventriculoarterial connection that links both ventricles to a single arterial trunk. This trunk provides flow to the aorta, pulmonary arteries, and coronary arteries. A singular valve, termed the truncal valve, is positioned above an outlet ventricular septal defect. With a prevalence of 1 in 10,000 pregnancies, truncus arteriosus accounts for less than 0.5% of congenital heart defects, making it one of the rarest diagnoses in this group. One in three cases is associated with 22q11.2 deletion syndrome, also referred to as DiGeorge syndrome, velocardiofacial syndrome, or CATCH22.

Embryologically, truncus arteriosus results from an aortopulmonary septation defect at three levels: great arteries, valvular, and subarterial. Several classification systems exist for truncus, from the classic Collet and Edwards system (1949), which identifies four types: Type 1 with a short pulmonary trunk, Type 2 where the pulmonary arteries emerge from the aorta, and Type 3 where the pulmonary arteries arise farther apart from the aorta. Type 4, which features no true pulmonary arteries but rather aortopulmonary collaterals, is no longer considered part of the truncus spectrum. Later, this congenital heart defect was reclassified using the Van Praagh system and its modifications. Currently, the classification proposed by Russell et al. (2011) is favored, which simplifies truncus types into two categories: aortic dominance and pulmonary dominance. This classification requires further anatomical description of the pulmonary artery branches, but it provides the best embryological and clinical correlation.

Truncus arteriosus exhibits several defining anatomical features. The subarterial outlet ventricular septal defect is often misidentified as a malalignment defect. The truncal valve, which can consist of 1 to 6 leaflets, is frequently dysplastic. Coronary arteries are anomalous by definition, as they do not originate from the aorta but from a common arterial trunk, with up to 64% of cases showing variations in origin and distribution. The neoaortic root is invariably large and grows over time, a phenomenon that remains unexplained.

The article aims to describe the natural history of truncal root dilatation following neonatal repair. This single-center, retrospective study evaluated all truncus arteriosus cases operated on at Boston Children's Hospital from 1984 to 2018. Echocardiographic measurements were collected during follow-up, focusing on diameters and z-scores of the annulus, sinuses of Valsalva (SV), and sinotubular junction (STJ) of the neoaorta. Trends over time were analyzed using a linear mixed-effects model.

During the study period, 255 patients underwent surgery, of whom 193 (75.7%) survived and were included in the study. The median age at correction was 12 days. More than half of the patients had tricuspid valves, and a quarter had quadricuspid valves. The median follow-up was 11.6 years, during which no cases of aortic dissection were reported. Twenty percent of the cohort (38 patients) required intervention on the truncal valve or root. The mean annual growth of the annulus, SV, and STJ was 0.7 mm/year, 0.8 mm/year, and 0.9 mm/year, respectively. Z-scores, although elevated, remained stable over time. Bicuspid valves were associated with larger SV (p = .003) and STJ (p

= .029) sizes, while quadricuspid valves showed larger STJ dimensions (p = .004). Over the follow-up period, patients with bicuspid and quadricuspid valves exhibited greater annular dilatation (p < .05). A high-risk group was identified: patients with truncal root growth above the 75th percentile had a higher incidence of truncal valve regurgitation (p = .019) and a greater need for reintervention (p = .002).

The authors concluded that truncal root dilatation persists beyond three decades after primary intervention. Patients with bicuspid and quadricuspid valves showed greater dilatation over time and required more frequent valve interventions, identifying them as a high-risk subgroup requiring closer follow-up.

COMMENTARY:

Truncal root dilatation is a consistent feature, progressively increasing over time, while aortic dissections remain anecdotal. The etiology of this dilatation is still unclear, whether due to altered hemodynamics from abnormal anatomy, a primary defect in the vascular wall, or a combination of both. According to clinical guidelines, replacement of the neoaorta is indicated if the diameter exceeds 55 mm. This recommendation applies equally to aortic dilatation in Fallot patients, those with transposition of the great arteries repaired by arterial switch surgery, and neoaortic dilatation in truncus arteriosus. Each condition has distinct pathophysiological substrates, yet the guideline remains the same due to the limited literature supporting individualized recommendations.

The study by Sengupta et al. explores the natural history of truncal neoaortic dilatation over a follow-up of up to 35 years, an achievement in itself. The authors demonstrate that, despite elevated z-scores, these remained stable over three decades. In a cohort of 193 patients, no cases of aortic dissection were recorded. They found that quadricuspid valves increase the likelihood of intervention on the valve or root tenfold and identify high-risk cohorts within the truncus spectrum requiring closer monitoring.

Despite being a valuable contribution, the study has limitations. It is retrospective and single-centered, analyzing a broad time frame due to the low incidence of the defect. Intraoperative data regarding truncal valve morphology, beyond leaflet count, are unavailable. Additionally, truncal annulus measurements were obtained using 2D echocardiography, providing only single-plane data despite the typically oval morphology of these annuli. Interobserver variability in echocardiographic measurements further complicates interpretation. The prevalence of 22q11.2 deletion syndrome is also unclear, as diagnostic techniques for this condition emerged in 1996.

Notably, this study still considers Type 4 truncus, which European guidelines no longer classify within the truncus spectrum.

In conclusion, this study follows the tradition of excellence from Boston Children's Hospital, offering pertinent and relevant insights to identify high-risk patients for truncal neoaortic dilatation after repair.

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Bunty Ramchandani

Mitral valve replacement in infants: "Highway to hell"

Experience at Emory Hospital with 15-mm St. Jude mechanical mitral valve replacement.

Mitral valve surgery in neonates or infants presents a challenge for any pediatric cardiac surgeon. In such patients, it is essential not to rush surgical indications, as the larger the patient, the higher the likelihood of successful repair. Several limitations hinder a durable repair: anatomical variations, small annular size, dysmorphic valvular tissue, underdeveloped subvalvular apparatus, papillary muscle anomalies, and a hypoplastic left ventricle. Nevertheless, all possibilities of repair must be exhausted before considering valve replacement.

Mitral valve replacement should be a therapeutic decision of last resort. Small annular options are limited; biological options such as the Melody valve in the mitral position or the Ross II procedure are available but come with early structural degeneration. Conversely, mechanical prosthetic replacement presents the disadvantage of lifelong anticoagulation. Experience with any of these options is limited, and outcomes are suboptimal, with mortality rates of 11-36%, increasing to 52% when analyzing children under 2 years of age.

In today's article, the Emory group describes their results with the 15-mm St. Jude mechanical mitral prosthesis. This is a single-center, retrospective study analyzing all cases of mitral valve replacement with this prosthesis. Over the 13 years analyzed (2009-2022), 16 mitral valve replacements were performed on 15 patients. The median age and weight were 6.2 months and 5.16 kg. Two-thirds of the patients had undergone prior mitral repair. The most common diagnosis in this cohort was atrioventricular (AV) canal defect with left AV valve lesions. Half of the cohort had a genetic anomaly. Ten prostheses were implanted in the supra-annular position. The median intubation time was 1.5 days, the median stay in the intensive care unit was 6 days, and the hospital stay was 17 days. Three patients experienced major postoperative complications, including diaphragm plication, cardiac arrest, and prosthetic re-replacement due to thrombosis. Another four patients required readmission within 30 days after discharge for anticoagulation imbalances, either below or above the therapeutic range. There was no in-hospital mortality, but four deaths occurred during follow-up (27%). Six patients required mitral prosthesis replacement after a median of 6.8 years, with one patient undergoing replacement 10 years after the initial implant. Currently, the series includes six patients with the 15-mm St. Jude mitral prosthesis, with a median follow-up of 4.7 years.

The authors conclude that their reported series demonstrates the lowest rate of adverse events and shows greater prosthetic durability compared to other groups. They emphasize the challenges in achieving and maintaining therapeutic anticoagulation ranges in these patients.

COMMENTARY:

One of the significant limitations of pediatric cardiac surgery is the lack of growth potential in the prostheses we implant, as well as the limited options for small sizes. In March 2018, following FDA approval, Abbott introduced one of the smallest commercially available mechanical prostheses, the 15-mm St. Jude Medical Masters HP. This

prosthesis is approved for children under five years old and required a prospective, multicenter, single-arm, non-randomized study of only 20 patients (the HALO study) for approval. Despite the small number of patients, Emory's cohort represents one of the largest reported experiences in the literature with the 15-mm St. Jude prosthesis.

The study's main contribution compared to the HALO study or other reported cohorts is the 13 years of follow-up in a homogeneous cohort. It reveals the realities of opting for the mechanical prosthesis route: 20% major postoperative adverse events, one case of acute thrombosis requiring replacement, and another during follow-up successfully treated with fibrinolysis using rtPA (a management strategy scarcely documented in children). Six patients were readmitted due to poor warfarin control, adding to the four who died during follow-up. The study also provides hopeful data: no patients developed heart block, prosthetic replacements to larger sizes after a median of 6.8 years, and one patient maintained the 15-mm prosthesis for a decade before replacement. Two-thirds of the implants were performed in the supra-annular position to accommodate larger prostheses. This implantation position is not usually preferred by certain groups due to the risk of disc obstruction, circumflex artery compression, and post-capillary pulmonary hypertension resulting from reduced left atrial compliance.

Biological alternatives do not yield better outcomes, except for the advantage of avoiding anticoagulation. Options include the pulmonary autograft in the mitral position (Ross II), which is technically complex, rarely documented, and presents the significant drawback of early degeneration, making its use anecdotal. Another alternative is the implantation of a bovine jugular vein bioprosthesis (Melody). It is a viable solution for small mitral annuli (<15 mm), allowing subsequent balloon dilation as the patient grows. However, it also suffers from structural degeneration, with most requiring replacement within two years of implantation. Additionally, it carries a higher risk of paravalvular leakage, left ventricular outflow obstruction, and pulmonary vein obstruction. Consequently, the decision between mechanical and biological valve replacement is not straightforward and is primarily guided by the mitral annular size, which must be 8 mm or larger. A mechanical prosthesis can be forced into annuli up to 12 mm, relegating the biological option to smaller annuli.

This study has multiple limitations: a very small sample size, its retrospective nature, and the inclusion of different implantation techniques (annular and supra-annular). No data are available for patients who died during follow-up. The favorable outcomes compared to similar series may be due to institutional idiosyncrasies.

In conclusion, mitral valve replacement should be avoided whenever repair is possible, even if suboptimal. However, if no other option remains, one must fasten their seatbelt and prepare for the "Highway to hell."

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Bunty Ramchandani

Pulmonary bioprosthesis; an unresolved issue

This is a single-center, retrospective study conducted at Minnesota Hospital, evaluating short-term outcomes of 27 patients with the Inspiris Resilia bovine bioprosthesis (Edwards) in the pulmonary position.

Pulmonary valve replacement (PVR) is the most frequent surgery in adults with congenital heart disease. The most common indication is pulmonary regurgitation after right ventricular outflow tract reconstruction. A competent pulmonary valve alleviates symptoms and preserves cardiac function.

There is significant controversy regarding the best bioprosthesis for the pulmonary position. The most common biological grafts are porcine and bovine valves. Evidence suggests that bovine bioprostheses are more durable in the aortic position; however, this difference has not yet been demonstrated in the pulmonary position.

In today's study, Said SM et al. report their experience with the Inspiris Resilia bioprosthesis (Edwards). They reviewed all PVR cases with the Inspiris Resilia bioprosthesis from August 2019 to October 2021. During this period, they operated on 27 patients (56% female) with a mean age of 22 ± 15 years. The majority had tetralogy of Fallot (48%) as their primary diagnosis. Five patients had been previously treated via catheterization. The indexed right ventricular end-diastolic volume was 164 mL/m², and the mean prosthesis size was 25 mm. Most patients (78%) had undergone at least one prior sternotomy.

In 22 patients, the procedure was performed using the standard technique, consisting of a longitudinal incision over the pulmonary artery or a patch in the right ventricular outflow tract. The remnants of the native pulmonary valve and muscular bands causing right ventricular outflow tract obstruction were removed. The bioprosthesis was implanted using a running suture, and a roof over the right ventricle and pulmonary artery was created with a patch of either pericardium or Contegra. In the remaining five patients, the prosthesis was implanted within a conduit.

As a result, six patients presented with trivial or mild pulmonary regurgitation at discharge. No in-hospital mortality was reported. After a mean follow-up of 16 months, there were no deaths or surgical reinterventions. However, half of the patients operated with the standard technique (13 patients) developed prosthetic regurgitation, which was moderate in six cases and severe in three. These three patients required a transcatheter valve-in-valve procedure. Interestingly, none of the five conduit-supported cases showed regurgitation during follow-up.

The authors expressed concern regarding the use of the Inspiris Resilia bioprosthesis in the pulmonary position. They proposed several theories about this early regurgitation: distortion of the prosthesis due to patch roofing techniques, changes in right ventricular geometry from reverse remodeling, or inadequate coaptation of the prosthetic leaflets in a low-pressure chamber.

COMMENTARY:

The Inspiris Resilia prosthesis is a next-generation biological prosthesis made from bovine pericardium modified through stable blocking and glycerolization. This process

permanently blocks free aldehyde groups in the tissue, preventing calcification and structural degeneration. It also eliminates the need for glutaraldehyde preservation, allowing dry storage without requiring rinsing before use. Furthermore, it is mounted on an expandable stent, enabling transcatheter valve-in-valve treatment in the case of structural degeneration. Various publications support its good short-term performance, with only two cases of early degeneration reported at 12 and 24 months, respectively.

PVR with a bioprosthesis is an off-label indication. Few studies report long-term outcomes. When interpreting these results, the diverse patient ages, procedural eras, and prosthesis sizes must be considered. Additionally, immunological factors and surgical complexity further complicate comparisons.

Hemodynamics differ between the heart's two sides in terms of pressure and rheology. Data from the aortic position should not be extrapolated to the pulmonary position. All bioprostheses are designed for the left heart. In vitro studies show varying behavior depending on the pressures they encounter. In low-pressure settings, such as the pulmonary position, prostheses exhibit slower leaflet coaptation, reduced insufficiency duration and volume, lower pressure gradients, and a decreased effective orifice area.

Broadly, the reported freedom from reintervention at five years is 95% (range 50–98%), and at 10 years, 81% (range 66–85%). At La Paz and Ramón y Cajal Hospitals, we compared porcine and bovine bioprostheses using propensity score analysis. The freedom from prosthetic degeneration at 3, 5, and 10 years was 97%, 93%, and 89% for porcine valves and 100%, 98%, and 79% for bovine valves. We found no differences between the two within the first five years; however, bovine prostheses showed greater structural degeneration afterward (HR = 6.99, p = .03).

The Minnesota group's study has multiple limitations: its retrospective nature, the small patient number (n = 27), and the absence of more precise complementary tests, such as 4-dimensional CT scans, to detect leaflet thrombosis. These shortcomings require cautious interpretation of the results and prevent drawing premature conclusions. Nonetheless, it is worth emphasizing that despite the limited number of patients, this represents the largest reported experience with the Inspiris Resilia bioprosthesis in the pulmonary position in the literature.

In conclusion, articles like the one analyzed today compel us to adopt a scientific mindset. With results challenging the *status quo*, they urge us to scrutinize innovations critically. In this case, the new Inspiris Resilia bioprosthesis (Edwards) does not offer reliable outcomes in the pulmonary position. As St. Augustine once said, "The appetite for novelty leads man to extreme anguish."

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Marta Gambra Arzoz

Congenital heart diseases, an overlooked cause behind out-of-hospital cardiac arrests

A nationwide nested case-control study conducted on the Danish population assessed the presence of congenital heart disease as a factor associated with out-of-hospital cardiac arrest events in patients aged 18 to 90 years.

In recent years, the prevalence of congenital heart disease in adults has been shown to increase (currently estimated at 0.3% worldwide), attributed largely to advancements in the diagnosis and treatment of this pathology. Mortality among patients with congenital heart disease is higher than in the general population, with sudden cardiac death estimated as the cause in up to 25% of cases. However, the literature describing and analyzing out-of-hospital cardiac arrest (OHCA) in adult patients with congenital heart disease—its physiology, prognostic factors, and episode survival—is scarce, heterogeneous, and subject to biases.

The purpose of this study was to investigate the association between OHCA and the presence of congenital heart disease in adult patients as the main associated factor and to analyze 30-day survival after the episode. The study included patients listed in the Danish out-of-hospital cardiac arrest registry with cardiac-cause OHCA (cases) between June 1, 2001, and December 31, 2019. This nested case-control study matched each case with up to five controls based on: 1) sex, 2) year of birth, 3) presence of ischemic heart disease, 4) heart failure or cardiomyopathy, 5) at least one cardiovascular risk factor (diabetes mellitus, hypertension, substance abuse, and/or peripheral arterial disease), and 6) associated comorbidity, which had to include at least one of the following: cerebrovascular disease, chronic obstructive pulmonary disease, or chronic kidney disease. Cases involving congenital heart disease were classified into three groups based on complexity (mild, moderate, or severe) following established guidelines in adult congenital heart disease (American Heart Association and European Heart Society). Cox regression analysis was used to predict time-to-event. Subanalyses were conducted on cases with identified shockable rhythms during the event and cases with autopsies confirming the cardiac cause of OHCA.

In total, 43,967 cases and 219,772 controls were included. Among cases, the prevalence of mild and moderate congenital heart disease was 0.3% each, and severe congenital heart disease was 0.1%. The presence of any type of congenital heart disease was statistically significantly associated with sudden cardiac death events, with the group of highest severity showing the highest risk. Statistical significance persisted after adjustment for sex and age, irrespective of the complexity of congenital heart disease. Additionally, stratified analyses by age, year of event, and previous cardiac surgery were performed:

Age: Risk was higher in younger patients within the moderate and severe congenital heart disease groups, disappearing in those older than 80 years. However, in the mild congenital heart disease group, incidence showed a U-shaped distribution, with higher incidence in patients under 50 years (with a stronger association in younger ages) and in those over 80 years. Year of event (2001–2006 versus 2014–2019): A decrease in association strength with the event was observed in the moderate-risk group, with no differences found in the other two groups. History of prior cardiac surgery: Associated

with higher risk in patients with moderate or severe congenital heart disease, but not in those with mild congenital heart disease.

Prognostic factors that showed better survival rates in congenital heart disease patients included: events occurring in public locations, witnessed arrests, early initiation of cardiopulmonary resuscitation (CPR), identification of a shockable rhythm, and early defibrillation, with the association being strongest in the severe congenital heart disease group. Factors associated with better 30-day survival after the episode were early CPR, identification of a shockable rhythm, and early defibrillation.

In the initial analysis, survival was higher in the congenital heart disease group. However, after adjusting for confounding factors, survival was similar between the groups. Subanalysis of cases with autopsies confirming the cardiac cause of the arrest showed no differences between groups.

COMMENTARY:

Advancements in the care and management of congenital heart disease patients over recent decades have led to increased survival rates, with a higher prevalence of congenital heart disease now observed in adulthood than in childhood. Although sudden cardiac death is one of the leading causes of mortality, the available literature on this subject remains limited. In this context, the present study was conducted to explore the association between congenital heart disease and OHCA events in adult patients.

The authors present a nested case-control study where congenital heart disease presence was statistically significantly associated with sudden cardiac death. Additionally, several important aspects of this study deserve attention:

- The strength of the association was higher in the group with more complex congenital heart disease and in those with prior cardiac surgery, likely due to a greater arrhythmogenic substrate in this population.

- The age-dependent association varied by the complexity of congenital heart disease.

- The risk of experiencing the event decreased in the moderate-complexity group during the second follow-up stage, likely due to improvements in diagnosis and treatment. However, this was not observed in the mild and severe complexity groups, highlighting the need to maintain cardiological follow-up into adulthood, even for patients with mild congenital heart disease.

- A significantly higher percentage of patients in the congenital heart disease group, especially in the severe group, underwent early CPR and defibrillation. This could be attributed to their younger age, lower comorbidity, and closer supervision by individuals trained to initiate basic life support maneuvers.

- Survival was initially higher in the congenital heart disease group, but this association disappeared after adjusting for confounding factors.

Limitations of the study:

- As a case-control study, it is observational, precluding causal analysis and the exclusion of residual confounding factors.

- The nested case-control design lacks data on potentially important confounding variables, such as echocardiographic findings (ventricular function, valvular pathologies, and residual lesions), which were not included in the matching process.

- Misclassification of congenital heart disease cases in the registry could lead to underestimation of congenital heart disease prevalence among cases.

This study is significant as it demonstrates that patients with any type of congenital heart disease have a higher risk of sudden cardiac death compared to the general population, emphasizing the need for early identification of candidates for implantable defibrillators and continued cardiological follow-up in mild congenital heart disease patients during adulthood. Moreover, the identification of factors associated with better 30-day survival—early CPR and defibrillation—highlights two key aspects crucial to the prognosis of any OHCA victim, including those with underlying congenital heart disease.

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Bunty Ramchandani

Clinical practice guidelines: a pending challenge in pediatric cardiac surgery

Experience of an American center implementing clinical practice guidelines for the surgical repair of ventricular septal defect.

Variation in clinical practice is inherent to the art of medicine, reflecting individualized and humanized care. The problem arises when the care provided lacks clear scientific evidence. While such variability may not result in differences in clinical outcomes, it can signal inefficiency in the system, leading to increased healthcare costs, inappropriate resource utilization, or even heightened morbidity due to unnecessary actions.

Today's article examines the variability observed at a center before and after implementing a clinical practice guideline for the surgical repair of simple ventricular septal defect (VSD) in a pediatric hospital. In line with previously published data, their aim was to reduce clinical variability, thereby shortening hospital stays without increasing adverse events. The study retrospectively compared outcomes over three years of experience with the guideline against two years prior to its implementation. Exclusion criteria included patients older than one year with nonrestrictive VSD, presence of additional cardiac defects other than patent ductus arteriosus or atrial septal defect, prematurity, chronic kidney disease, chromosomal anomalies, significant comorbidities from other systems, and those requiring intubation for more than six hours. A total of 43 milestones were evaluated within the clinical pathway, of which 5 were deemed essential for successful postoperative outcomes. These included: scheduling the intervention as the first case of the day, ICU admission before 2:00 PM, administering the first dose of furosemide within the first 4 postoperative hours, initiating oral feeding within the first 4 hours, transitioning to oral analgesia by postoperative day one, and avoiding continuous infusions of sedatives or opioids.

The analysis included 23 patients managed under the clinical guideline and 25 from the pre-guideline period. Demographics were comparable between groups. Patients following the clinical pathway achieved, on average, 80% of evaluated milestones. Univariate analysis showed earlier initiation of oral feeding in patients under the guideline, with a mean time of 180 minutes versus 360 minutes in the pre-guideline group ($p < .01$). Additionally, the clinical pathway group reduced hospital stays by one day ($p = .04$). No differences were observed regarding adverse events, including mortality, reintervention rates, acute kidney injury, chest tube output, or readmissions.

The authors concluded that implementing clinical guidelines improved oral tolerance times and reduced hospital stays. Such guidelines in surgical settings could reduce clinical variability and enhance the quality of medical care.

COMMENTARY:

The best healthcare practice is one centered on patients and grounded in effectiveness, efficiency, and scientific evidence. Reducing variability fundamentally requires the creation of clinical protocols based on robust evidence. To this end, the authors established a working group tasked with defining care standards through evidence and

consensus. The protocol was reinforced with continuous education and training, including monthly sessions with nursing units and multidisciplinary medical meetings.

This study highlights how early enteral feeding reduces unnecessary intravenous fluid administration, thereby preventing fluid overload. In pediatric patients, agitation is often linked to thirst or hunger. Their limited communication abilities can lead to the administration of sedatives or opioids to manage agitation. Early enteral feeding offers the added benefit of improving patient comfort, which in turn decreases the need for sedatives and/or opioids.

Clinical guidelines, like those described in this article, are essential steps toward enhanced recovery after surgery (ERAS) in pediatric cardiac surgery. ERAS is a relatively new concept in cardiac surgery, with the first guidelines emerging in 2019. Standardizing care allows the identification of patients who might benefit from fast-track management. Moreover, care standardization positively impacts the acute postoperative cardiac care of other patients in the unit.

This retrospective single-center study involved a small number of patients. One key limitation of such studies is the Hawthorne effect, where subjects alter their behavior due to awareness of being observed. This effect can also extend to healthcare personnel, potentially modifying their practices beyond adherence to the new protocol, leading to improved care delivery compared to the pre-guideline phase. Importantly, patients requiring intubation for more than six hours were excluded. Thus, the analysis aligns more with a per-treatment criterion than an intention-to-treat criterion, which might be more accurate. The authors justified this exclusion by arguing that such cases could not adhere to the clinical pathway's milestones. However, this compromises the study's internal validity, as it would be crucial to understand the reasons behind deviations from the protocol, such as delayed extubation.

In conclusion, the goal is not to eliminate variability entirely but to minimize it. However, it is critical to eliminate decisions that do not contribute to the objective benefit of our patients.

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Bunty Ramchandani

Atrioventricular block after surgery: the minesweeper game?

A prospective study conducted at Boston Children's Hospital aimed at mapping the conduction system in various congenital heart defects to create a predictive model of conduction tissue anatomy.

Postoperative atrioventricular block (AVB) in the correction of complex cardiac defects has been the Damocles' sword of congenital heart surgery. In the early days of this specialty, one in ten patients developed AVB after surgery, treated with adrenaline, atropine, and the newly discovered isoproterenol. These treatments were useful but temporary, condemning patients with permanent AVB. Temporary epicardial pacemaker wires were designed and first used by Walton Lillehei in the 1950s. However, the generator they were connected to was a bulky, mains-dependent device. If power failed, so did the generator and, consequently, cardiac stimulation. Unfortunately, Dr. Lillehei faced this tragic situation with one of his pediatric patients, with fatal results. This led him to seek Earl Bakken, an electrical engineer and hospital technician, who developed the first portable pacemaker in his small garage. Earl Bakken likely never imagined the significance of this milestone for the company he co-founded, Medtronic®.

We have made significant progress since then, but postoperative AVB remains the Achilles' heel of our interventions. In less complex congenital surgeries, the incidence is approximately 1%. However, with greater complexity comes a higher risk, reaching up to 20% in conditions such as heterotaxy/isomerism syndrome.

The Boston Children's study reports its experience with intraoperative conduction system mapping in various congenital heart defects. Their objective is to develop a predictive model of conduction tissue anatomy based on the specific congenital condition. From February 2020 to December 2021, mapping was performed in all complex congenital surgeries. Using a multielectrode catheter, electrograms were obtained in a decompressed, beating heart. They recorded patient anatomy, surgical procedures, the location of the His bundle, and conduction system status post-surgery. A classification and regression tree analysis was used to develop a predictive model of conduction tissue location based on the type of congenital defect.

A total of 109 patients were mapped, with median weight and age of 10.8 kg and 1.8 years, respectively. The conduction system was identified in 96% of cases, with a median mapping time of 6 minutes. The anatomies evaluated included atrioventricular canals, double outlet right ventricles, complex transposition of the great arteries, and multiple ventricular septal defects. The classification and regression tree analysis identified ventricular looping and visceroatrial situs as key discriminators for conduction system location. As a result, 89.5% of patients were free of AVB postoperatively. Only one patient (2.9%) with heterotaxy syndrome developed postoperative AVB.

The authors concluded that intraoperative mapping allows identification of the His bundle location and enhances understanding of the anatomical factors influencing its position. The predictive model provides additional insight into the conduction system in these patients, aiding surgeons in anticipating its location and avoiding injury.

COMMENTARY:

It has been just over a century since the anatomical localization of the cardiac pacemaker by Keith and Fick and the identification of the atrioventricular node by Sunao Tawara. Over recent decades, knowledge of the cardiac conduction system has advanced significantly thanks to genetic and molecular developments. For simple congenital defects, the location of the AV node and His bundle is relatively predictable; however, in complex cases, it becomes a guessing game. Experience has shown that the conduction system rotates with ventricular looping. This explains its anterosuperior position in patients with congenitally corrected transposition of the great arteries. However, ventricular looping is not the only factor; misalignment of the atrial and ventricular septa, as well as the atresia of a cardiac chamber, also play a role. In some cases, multiple AV nodes exist, and determining the functionally relevant one remains a mystery.

This novel study from Boston Children's is the first large-scale investigation into the conduction system in patients with complex congenital heart defects. It is conducted in a beating, decompressed heart without complications related to the procedure. Despite their efforts, 4% of patients could not have their conduction system mapped, and in 10%, AVB could not be avoided. However, in heterotaxy patients, this technique reduced AVB from a reported 14% in their series to 3%.

This technique has several limitations, including catheter design, which was initially intended for percutaneous studies. This is evidenced by the 4% of patients whose mapping was unsuccessful due to size issues. Another limitation lies in logistics and resources; not all hospitals can afford to have an electrophysiologist in the operating room for intraoperative studies.

The beginnings of any innovation are cumbersome, but as more experience is gained in mapping, I am confident it will become more efficient with devices specifically designed for this purpose.

In conclusion, while we may not achieve a universally predictable conduction system pattern for all congenital defects, studies like this one provide roadmaps to avoid stepping on mines with our sutures.

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Bunty Ramchandani

Half a century of experience in heterotaxy syndrome

Long-term outcomes at Mayo Clinic in the management of patients with heterotaxy syndrome.

Heterotaxy syndromes or cardiac isomerisms, depending on the morphological school of thought employed, encompass a highly heterogeneous group of cardiac and extracardiac anomalies. These conditions represent some of the most complex profiles encountered in congenital heart disease units. Long-term data on treatment and prognosis for these patients are scarce. Identifying cases amenable to biventricular repair is essential, as univentricular pathways are associated with poorer short- and long-term outcomes within this patient population.

This study is a historical review analyzing five decades (1973–2021) of heterotaxy syndrome management. Its objective was to compare long-term outcomes of univentricular versus biventricular strategies. Patients were categorized by asplenia and polysplenia (Van Praagh's school) instead of defining atrial appendage morphology, which provides insights into isomerism type and laterality (Anderson's school). The primary endpoint was survival after birth.

A total of 230 patients were identified: 107 (47%) with polysplenia and 123 (53%) with asplenia. The majority (87%) followed a single-ventricle pathway, with 90% reaching the Fontan stage. Most patients exhibited a dominant right-ventricular morphology. One-third had total anomalous pulmonary venous drainage, and another third showed inferior vena cava interruption. The mean age for Fontan completion was 7.5 years, with an overall hospital mortality of 17%, decreasing to below 10% since 1995. Only one death occurred in the biventricular group.

With a median follow-up of 20 years, 43% of the cohort had died within 15 years. At 30 years, survival was markedly lower in the single-ventricle cohort compared to the biventricular group (53% vs. 93%; $p = .001$). Among single-ventricle patients, those achieving Fontan showed slightly higher survival rates at 20 years compared to those who did not (68% vs. 63%). Overall, asplenia patients had worse survival compared to those with polysplenia (63% vs. 80%; $p < .001$). Stratified analysis within Fontan patients showed worsening outcomes for asplenia compared to polysplenia (39% vs. 56%; $p < .001$).

Approximately 23% of the cohort required permanent pacemaker implantation. Multivariable analysis revealed independent mortality risk factors: univentricular physiology (OR = 7.2), absence of prior Glenn (OR = 3.6), asplenia (OR = 2.7), and the need for a permanent pacemaker (OR = 2.3).

The authors concluded that asplenia subtype presents worse survival, and univentricular pathways are associated with inferior outcomes compared to biventricular repair.

COMMENTARY:

Discussing heterotaxy syndromes necessitates explaining the two schools of thought to avoid misunderstandings. Terminological inconsistencies in the literature complicate comparisons between studies.

On one side, Richard Van Praagh's American school identifies three types of heterotaxy syndromes: asplenia, polysplenia, and a normal right spleen (mirror image of normal situs). Asplenia is associated with an intact inferior vena cava and higher prevalence of atrioventricular canal defects, often resulting in interatrial defects. Conversely, polysplenia frequently exhibits inferior vena cava interruption between the subhepatic and suprarenal segments, with venous blood reaching the superior vena cava through the azygos/hemiazygos system.

Robert H. Anderson's European school, on the other hand, categorizes patients based on isomerism rather than abdominal organ arrangement. Differentiation relies on atrial appendage morphology, considered the most constant atrial structure. Anderson's descriptions include atrial morphology, ventricular mass, and arterial trunks, along with atrioventricular and ventriculo-arterial connections.

Like any published study, it is crucial to highlight limitations. This is a retrospective, single-center study spanning five decades. Its applicability to smaller centers is limited due to the quaternary nature of the hospital. However, such patients should ideally be treated in highly specialized centers. The lengthy study period explains the predominance of single-ventricle pathways and delayed Fontan surgeries.

In conclusion, the findings of Graham et al. confirm and quantify pre-existing notions. Publishing such extensive experiences is a milestone, offering valuable guidance for managing this heterogeneous group of patients.

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Bunty Ramchandani

Fontan-associated liver disease: what is the value of liver fibrosis scores?

A retrospective, observational study of 159 adults with Fontan circulation analyzed the correlation between two liver fibrosis scores, haemodynamic status, degree of liver damage, and long-term mortality.

Fontan circulation is rooted in the concept of perpetual fluid motion described in the mid-17th century. However, after half a century of experience, the reality is markedly different; it represents a state of "chronic heart failure" created by surgical intervention. This failure is rarely attributable to the heart itself but rather to an insufficient circulation.

One of the organs profoundly affected by this circulatory insufficiency is the liver. Elevated central venous pressure and impaired hepatic lymphatic drainage contribute to liver fibrosis, which becomes severe in over 65% of patients. Fontan-associated liver disease (FALD) encompasses a wide spectrum of hepatic conditions ranging from mild biochemical alterations indicative of cytolytic and/or cholestatic liver injury to advanced fibrosis, compensated or decompensated cirrhosis, focal nodular hyperplasia, and even hepatocellular neoplasms.

The study under review investigates the correlation of liver fibrosis scores with haemodynamic status, degree of liver cirrhosis, and prognosis in adults with Fontan circulation. Two non-invasive scores were assessed: the APRI ratio [AST/platelet count] and FIB-4 [(age x AST)/(platelet count x √ALT)]. The study included 159 adults with Fontan circulation who underwent catheterisation at Mayo Clinic between 1999 and 2017. Haemodynamic, laboratory, imaging, and pathological data were collected.

Both scores showed weak correlations with Fontan circulation resistances and pulmonary capillary wedge pressure. No correlations were found between liver fibrosis indices and ventricular end-diastolic pressure, arterial oxygen saturation, cardiac index, or pulmonary vascular resistance. Among 31 patients who underwent liver biopsy, no correlations were observed between the degree of fibrosis and liver fibrosis scores. In fact, most liver fibrosis markers failed to correlate with the indices studied. However, a significant association was found with prognosis: over a mean follow-up of 9 years, 64 patients (40.8%) died. Multivariable analysis, which incorporated prognostic factors described in the literature, revealed that each unit increase in the APRI score was associated with a hazard ratio (HR) for mortality of 1.31, and each unit increase in the FIB-4 score was associated with an HR of 2.15 (p=.003 for both).

The authors concluded that APRI and FIB-4 scores were associated with long-term mortality in adults with Fontan circulation. However, these scores were not useful for determining haemodynamic status or the degree of liver fibrosis.

COMMENTARY:

Cirrhosis, a key feature of FALD, represents a late-stage consequence of Fontan circulation. Progressive liver fibrosis caused by congestion disrupts hepatic architecture, leading to hepatocyte regeneration and nodule formation. Metabolic liver function typically declines in advanced stages. However, there is limited correlation between the

degree of liver fibrosis and the clinical manifestations or non-invasive diagnostic tests. Currently, there are more adults than children living with Fontan circulation worldwide, bringing FALD into sharper focus as a disease that takes decades to develop.

Liver biopsy remains the gold standard for diagnosis. However, the heterogeneous nature of hepatic involvement in FALD means that significant lesions can be missed. APRI and FIB-4 are inexpensive, easy-to-calculate indices derived from laboratory tests originally designed for viral hepatitis. Their non-invasive nature makes them attractive for studying Fontan patients. This study is the first to evaluate the correlation between these indices, clinical outcomes, and haemodynamic status in adult Fontan patients. The lack of correlation with haemodynamic status suggests that the pathophysiology of FALD is more complex than sustained elevated central venous pressure alone.

Regarding the study's limitations, it is important to note that the Mayo Clinic is a quaternary center for congenital heart disease, introducing selection bias as the most complex cases are referred there. Furthermore, nearly two-thirds of the cohort had an atriopulmonary connection, a technique now largely abandoned due to its high rate of long-term complications. Currently, extracardiac conduit Fontan circulation is the most commonly employed technique, yet it represented less than 10% of the study cohort, affecting the external validity of the findings.

In conclusion, FALD, particularly cirrhosis, will become increasingly prevalent among Fontan patients simply due to the growing number of adults with this circulation type and the decades-long course of the disease. The complex pathophysiology underlying FALD cannot be adequately assessed using scores designed for other diseases, even those affecting the same organ. Non-invasive alternatives and multidisciplinary teams are essential for studying and managing this unique aspect of Fontan circulation.

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Bunty Ramchandani

Adults with congenital heart disease: challenging the theory of evolution

A national Swedish study analyzing morbidity and mortality among over 37,000 adults with congenital heart disease.

Congenital heart disease (CHD) is the most common congenital malformation, with an incidence of 1% of all live births. It is thirty times more common than cystic fibrosis and fifty times more frequent than pediatric cancer. Over the past 70 years, CHD has transformed from a fatal diagnosis to one where more than 97% of diagnosed individuals reach adulthood. This revolutionary change in treatment has led to a situation in many countries where adults with congenital heart disease (ACHD) now outnumber children with CHD. These advancements are largely due to continuous technological progress and the perseverance of the medical community. Special recognition goes to Helen Taussig and Maude Abbott, the pioneering cardiologists who first studied and treated CHD.

This study provides a retrospective analysis of the impact of this revolution in Sweden. Researchers reviewed various national databases of inpatient, outpatient, and mortality records. The analysis included all individuals with CHD born between 1950 and 1999 who survived beyond 18 years of age. For every CHD patient, ten matched controls were selected from the same databases. Follow-up was conducted from 1968 to 2017, tracking all adults until death. Patients who died before 18 years of age were excluded. The primary aim was to assess the mortality and cardiovascular morbidity of ACHD patients during adulthood in Sweden.

Given the heterogeneity of this population, patients were categorized into six groups (following methodologies from similar studies):

- Group 1: Conotruncal defects (e.g., truncus arteriosus, transposition of the great arteries, double-outlet right ventricle, aorto-pulmonary window, tetralogy of Fallot).
- Group 2: Severe non-conotruncal defects (e.g., single ventricle, hypoplastic left heart syndrome, atrioventricular canal defects).
- Group 3: Coarctation of the aorta.
- Group 4: Ventricular septal defect.
- Group 5: Atrial septal defect.
- Group 6: Miscellaneous defects not classified into the above groups.

A total of 37,278 ACHD patients were included and compared with 412,799 controls. The average follow-up period was 19.2 years. During this time, 1,937 ACHD patients (5.2%) and 6,690 controls (1.6%) died, resulting in mortality rates of 2.73 and 0.84 per 1,000 person-years, respectively. Mortality among ACHD patients was 3.2 times higher ($p <$

.001) compared with controls. After up to 50 years of follow-up, over 75% of ACHD patients were still alive, and 75% reached the age of 60 years. Mortality consistently declined over time ($p < .001$), with the decline beginning in the 1970s. Adjusted mortality was elevated across all groups ($p < .001$), with the highest hazard ratio (HR: 10.03) observed in conotruncal anomalies, followed by severe non-conotruncal defects (HR: 7.36). Even conditions traditionally considered "curative," such as atrial septal defect, showed a slightly elevated mortality (HR: 1.36).

The authors concluded that ACHD patients had more than three times the mortality risk of individuals without CHD. Despite this, 75% of ACHD patients who survived to age 18 reached their sixth decade of life. Patients born after 1975 experienced a lower subsequent mortality risk.

COMMENTARY:

What is CHD? It is an abnormality of one or more cardiac or vascular structures present at birth. Achieving a complete, closed, and dual circulatory system has required millions of years of evolution. Unlike the left ventricle, which has undergone natural selection since the Devonian period 500 million years ago, the right ventricle only emerged 180 million years ago during the Jurassic period. The need for continuous terrestrial respiration demanded an auxiliary circulatory pump to direct blood flow to the lungs, leading to the development of the subarterial conal free wall and the septation of systemic and pulmonary circulations. These evolutionary changes are highly complex, making it unsurprising that occasional errors still appear in the developmental "symphony" of the cardiovascular system.

The need to address these anomalies gave birth to the specialty of congenital heart disease. Soon, the number of adults with CHD (ACHD) will surpass the number of children with CHD in Spain. As Lady Somerville predicted in her Lancet article more than 40 years ago, "we expect a tsunami of ACHD" in the coming decades.

The successes of previous generations in CHD management have led to a growing cohort of ACHD patients. In the years to come, colleagues from various specialties will face these patients, either directly or indirectly, requiring specialized care. In cardiology, ACHD patients present with arrhythmic, vascular, and valvular complications, complex management of pulmonary hypertension and residual shunts, and most notably, advanced heart failure. For this reason, it is essential to care for this population in specialized CHD centers to ensure proper management.

No study is without limitations. While this study analyzes outcomes from nearly 9 million patient-years with minimal loss to follow-up, it relies on administrative records. The results depend on accurate coding of morbidity, mortality, and patient diagnoses. The study lacks access to clinical data, which limits insight into disease progression and terminal events. Additionally, some conditions share a single code (e.g., atrial septal defect and patent foramen ovale), complicating the interpretation of results. Furthermore, technological advancements, such as the routine use of echocardiography, have likely added patients with simpler defects who were previously undiagnosed, making comparisons across time periods challenging. These data must be interpreted cautiously, as demographic analyses of ACHD patients may oversimplify the complexity of these conditions.

In conclusion, CHD has undergone a revolution over the past century, transforming from an incurable disease to a chronic condition. Studies like that of Dellborg et al.

demonstrate that while significant progress has been made, there is still work to do to improve outcomes that are already remarkable.

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Bunty Ramchandani

Results of Systemic-to-Pulmonary Shunt in Pulmonary Atresia With Ventricular Septal Defect

30 Years of Experience at the Royal Children's Hospital of Melbourne in Managing Pulmonary Atresia With Ventricular Septal Defect Without Major Aortopulmonary Collateral Arteries

The coexistence of pulmonary stenosis and ventricular septal defect is commonly referred to as a Fallot-type situation. Pulmonary atresia with ventricular septal defect (PA-VSD) represents the extreme end of this spectrum. This conotruncal anomaly is characterized by the absence of luminal continuity between the right ventricle and pulmonary arteries. The symptomatology depends on the degree of pulmonary blood flow, which dictates the clinical management of these patients.

There are three subgroups of PA-VSD:

1. Normal pulmonary arteries with typically ductal-dependent flow.

2. Hypoplastic pulmonary arteries with variable arborization defects (absence of blood flow to certain pulmonary segments), frequently accompanied by major aortopulmonary collateral arteries (MAPCAs) with variable distribution and number.

3. Absence of pulmonary arteries with exclusive flow from MAPCAs.

This discussion focuses on the first subgroup—those with normal pulmonary arteries—and specifically on their treatment options. Currently, these patients can be managed through various equally valid approaches. One strategy involves early complete repair, including VSD closure and implantation of a conduit between the right ventricle and pulmonary arteries, to avoid morbidity and mortality associated with shunts and the need for subsequent surgeries. Another approach is staged repair, beginning with systemic-to-pulmonary shunting for palliation, followed by definitive repair at a later stage to mitigate the risks of complex neonatal surgeries and the frequent reoperations required for small conduits. Some groups advocate for a hybrid correction—resolving right ventricular outflow obstruction with a conduit or transannular patch in one stage, followed by VSD closure in a second stage. There is no perfect solution; the strategy should be tailored to the individual patient.

In this article, Macalister et al. describe a 30-year experience (1989–2019) at the Royal Children's Hospital of Melbourne in managing PA-VSD with systemic-to-pulmonary shunts. Patients included were those with PA-VSD without MAPCAs, even if the initial palliation was performed at another institution. Excluded were patients unsuitable for biventricular repair, those undergoing primary complete repair, and one patient who received a transannular patch during palliation. Management involved various shunt types: modified Blalock-Taussig shunts from the innominate or ipsilateral subclavian artery, central Gore-Tex shunts via sternotomy or thoracotomy, with or without cardiopulmonary bypass. The ductus arteriosus was not ligated in all cases. Final repair utilized diverse conduits and patches. The cohort was divided into two periods before and after 2009, reflecting a shift in preference for central shunts and systematic ductal closure.

Among 107 patients analyzed, 91 (85%) achieved complete repair at a median age of 1 year. Median follow-up was 10.5 years. Survival at 6 months, 20 months, and 10 years was 90%, 85%, and 81%, respectively. Chromosomal abnormalities were present in one-third of patients, with no significant differences between periods. During the second period (n = 40), cardiopulmonary bypass use increased (72% vs. 20%; $p < .001$), primarily due to the choice of central shunts. This period saw reduced early mortality, decreased interstage mortality (not statistically significant), and earlier completion of repair (0.7 years vs. 1.3 years; $p < .001$). Ninety percent of patients treated in the second period achieved complete repair. Logistic regression identified that shunts <3.5 mm ($p < .006$) and those performed post-2009 ($p < .001$) facilitated earlier complete repair. However, smaller shunts were an independent risk factor for morbidity (HR = 4.2; $p < .039$) without increasing mortality or impeding repair rates. Atrioventricular discordance and genetic syndromes independently increased mortality risk before complete repair ($p < .05$).

The authors concluded that survival following staged repair of PA-VSD is high. Smaller shunts allow earlier repair without increasing mortality but are associated with higher morbidity.

COMMENTARY:

Scientific evidence guides clinical practice, and the highest level of evidence comes from randomized controlled trials. However, in pediatric cardiology, such trials often pose ethical challenges. This limitation forces practitioners to rely on institutional experiences described in the literature. PA-VSD is a complex condition, with outcomes influenced not only by surgical decisions but also by pre- and postoperative management. Adding to this complexity are genetic anomalies with extracardiac malformations, which independently worsen outcomes regardless of the surgical technique employed.

The results reported by Macalister et al. represent some of the best published outcomes for staged PA-VSD repair. Their complete repair rate of 85% and 10-year survival rate of 81% rival outcomes reported for primary early repair. It is worth noting that outcomes for staged repair in other studies have been inferior due to higher proportions of patients with genetic anomalies. This study's findings should be interpreted with caution, given its retrospective nature, long study period, and heterogeneous cohort in terms of surgical techniques, reconstruction materials, and ductal ligation during palliation. Postoperative management of palliated patients is challenging, requiring a highly experienced team. Thus, the results reported by Macalister et al. may not be generalizable to other centers.

In conclusion, with the current evidence, both early repair and staged approaches are equally valid for managing PA-VSD. The most reasonable approach is to select the technique and strategy best suited to the experience and outcomes of the treating institution.

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Bunty Ramchandani

Experience of Mayo Clinic with Repair of Anomalous Aortic Origin of a Coronary Artery

Experience of Mayo Clinic with the unroofing technique for anomalous aortic origin of a coronary artery with an intramural course.

Anomalous aortic origin of a coronary artery (AAOCA) is the second leading cause of sudden cardiac death in young athletes, with a prevalence of 0.1%-0.7% in the general population. This figure likely underestimates the actual prevalence, as routine screening tests are not typically performed without clinical indications. AAOCA may involve both the left (AAOLCA) and right coronary artery (AAORCA) origins. It can also affect the coronary artery's course, which may be prepulmonary, interarterial, subpulmonary, retroaortic, intraseptal, or retrocardiac. Right coronary involvement is 3-6 times more frequent than left coronary involvement; however, AAOLCA carries a higher risk of sudden cardiac death, particularly during or immediately after exercise. Furthermore, certain anatomical variants increase the risk of ischemia and sudden death. High-risk anatomies include a slit-like orifice, interarterial course, intramural course, acute take-off angle, high origin, and proximal stenosis due to an elliptical vessel shape.

The team led by Dearani et al. at Mayo Clinic reported outcomes of the unroofing technique in 148 patients with intramural AAOCA from 2003 to 2020. Patients with intraseptal AAOCA or anomalous left anterior descending artery originating from the right sinus and crossing the right ventricular outflow tract were excluded. The article provides a brief overview of their preoperative and postoperative study protocol, which utilized echocardiography, coronary computed tomography angiography (CTA), catheterization (in adults with risk factors), stress echocardiography, or nuclear medicine testing. They also describe a standardized surgical technique.

The study included 130 patients with AAORCA and 18 with AAOLCA, with a median age of 44 years. In 80% of cases, the anomaly was corrected as an isolated procedure, yielding an in-hospital mortality of <1% (2 deaths, both adults >55 years with postoperative complications following reoperations for aortic root or valve replacement associated with AAOCA repair). Commissural resuspension of the aortic valve was required in 25 cases to achieve adequate unroofing. No cases of iatrogenic worsening of aortic valve function were observed. Over a median follow-up of 9.5 years, 5 deaths were reported—3 from non-cardiovascular causes and 2 from unknown causes. No pediatric patients (n = 29) died during the postoperative period or follow-up. Post-repair survival for AAOCA was 94.5% at 15 years. Clinical follow-up data were available for nearly 75% of the cohort. During a median follow-up of 3.9 years, approximately one-third of patients reported chest pain; however, ischemia screening revealed no correlation between chest pain and the unroofed coronary artery.

No dysfunction of native aortic valves was observed in patients undergoing unroofing as an isolated procedure for anomalous coronary arteries.

The authors concluded that unroofing of intramural AAOCA is a safe technique with low postoperative mortality, even when performed alongside concomitant procedures in previously operated patients. Long-term survival is excellent, with most patients asymptomatic and resuming their lives without limitations.

COMMENTARY:

The 2020 ESC guidelines on congenital heart diseases in adults recommend surgery in symptomatic AAOCA patients with evidence of ischemia in the corresponding territory or high-risk anatomies. Surgery is also recommended for asymptomatic AAOLCA patients with myocardial ischemia or high-risk anatomy. Surgery is discouraged in asymptomatic AAORCA patients without evidence of myocardial ischemia or high-risk anatomy. Traditionally, AAOLCA is considered high risk due to its strong association with sudden cardiac death. However, Jegatheeswaran et al. from the Toronto group demonstrated in a multicenter study that AAORCA accounted for one-third of sudden cardiac deaths related to AAOCA, indicating it should not be considered benign. In fact, in their study, 3 of the 4 pre-hospital cardiorespiratory arrests related to AAOCA involved anomalous right coronary arteries.

The goal of surgery is to address four potential mechanisms of ischemia: 1) slit-like orifice geometry and dynamic stenosis causing pressure loss and turbulent flow; 2) systolic collapse of the thin-walled intramural segment; 3) systolic stretching of the aortic wall at the intramural segment; and 4) extrinsic compression of the interarterial segment between the aorta and pulmonary artery.

This study focused on the unroofing technique, but other approaches not discussed in the article include coronary reimplantation, pulmonary artery translocation, and, as a last resort, coronary artery bypass grafting (CABG). CABG should only be employed when fixed stenosis >50% is present in the anomalous vessel. Otherwise, there is a high risk of early graft failure due to competitive flow, as coronary perfusion impairment in AAOCA is often phasic and physiologically specific, unlike atherosclerotic disease.

The Mayo Clinic's algorithm closely resembles protocols published by other institutions, emphasizing imaging studies and ischemia-provoking tests. This is particularly important for identifying asymptomatic patients post-surgery. Relying solely on the absence of contractility abnormalities during echocardiographic follow-up may lead to false negatives, as these lesions are dynamic. The appropriate screening test remains contentious. Some groups use dobutamine stress echocardiography, nuclear medicine tests, cardiac functional MRI, or, in rare cases, catheterization with fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR). However, no validated data exist for dynamic stenoses. In light of this variability, future efforts should aim to standardize diagnostic procedures and align clinical findings with patient outcomes.

Despite being an insightful study with a large cohort for this rare pathology, several limitations must be acknowledged. The data are retrospective from a single center, potentially limiting generalizability. Clinical follow-up was unavailable for nearly 25% of patients, and the median follow-up period of 3.9 years may underestimate ischemia incidence.

In conclusion, this study provides three key takeaways: unroofing surgery has low short- and long-term mortality; outcomes in pediatric populations are particularly favorable; and AAORCA should not be considered benign.

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Bunty Ramchandani

New responses to the prothrombotic state of Fontan circulation

A multicenter observational study with a control group evaluates differences in thrombin generation in patients with Fontan circulation.

The Fontan pathway represents the surgical solution for all “non-septable” hearts, either due to underdevelopment or the complete absence of a cardiac chamber. In other words, the Fontan procedure is the definitive strategy for managing single-ventricle physiology. Achieving the Fontan stage requires two prior surgeries. In the neonatal period, based on the infant’s primary issue, one of the following procedures is performed:

- Reduced pulmonary flow: systemic-to-pulmonary shunt.
- Reduced systemic flow: stage 1 Norwood.
- Pulmonary hyperflow: pulmonary banding.

Subsequently, at 4-6 months of age, once the initial treatment becomes insufficient, the Glenn surgery (superior cavopulmonary connection) is performed. Finally, between 2 and 4 years of age, the child’s growth allows the Fontan surgery to be carried out.

In his seminal 1971 article in *Thorax*, Francis Fontan clarified the intent of his procedure: “This is not an anatomical correction, which would necessitate the creation of a right ventricle, but rather a physiological restoration of pulmonary flow along with the suppression of left and right blood mixing.” This physiological solution comes at a price, leading to several maladaptations, including an increased prothrombotic state with unclear etiology.

Standard hemostasis tests do not provide sufficient information on coagulation status, particularly in Fontan circulation (FC) patients. In recent years, clinical practice has incorporated new technologies offering a more comprehensive assessment of coagulation. Among these, calibrated automated thrombography (CAT) evaluates the impact of various factors on thrombin formation. This technological advancement underpins the study we analyze today.

This research, conducted by a Polish team, included 81 adult FC patients from three tertiary hospitals. Healthy volunteers aged 18-40 years (n = 54) served as controls. Individuals with elevated total cholesterol levels, suspected thrombophilia, or pregnancy were excluded. To minimize confounding factors, anticoagulant and/or antiplatelet therapies were discontinued with sufficient lead time to obtain baseline hemostatic profiles. Three thrombin formation scenarios were evaluated: the influence of platelets, coagulation factors, and tissue factor derived from microparticles. Interest in microparticles has surged due to their apparent role in thrombus formation in systemic processes, including oncologic, inflammatory, and cardiovascular conditions.

Upon analyzing the data, Skorek et al. observed that 40% of the FC group exhibited thrombocytopenia, while most patients had elevated liver enzymes. Seventy percent

were classified as NYHA functional class II, and half of the cohort was receiving anticoagulant or antiplatelet therapy. These findings align with expectations, including the decreased activity of coagulation factors V, VII, and X reported in FC patients. However, a 185% increase in microparticle-derived tissue factor was identified in the Fontan group ($p < .001$). Platelet influence demonstrated a reduced thrombin formation potential in the FC group ($p < .001$), persisting across subgroups stratified by antiplatelet use and thrombocytopenia ($p < .001$). These results were consistent regardless of systemic ventricle type or anastomosis configuration (extracardiac conduit/intracardiac conduit/atriopulmonary). Conversely, microparticle-derived tissue factor influence indicated greater thrombin formation potential ($p < .001$).

The authors concluded that microparticles, particularly their tissue factor, may significantly contribute to the prothrombotic state in FC.

COMMENTARY:

Interest in FC has risen in the literature, partly due to data emerging from national registries such as those in Australia and New Zealand. We know Fontan survival exceeds 80% at 30 years, with patients often enjoying a good quality of life, engaging in work, and leading nearly normal lives. Most patients will not require further surgical interventions, and fewer than 5% will undergo cardiac transplantation. These registries provide a more contemporary perspective, revealing outcomes better than expected. As a result, a growing cohort of patients with this unique circulation is likely to lead long lives. However, not all outcomes are favorable. Eight percent of these patients will experience symptomatic thrombotic events, with subsequent mortality exceeding 30%. Identifying, understanding, and addressing the complications associated with this circulation is imperative.

Non-pulsatile pulmonary flow, slowed venous return, hepatic congestion, Fontan prosthetic material, hypoxemia, and turbulence at cavopulmonary anastomoses cause endothelial damage. Damaged endothelial cells release microparticles and von Willebrand factor into the bloodstream. This groundbreaking study by Skorek et al. establishes a strong association between these microparticles and the prothrombotic state of FC. Their findings shed light on anticoagulation management in this population, an area with no scientific consensus. The endothelial involvement suggests new therapeutic targets.

Despite its novel contributions, the study has limitations. The sample size is small, although it represents the largest cohort of FC patients in Poland. The FC group is heterogeneous in anastomosis techniques, systemic ventricle types, and baseline medications (some on antiplatelets, others on anticoagulants). Additionally, the lack of follow-up data precludes evaluating the progression of the studied variables.

Thanks to studies like this, we begin to address some unanswered questions, though much remains to be learned regarding optimal treatment for single-ventricle hearts.

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Bunty Ramchandani

Methylprednisolone in Pediatric Cardiac Surgery: The End of a Religion?

A multicenter, prospective, randomized, double-blind, placebo-controlled trial utilizing the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) was conducted to evaluate perioperative prophylactic glucocorticoid use.

Cardiopulmonary bypass (CPB) represents one of the primary sources of inflammation in cardiac surgery. Corticosteroids, synthetic analogs of glucocorticoids, exert anti-inflammatory effects by suppressing various pro-inflammatory genes (cytokines, cell adhesion molecules, enzymes, and receptors). It is logical to hypothesize that glucocorticoid administration might reduce CPB-induced inflammation; however, the scientific evidence remains inconclusive.

Two randomized clinical trials in adults, Dexamethasone for Cardiac Surgery (DECS) and Steroids in Cardiac Surgery (SIRS), demonstrated no benefits from glucocorticoid use. On the contrary, they reported increased risks of myocardial injury and postoperative hyperglycemia. These findings cannot be extrapolated to pediatric populations, as the inflammatory response to CPB differs significantly. Consequently, prophylactic glucocorticoid usage varies considerably across countries, hospitals, and even among practitioners within the same institution.

In this clinical trial, K.D. Hill et al. analyzed 1,200 patients under one year of age undergoing elective cardiac surgery with CPB. Participants were randomized into two groups of 600 patients each: one receiving 30 mg/kg of methylprednisolone (MP) in the CPB priming solution and the other receiving a placebo. MP was selected due to its widespread use in pediatric cardiac surgery. Patients were recruited from 24 U.S. hospitals, all of which participated in the STS-CHSD registry and had undergone stringent quality control audits. The primary endpoint was a hierarchical composite of death, heart transplantation, and 13 other complications. In patients without primary events, secondary endpoints included hospital length of stay.

No statistically significant differences were found in primary or secondary endpoints, except for a reduced rate of reoperation due to bleeding in the MP group (OR = 0.34; p = .016). As an adverse effect, MP was associated with higher postoperative hyperglycemia requiring insulin treatment (19% vs. 6%; $p < .001$). Subgroup analyses revealed statistically significant benefits of MP in patients with lower surgical complexity (STAT 1–3, OR = 0.75), CPB duration >180 minutes (OR = 0.77), and preterm infants (OR = 0.80).

The authors concluded that MP did not significantly reduce adverse postoperative outcomes but led to an increased incidence of insulin-requiring hyperglycemia.

COMMENTARY:

The results of this trial align with those of smaller studies published in the literature. The DECISION trial (Dexamethasone in Pediatric Cardiac Surgery), involving 394 children (85% low-complexity surgeries), found no benefits from glucocorticoid use. Another

study by Graham et al. on 176 neonates undergoing high-complexity procedures reached the same conclusion. However, both studies noted slight advantages, including reduced inotropic support and benefits in palliative surgeries.

Although no global benefits were observed, certain subgroups appeared to derive advantages. Glucocorticoids may provide modest benefits, particularly in surgeries involving prolonged CPB times. Nonetheless, many clinical factors may negate these benefits entirely.

A notable aspect of this trial was its pragmatic cost-reducing design. By utilizing the STS-CHSD database, the trial's cost was reduced to one-third, making it the largest published trial in pediatric cardiac surgery.

Finally, in response to the question posed in the title, this is not the end of prophylactic glucocorticoid use in pediatric cardiac surgery. However, justifying its use will become increasingly challenging.

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Bunty Ramchandani

Aortic Dilatation in Tetralogy of Fallot: A Real Threat?

A single-center, retrospective study conducted by Boston Children's Hospital evaluates the longitudinal progression of aortic root dilatation and the development of aortic regurgitation (AR) based on 60 years of clinical experience.

Tetralogy of Fallot (TOF) is one of the most common cyanotic congenital heart defects, with an incidence of 5 cases per 10,000 live births. A late complication of TOF includes progressive aortic root dilatation and AR. The prevalence of this complication varies widely, depending on the population studied, follow-up protocols, and the stage of life during evaluation. Additionally, the prevalence is influenced by whether measurements are reported as absolute values, indexed values, or z-scores; the specific region of the aorta assessed; and the imaging modality used. Consequently, aortic dilatation prevalence in this population ranges from 7% to 88% depending on these factors. The clinical significance of this dilatation is debatable, as aortic dissection in these patients is exceedingly rare. A study evaluating 18,000 emergency department admissions of adults with TOF reported aortic dissection in only 0.06% of cases. In fact, the literature documents only five deaths due to aortic dissection in this population. This study aims to establish a foundational understanding of the natural history of this late complication, leveraging six decades of institutional experience.

All medical records of patients with TOF repair at Boston Children's Hospital from 1960 to 2022 were reviewed. Patients were categorized into two groups: those with TOF and pulmonary stenosis (TOF-PS) and those with TOF variants, which included TOF with pulmonary atresia with or without major aortopulmonary collateral arteries (MAPCAs). Variants such as double-outlet right ventricle, TOF with atrioventricular canal, and TOF with absent pulmonary valve syndrome were excluded. Echocardiograms performed preoperatively and during follow-up were analyzed. Measurements of the aortic annulus, sinuses of Valsalva, and sinotubular junction were collected, and z-scores were calculated. Longitudinal trends in these parameters were evaluated using linear mixed-effects models.

A total of 2,205 patients underwent TOF repair at a median age of 4.9 months. Among them, 72.9% (1,608 patients) had TOF-PS, while 27.1% (597 patients) had TOF variants. With a median follow-up of 14.4 years (range, 0.1–62.6 years), 313 patients (14.2%) developed mild or greater AR, and 34 patients (1.5%) required interventions involving the aortic valve or root. The mean growth rates of the aortic annulus, sinuses of Valsalva, and sinotubular junction were 0.5 mm/year, 0.6 mm/year, and 0.7 mm/year, respectively, while z-scores remained stable over time. Patients with TOF variants exhibited larger aortic root dimensions compared to those with TOF-PS ($p < .05$). During follow-up, TOF variants demonstrated greater growth of the aortic annulus ($p = .02$), sinuses of Valsalva ($p < .001$), and sinotubular junction ($p < .001$).

High-risk patients, defined as those with measurements above the 75th percentile, had increased incidence rates of mild or greater AR ($p < .001$), moderate or greater AR ($p < .001$), and higher rates of aortic valve intervention ($p = .045$). No cases of aortic dissection or rupture were observed in the entire cohort.

COMMENTARY:

The pathophysiology of aortic dilatation in conotruncal anomalies remains unclear. Early studies attributed the condition to hemodynamic stress on the aortic wall prior to surgical repair. However, intrinsic abnormalities in the aortic wall—including defects in smooth muscle, elastic fibers, and collagen—have also been observed in neonates undergoing early repair, suggesting that prolonged hemodynamic stress is not the sole factor. Regardless of the timing of complete repair, all TOF patients exhibit intrinsic aortic root abnormalities exacerbated by hemodynamic factors that increase stiffness and reduce distensibility, leading to focal smooth muscle loss, cystic medial degeneration, and elastic fiber fragmentation. It is now believed that TOF-related aortic dilatation arises from a combination of hemodynamic and genetic factors contributing to asymmetric development of conotruncal structures.

Applying standard aortopathy guidelines to TOF-related dilatation can lead to misguided clinical decisions. The natural history of TOF-associated aortic pathology differs significantly from conditions like bicuspid aortic valve disease or Marfan syndrome. For instance, TOF variants with pulmonary atresia—representing extreme cases of obstruction—are associated with greater aortic root dimensions due to sustained volume overload and longer periods of hemodynamic stress, as these patients typically undergo palliative procedures before definitive repair.

Despite being an excellent study with the longest longitudinal follow-up of TOF patients to date, this research has limitations. It is a single-center retrospective study with inherent selection biases, particularly as it originates from a quaternary care hospital. Measurement reliability varied over decades as echocardiographic technology evolved. Additionally, z-scores were analyzed only up to the age of 20 years, as these scores are not validated beyond this age.

The study by Sengupta et al. sheds light on the natural history of aortic dilatation and AR in TOF. It highlights the importance of differentiating high-risk variants that require closer surveillance. Most notably, the rarity of dissection and rupture emphasizes the need to avoid over-treatment and to tailor follow-up strategies based on individualized risk profiles.

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Pablo Merás Colunga

Single ventricle without Fontan circulation: the importance of the type of palliation

This multicenter retrospective study analyzes prognostic differences in three groups of single-ventricle patients who, for various reasons, do not achieve Fontan circulation: those with restrictive pulmonary flow (native pulmonary stenosis or banding), superior vena cava-to-pulmonary artery connection (Glenn), and systemic-pulmonary shunts (with or without Glenn).

The term "single ventricle" encompasses multiple anatomies in which two fully developed ventricles capable of sustaining the systemic and pulmonary circulations are absent. These cases represent 7.7% of congenital heart diseases. Currently, the standard surgical solution involves several interventions to separate both circulations, establishing what is known as Fontan circulation, where the systemic venous return from the caval veins is directly connected to the pulmonary arteries, creating a passive pulmonary circuit. However, many patients fail to complete Fontan circulation, remaining at intermediate stages of palliation or even retaining their native anatomy. The prognosis and natural history of these patients are not well described in the literature.

The study by Gordon et al. aims to analyze the survival and complications in these patients, categorized into three groups according to the palliation stage:

- G1: Patients with restrictive pulmonary flow (native pulmonary stenosis or banding).
- G2: Patients with Glenn (superior vena cava-to-pulmonary artery connection).
- G3: Patients with systemic-pulmonary shunts (with or without Glenn).

Patients with Eisenmenger syndrome or segmental pulmonary hypertension were excluded.

A total of 120 patients from seven reference centers in Spain were retrospectively included (mean age 32 years, mean follow-up 7.1 years). Mortality, heart transplant rates, hospitalizations for heart failure (HF), the development of atrial arrhythmias (atrial fibrillation and flutter), and reintervention rates were analyzed. Additionally, clinical, laboratory, and ventricular function parameters were assessed at baseline and follow-up, including their longitudinal changes.

The study population represented 22.6% of the total cohort of patients with single-ventricle physiology. The remaining patients were excluded for having completed Fontan circulation (72.5%) or for being in Eisenmenger physiology (4.9%).

Each group displayed a distinct prognostic profile:

- G3 (systemic-pulmonary shunts, n=35): This group exhibited the worst prognosis, with the highest mortality (34.3%), HF hospitalizations, atrial arrhythmias, and reintervention rates. Baseline ventricular and renal function parameters were worse in this group, and they experienced greater ventricular function deterioration during follow-up.

- G1 (restrictive pulmonary flow, n=55): This group had the lowest mortality (12.7%) and more favorable characteristics, including better ventricular function, functional class, and oxygen saturation.

- G2 (Glenn, n=30): This group presented an intermediate prognosis (mortality 16.7%), with a notably lower incidence of HF hospitalizations.

The authors concluded that the type of palliation in patients with single-ventricle physiology and restrictive pulmonary flow who do not undergo Fontan surgery defines distinct profiles. Patients palliated with systemic-pulmonary shunts have a worse prognosis, with increased morbidity and mortality.

COMMENTARY:

This is the largest study to date on single-ventricle patients with restrictive pulmonary flow who reach adulthood without completing Fontan circulation, establishing several phenotypes with distinct physiology. This classification allows for defining the characteristics and prognosis of each group based on the type of palliation.

One key finding is that this population represents nearly a quarter (22.6%) of single-ventricle patients. Reasons for not completing Fontan were varied and often predictable, such as the presence of pulmonary hypertension, hypoplastic pulmonary branches, or high surgical risk. However, the most frequent reason was patient or family refusal, particularly in patients with restrictive pulmonary flow, likely due to their well-balanced physiology and "stable" clinical status.

The better prognosis observed in G1 may stem from several factors:

1. 75% had a native anatomy with a well-balanced circulation requiring no intervention.

2. The dominant anatomy was double-inlet left ventricle, typically associated with a more favorable prognosis.

3. They were older at the first visit, suggesting a survival bias in this group.

4. Their oxygen saturation was better than patients with Glenn, where upper body circulation flows directly into the lungs without systemic mixing, reflecting good hemodynamic balance.

The poorer prognosis in G3 may be explained by greater baseline cyanosis and both systolic and diastolic volume overload due to systemic-pulmonary shunts (compared to systolic overload alone in G1). This likely leads to greater ventricular dilatation and dysfunction, increased arrhythmias, HF, and ultimately higher mortality.

Mortality was high across all groups (20% overall), highlighting the need for caution when managing these patients, regardless of palliation type. HF and atrial arrhythmias (31.7% and 17.5%, respectively) were also common. Despite the high mortality, the proportion of transplants (8.3%) seems low, particularly given that patients with native anatomy might be good candidates with potentially suitable anatomical and hemodynamic characteristics.

Sudden cardiac death (38%) and HF (33%) were the leading causes of mortality, with no differences between groups. Risk stratification and sudden death prevention in these patients remain complex, as causes may extend beyond ventricular arrhythmias. The inherent anatomical limitations of this population also challenge device implantation.

The primary limitation of the study lies in its retrospective design, with potential confounding and information biases, as well as the inclusion of a highly selected population of adult survivors, introducing survival bias.

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Bunty Ramchandani

Management of adults with anomalous aortic origin of the coronary arteries

Systematic review and critical appraisal of evidence on the treatment of adults with anomalous aortic origin of the coronary arteries.

Advances in imaging techniques and the widespread adoption of screening protocols have led to a significant increase in the diagnosis of anomalous aortic origin of the coronary arteries (AAOCA) in recent years. Patients with AAOCA may present with a wide range of clinical manifestations, making diagnosis challenging and sparking debates regarding treatment, particularly in asymptomatic individuals. While various management approaches exist for this condition, there is no consensus on the optimal treatment strategy. In today's article, a group of 23 experts in the field created a consensus document after reviewing 158 publications.

One of the primary challenges faced is the lack of consensus on nomenclature used to describe these anomalies. Consequently, there is no standardized approach to identifying, describing, or classifying them. For example, articles using Angelini's classification may differ significantly from those employing the 11th edition of the International Classification of Diseases. The prevalence of AAOCA in the general population is less than 1%. These anomalies may occur in isolation or in association with syndromes. For instance, they are observed in 6% of patients with tetralogy of Fallot and are twice as common in bicuspid aortic valves compared to tricuspid valves. An association with connective tissue disorders, such as Marfan syndrome, has also been documented. Depending on the source, prevalence rates vary from 0.6% (in autopsy series of sudden cardiac death) to over 5% in noninvasive screening protocols. The most common form is the anomalous origin of the circumflex artery from the right coronary artery or the right sinus of Valsalva. A study of more than 5000 adolescents found that anomalous origin of the right coronary artery from the left sinus of Valsalva (R-AAOCA) was three times more common (0.33%) than anomalous origin of the left coronary artery from the right sinus of Valsalva (0.12%).

The primary concern with these anomalies is not the anomalous origin itself but the potential mechanisms of ischemia they may induce, which can be fixed or dynamic. Fixed stenoses involve ostial narrowing or proximal coronary narrowing, while dynamic stenoses are associated with coronary spasm and/or the intramural or intramyocardial course of the artery. Traditionally, interarterial compression between the aorta and pulmonary artery was believed to be a key mechanism of ischemia. However, recent studies challenge this hypothesis, identifying the intramural segment as the true ischemic mechanism. Under conditions of increased cardiac output, such as stress, dynamic compression of the intramural portion of the coronary artery occurs, reducing the cross-sectional area of the typically oval-shaped vessel. Combined with increased flow resistance due to Hagen-Poiseuille's law, this leads to distal hypoperfusion and myocardial ischemia. Ostial abnormalities, such as slit-like ostia, hypoplastic ostia, or a coronary takeoff angle of less than 45º (which may act as an intermittent valvular obstruction), also pose high risks for ischemia.

In non-coronary cardiac surgeries, the presence of AAOCA and its variants must be identified. The most common scenario arises in bicuspid aortic valve surgeries, where the circumflex artery may originate from the right sinus of Valsalva and take a posterior course toward the atrioventricular groove, posing a risk of injury during aortotomy. Additional challenges include inadequate myocardial protection and potential coronary

compromise by prosthetic sutures. Cases of circumflex artery compression following transcatheter aortic valve implantation have also been described.

To assess the risk associated with a specific AAOCA variant, comprehensive imaging studies are essential. Invasive modalities, such as catheterization with intravascular ultrasound (IVUS), enable functional assessments. However, noninvasive modalities, such as computed tomography (CT), have gained prominence due to their submillimeter spatial resolution, allowing detailed visualization of the origin, course, luminal narrowing, and atherosclerosis. Magnetic resonance imaging (MRI) offers a radiation-free alternative, albeit with limitations such as susceptibility to metallic artifacts and lower spatial resolution. Echocardiography is primarily used in pediatric populations and is not recommended for AAOCA evaluation in adults. For functional analysis, European guidelines explicitly recommend non-pharmacologic imaging tests. Exercise-based or dobutamine stress tests are generally preferred, as they better reflect dynamic coronary flow behavior. While perfusion imaging holds promise, there is no consensus on its protocols, and most studies focus on left ventricular perfusion, with right ventricular perfusion remaining an area for further validation. CT-derived fractional flow reserve is a promising technique, although its application in AAOCA requires further validation. Computational models simulating fluid-structure interactions are emerging as tools to predict coronary flow anomalies and potential solutions.

Both European and American guidelines agree on treating symptomatic patients or those with evidence of ischemia. European guidelines go a step further, recommending surgery in asymptomatic patients with high-risk anatomies (Class IIa recommendation), while American guidelines assign a lower recommendation level (Class IIb). Clinical evaluation of ischemia must consider the AAOCA variant, the patient's age and activity level (sudden cardiac death risk is higher in individuals under 30), surgical risks, and patient preferences. Anxiety related to sudden cardiac death or the implications of this anomaly in competitive athletes can significantly influence decision-making.

Various surgical techniques are tailored to address the specific mechanisms of ischemia in AAOCA. The most common procedure is "unroofing" for intramural AAOCA, which may include creating a neo-ostium in cases involving the commissure. In centers with experience, surgeons may detach the aortic commissure, perform unroofing, and resuspend the commissure. Ostial stenosis due to hypoplasia or an acute takeoff angle may be corrected with ostioplasty, while reimplantation of the coronary artery into the appropriate sinus is another option. For extrinsic compression caused by the pulmonary artery, lateral translocation or the LeCompte maneuver may be performed. Transseptal AAOCA may require transconal or transinfundibular unroofing. In select cases, surgical revascularization may be employed, although it is not a first-line option due to the dynamic nature of ischemia, which could compromise graft function. Percutaneous treatment is limited by a 13% in-stent restenosis rate at 5 years and should be reserved for non-surgical candidates.

COMMENTARY:

Today's review article is essential reading for anyone seeking a quick update on the literature surrounding AAOCA. With its iconography and schematic tables, it covers the diagnostic and therapeutic algorithms for these coronary anomalies comprehensively. However, it is worth emphasizing that a significant proportion of AAOCA cases involve multilevel obstructions, and failure to address all levels may result in persistent or recurrent ischemia. Beyond the anatomy of the coronary ostium and the AAOCA course, it is crucial to identify myocardial bridges, which coexist in up to 5% of cases. Failure to

treat these segments negates the benefits of other techniques used to repair the proximal segment. For unroofing procedures, it is critical to adequately release the coronary exit from the aorta to effectively address the intramural segment's ischemic mechanism. Insufficient release renders the length of unroofing futile.

Advances in imaging modalities have illuminated the complexity of this pathology. As a result, it is imperative that these patients are treated in referral centers with multidisciplinary teams experienced in imaging, congenital heart disease, and surgical techniques. Customization of surgery is paramount in this condition.

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Section IV:

Heart transplant, heart failure and mechanical circulatory support

Alessia Miraglia

New Horizons for Heart Transplantation: The American Experience with HCV-Positive Donors

A prospective cohort study at the Medical University of South Carolina analyzed the United Network for Organ Sharing (UNOS) database to assess mid-term survival in patients receiving transplants from hepatitis C virus (HCV)-positive versus HCV-negative donors.

Spain has long stood out globally for its leadership in organ donation. In 2021, Spain and the United States led worldwide transplant rates, with 102.4 and 126.8 transplants per million people, respectively, according to the latest report from the World Observatory on Donation and Transplantation (September 2022). Nevertheless, transplant waiting lists, particularly for heart transplants, are often saturated, leading to numerous patient deaths while awaiting organs. In efforts to increase the donor pool, reduce bridge-to-transplant therapies, and decrease waitlist mortality, recent decades have seen expanded donor age criteria, inclusion of new donor profiles, such as diabetic individuals, and more recently, acceptance of HCV-positive (HCV+) donors.

Kwon et al. discuss this subject in their recent article published in *Annals of Thoracic Surgery*, presenting a prospective cohort study conducted at the Medical University of South Carolina that analyzes the UNOS database. Data from 1,170 transplants (7% of total heart transplants) involving HCV+ donors were collected between March 2015 and June 2021. Exclusion criteria included recipients under 18, multiorgan transplants, and non-HCV recipients. Donor criteria were HCV+ based on antibody presence and/or viral load, with the majority being brain-dead patients who had suffered opioid overdose. Among the 1,170 transplants performed, 772 recipients (62.7%) were HCV+ prior to the transplant. The primary outcome was 1-year post-transplant survival, with secondary outcomes including 3-year survival, dialysis rates, stroke, adverse drug reactions before rejection and/or within the first year post-transplant. Statistical analyses included Cox multivariable regression and Kaplan-Meier survival curves. Analyzing total heart transplants within the study period (n=16,648), a significant rise in HCV+ transplants was observed, increasing from 0.12% to 12.9% (Pearson correlation coefficient r = 0.967, $p < 0.001$). Notably, HCV+ recipients experienced reduced waitlist time (58 vs. 71 days, $p < 0.004$), consequently minimizing bridge therapy duration. Unadjusted 1- and 3-year survival rates showed no statistically significant differences between HCV-negative and HCV+ recipients. Risk-adjusted rates confirmed similar outcomes, demonstrating that donor HCV+ status did not affect patient mortality.

In conclusion, this study demonstrates that recipients of hearts from HCV+ donors have mid-term survival outcomes comparable to those receiving hearts from HCV-negative donors.

COMMENTARY:

Although based on American registry data, this study is the largest to date in terms of follow-up duration and patient inclusion. However, it has limitations: heart transplants using HCV+ donors is a relatively recent practice in the United States, meaning that most patients included in the analysis had not reached the 3-year follow-up by the study's end date. Consequently, ongoing follow-up is essential to ensure long-term safety. Another limitation is that the study was conducted during the SARS-CoV-2 pandemic, where emergency conditions may have influenced donor profiles, transplant volume, and outcomes.

Compared to other organ transplant types, the number of heart transplants remains stagnant, primarily due to the scarcity of suitable organs (according to Colvin et al., the number of donors remains less than half of the patients on the waiting list). Thus, identifying new strategies to increase the availability of viable organs is critical.

Beyond survival outcomes, the most innovative aspect of this study lies in evaluating the potential of expanding the donor pool to include HCV+ donors. Historically, active HCV infection was an exclusion criterion due to the lack of effective treatments. However, thanks to the development of new antiviral drugs over the last decade, we can now treat HCV infection with cure rates close to 95%. Supported by emerging data from studies in Spain, we may expect an increase in this type of donor in future heart transplant waitlists.

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José Manuel Martínez Comendador

Donor after Cardiac Arrest for Heart Transplantation in the United States: Hope Becoming Reality

This study compares the use and outcomes of heart transplants utilizing donation after circulatory death (DCD) versus donation after brain death (DBD) in the United States.

Heart transplantation (HT) is an effective technique for patients in the end stage of heart failure. Unfortunately, its use is limited by a shortage of donor hearts, resulting in a waitlist mortality rate exceeding 30% per year. Most heart donors are patients whose circulatory function remains intact after the diagnosis of brain death, known as donation after brain death (DBD). Recently, another type of donor, where donation occurs after circulatory death, known as controlled DCD, has become available. These donors suffer irreversible brain damage but do not meet the criteria for brain death, meaning their lives are sustained by mechanical respiratory and circulatory support. The decision to withdraw this support is made independently of their potential as organ donors. In DCD, death is diagnosed after a specific period following the cessation of spontaneous breathing and circulation, without natural resumption. The required period for confirming death varies by different agencies and governing bodies overseeing organ donation.

In recent years in the United States, the increase in DCD has significantly raised the number of kidney, liver, pancreas, and lung transplants, representing about one-quarter of all donors. However, its utilization in heart transplantation has been limited due to technical and ethical reasons, with recent reintroduction aimed at expanding donor availability.

To examine the use and outcomes of heart transplants in these cases, a nationwide study was conducted using the United Network for Organ Sharing (UNOS) database. A total of 266 adult patients who received DCD heart transplants were identified and compared with 5,998 DBD transplants, using a propensity score–adjusted model for group balancing. Cardiopulmonary transplants were excluded from the study. During the period from December 2019 to December 2021, the monthly percentage of DCD HT increased significantly from 2.5% to 6.8% ($p < 0.001$). Twenty-two centers performed these transplants, ranging from 1 to 75 transplants per center. Four centers accounted for 70% of the national volume. Recipients of hearts from DCD donors demonstrated greater clinical stability compared to DBD recipients (80.4% vs. 41.1% in status 3-6, respectively; $p < 0.001$). Additionally, recipients of DCD hearts were more likely to have type O blood (58.3% vs. 39.9%; $p < 0.001$) and to have waited longer after being listed (55 days vs. 32 days; $p = 0.003$). No significant differences were found in six-month survival between the two groups, with a survival rate of 92.1% for DBD transplants and 92.6% for DCD transplants. Outcomes in propensity score–matched patients were similar, except for higher rates of treated acute rejection in DCD transplants prior to discharge (14.4% vs. 8.8%; $p = 0.01$). Furthermore, the outcomes of DCD heart recipients did not differ based on procurement and preservation techniques used, with outcomes remaining consistent between simple retrieval and normothermic regional perfusion (NRP).

According to the study authors, DCD HT is comparable to DBD transplantation in terms of short-term survival. Furthermore, broader implementation of this donation technique could significantly enhance organ availability for transplantation.

COMMENTARY:

The history of DCD HT began in 2004, but it was not until 2015 that the first series was published in Australia using a protocol for rapid surgical heart explant and subsequent preservation in an ex situ perfusion device (Organ Care System® [OCS®] by Transmedics®). The United Kingdom also developed a similar protocol, with the option to perform NRP after diagnosing the donor's death, using an extracorporeal membrane oxygenation (ECMO) device. In both series, short- and long-term survival was comparable to DBD HT series. Subsequently, other groups published cases of DCD HT using a modified protocol involving peripheral cannulation before donor death, NRP, and static cold preservation after explantation without using an ex situ perfusion device, also yielding excellent results.

This American registry suggests that six-month survival rates and in-hospital adverse events are similar for DCD and DBD HT. These figures align with results from previous registries in the United Kingdom and Australia. Although patients selected for DCD transplantation had lower baseline risk, were younger, and had better ejection fraction than DBD patients in the study by Chen et al., after propensity score adjustment, both heart donation techniques achieved similar short-term survival. This supports the theory that the warm ischemic period experienced in DCD does not significantly impact post-transplant outcomes when donors and recipients are properly selected. However, for the first time, a higher rate of treated acute rejection before discharge in DCD transplants is reported. The lack of information on pretransplant sensitization status and other relevant data prevents full validation of these findings.

In practice, two techniques are currently used to retrieve DCD hearts for transplantation: simple retrieval and NRP, both with static cold or ex situ perfusion preservation using the OCS® device. Evidence on which method is superior is limited. The ongoing US DCD Heart Trial only uses simple retrieval with ex situ perfusion. European centers that used NRP achieved 100% short-term survival, though with primary graft dysfunction between 12-60%. In the UK, one-year survival was 100% with NRP compared to 91% with simple retrieval. In the OCS Heart EXPAND study, which uses the OCS® system after DBD donation, 30-day and six-month survival rates were 94.7% and 88%, respectively. In the study by Chen et al., while no significant differences were observed, NRP had a lower organ rejection rate compared to simple retrieval. Remaining outcomes were similar with both techniques.

The findings of this registry are of critical importance, reinforcing and confirming that DCD HT, along with other published registries in Europe and Australia, constitutes a viable alternative with outcomes comparable to DBD HT. Nonetheless, this study has some limitations, including a follow-up period for transplanted patients that is too short to draw conclusions on long-term outcomes. Additionally, there is no information on times between asystole and reperfusion, which could be a key factor in post-surgical outcomes. Exact total ischemia times are also unknown, as some organs were perfused with an ex situ perfusion platform, which cannot be considered true ischemia. Lastly, for classification purposes, it was assumed that those patients with intervals of less than 15 minutes between death and aortic clamping had undergone simple retrieval, while the rest underwent NRP, though this assumption is not precise.

In Spain, a national DCD HT protocol has recently been established, endorsed by the Standing Commission for Transplant of the Interterritorial Council of the National Health System. This protocol primarily involves peripheral ante mortem cannulation, NRP, and static cold preservation prior to implantation. The first DCD HT using this protocol was performed in Spain in January 2020, and since then, more than 60 DCD HTs have been carried out across 12 different Spanish centers, adding to the over 295 procedures

conducted in six European countries. Initial published results support the positive DCD outcomes described in this article. Additionally, the NRP cardiac preservation technique used in DCD in Spain offers numerous advantages, such as reducing ischemia-reperfusion injury and enabling multiple organ preservation simultaneously, avoiding costly ex situ preservation techniques. Furthermore, it allows for elective organ retrieval and evaluation before extraction.

It is believed that DCD HT could increase transplant activity by 10-15% in Spain, making it a real and viable alternative to meet the growing global demand for organs. Optimism is the hope that leads toward achievements, and in this case, with this new cardiac donor modality, we can say that hope is becoming reality.

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José Cuenca Castillo

New Prioritization Criteria for Heart Transplantation in Spain: Expert Opinion

An expert commentary by Dr. J. Cuenca on the past, present, and future of prioritization criteria for heart transplantation in Spain, recently updated in April 2023.

All organ transplant programs must continuously review their allocation criteria, prioritizing patients in the most critical clinical condition, provided they maintain a high probability of success after the procedure to prevent futility in such a limited resource.

Each year, all Spanish heart transplant (HT) teams meet with the National Transplant Organization (ONT) to ratify or modify the criteria for the distribution of donor hearts, for both adult and pediatric HT. Over the years, and with the aim of meeting the objective outlined above, several modifications to these criteria have been implemented, the most recent being in 2017.

In June 2022, a consensus conference was held at Casa del Corazón in Madrid, organized by the Heart Failure Association of the Spanish Society of Cardiology (SEC) and the ONT, with the participation of cardiologists, cardiac surgeons, and transplant coordinators from hospitals, regional organizations, and the ONT itself.

The objectives of this consensus conference were:

To analyze the current organization and management of patients with advanced heart failure and cardiogenic shock in Spain.

To conduct a critical review of HT distribution and urgency criteria applied in other countries.

To assess outcomes in Spain concerning patients on the waiting list, donors utilized, and post-HT clinical results, following the 2017 revision of HT urgency criteria.

To establish a national protocol for cardiac donation after circulatory death.

To propose new prioritization criteria for HT in Spain.

At the conference, for each of these objectives, multidisciplinary working groups were formed with representation from transplant centers and the ONT. These groups developed reports and their conclusions by the end of 2022. A summary of these reports and conclusions will be published in an upcoming issue of *Revista Española de Cardiología*.

In February 2023, the customary meeting between Spanish HT groups and the ONT took place at the ONT facilities to discuss the working group's proposal and agree on the "2023 HT Distribution Criteria in Spain," which took effect on April 1, 2023.

The prioritization criteria adopted represent the most profound change ever made compared to the previous standards. Notably, there is now an objective definition of "multiorgan failure (MOF)," as its presence leads to either temporary exclusion or inability to be listed for HT. MOF is defined by the presence of any of the following five criteria:

A score >11 points on the SOFA (Sepsis-related Organ Failure Assessment) scale for 48 hours. A patient with a creatinine level of 2.1 mg/dL, bilirubin level of 2.1 mg/dL, 90000

platelets/mm³, PaO_2/FiO_2 < 300 mmHg, and norepinephrine dosage of 0.2 mcg/kg/min would meet this criterion.

Patients on invasive mechanical ventilation (IMV) for seven consecutive days, except for patients in electrical storm.

Acute or chronic renal failure requiring renal replacement therapy (RRT), except cardio-renal transplant candidates and patients with anuric acute tubular necrosis following at least four weeks of short-term mechanical circulatory support, prior glomerular filtration rate >60 mL/min, and a SOFA score <6 points. Ultrafiltration for managing patient volemia is not considered RRT.

Patients on IMV for more than five days who, after extubation, exhibit critical illness myopathy, defined by a score <36 points on the Medical Research Council (MRC) scale.

Patients on circulatory support and vasoactive drugs with a vasoactive-inotropic score (VIS) >20 points. This score is reached with an isolated dose of 0.2 mcg/kg/min of epinephrine or norepinephrine, or with 5 mcg/kg/min of dobutamine and 0.15 mcg/kg/min of epinephrine or norepinephrine.

The second significant change in the new criteria refers to the classification within the highest prioritization level. In the absence of MOF, Urgency O is divided into two grades: OA for patients supported with veno-arterial ECMO or biventricular mechanical assistance and patients with long-term ventricular assist devices (LVAD) experiencing severe mechanical dysfunction or thromboembolic complications, and grade OB for patients supported with short-term univentricular full-support circulatory assist devices (such as Centrimag®, Impella® 5.0, 5.5, or CP if the patient has a body surface area <1.7 m²) and patients with refractory electrical storm (three or more episodes of at least five minutes within 24 hours, requiring cardioversion or pacing and unresponsive to treatment within four days) without circulatory assist device support.

Thirdly, priority level 1 (third clinical severity level) has been expanded to include not only LVAD dysfunction due to driveline infection, persistent gastrointestinal bleeding, or severe right ventricular dysfunction but also certain uncommon yet challenging clinical situations. These include adult patients with univentricular physiology requiring continuous intravenous treatment, adult Fontan surgery patients with severe protein-losing enteropathy, and patients with cardiomyopathies with reduced cardiac chambers who are not candidates for mechanical assist devices.

As previously mentioned, this is the most profound modification made to date in HT prioritization criteria. Its purpose, developed through a multidisciplinary consensus conference, is to prioritize patients in the most critical clinical situations without reaching the MOF threshold, aiming to optimize the efficient use of the highly limited resource that is the donor heart.

For future analysis of the impact of these new HT prioritization criteria in Spain, it is essential to remember some figures and their evolution over recent years, examining the results of the 2017 changes, which serve as a starting point for future analysis.

According to data from the 2022 Spanish Heart Donation and Transplant Activity Report, the number of HTs in Spain peaked in 2000 with 353 implants (8.9 per million population). The enactment of the new Road Safety Law in Spain, fortunately, led to a significant decline in donors from brain death due to traumatic brain injury, resulting in a decrease in HT numbers, reaching a low in 2011 with 237 implants (5.0 per million population).

Since then, activity has slowly but steadily increased due to a greater use of hearts from donors after brain death secondary to stroke and, over the past two years, controlled circulatory death donations. In 2022, 311 procedures were performed (6.6 per million population).

From 2013 to 2018, between 45-49% of heart transplants in Spain were performed on an urgent basis. This figure has decreased significantly since 2019, possibly influenced by the 2017 changes in HT prioritization criteria, dropping to 38%. Although these percentage changes have not significantly altered the likelihood of transplantation for a patient listed as urgent, which has remained between 75-80% over the past 10 years, there has been an increase in the probability of transplantation for a patient listed as elective. This probability has risen from an average of 40% until 2016 to 50-55% since then.

Analyzing the results, survival rates from 2013 to 2022 are 81.4% one year post-transplant and 73.4% at five years, significantly higher than those observed in the earlier series. There has been no statistically significant improvement in survival over the last decade; however, there is a constant numerical improvement in one-year survival: 79.7% in the period 2013-2015, 81.7% in 2016-2018, and 82.2% in 2019-2021.

Clinical outcomes over the coming years will allow us to evaluate whether this modification of HT distribution and prioritization criteria in Spain has been an effective tool in achieving a difficult balance between accessibility and futility for this complex therapy.

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José Manuel Martínez Comendador

Spanish Heart Transplant Registry 2022: Stabilization in Characteristics and Outcomes

This article analyzes the results of the Spanish Heart Transplant Registry for 2022, including trends since 2013. The Spanish Heart Transplant Registry is dedicated to annually updating its most crucial data. This article details the most significant clinical characteristics, treatments administered, and outcomes related to the survival of procedures conducted in 2022. Additionally, trends in these aspects since 2013 are explored.

In 2022, a total of 311 heart transplants were performed, representing a 3% increase from the previous year. No significant changes in demographic and clinical characteristics were observed compared to prior years, supporting trends identified over the past decade. These trends highlight a reduction in urgent procedures and an increase in the use of pre-transplant circulatory support, particularly with ventricular assist devices. Over the last decade, survival rates reached 81.4% at one year and 73.4% at three years, showing numerical improvements that, while not statistically significant, are promising.

These results lead the authors to assert that, over the past decade, stabilization has been observed in the characteristics of heart transplant procedures and their outcomes.

COMMENTARY:

The 2022 Spanish Heart Transplant Registry stands out compared to the two previous years for being entirely free from the impacts of the SARS-CoV-2 pandemic. This period translated only into a slight increase in the total number of transplant patients without affecting outcomes. Consequently, we can assert that the experience and resilience of the Spanish heart transplant system enabled it to overcome the challenges of the pandemic in terms of activity and outcomes.

Analysis of temporal trends reveals the consistency of heart transplantation in Spain regarding the characteristics of recipients, donors, surgical procedures, and immunosuppressive treatments.

In recent years in Spain, most heart transplant recipients are men, representing approximately 75% of cases, with an average age close to 50 years. Additionally, in over one-third of cases, these patients undergo transplants urgently, often relying on pre-transplant ventricular assist devices, with a plateau or slight reduction in the use of VA-ECMO. This significant reduction in urgent transplants over the last four years is a clear outcome of the changes in the waitlist inclusion criteria implemented in July 2017. Furthermore, in half of the cases, transplants are performed with donors typically considered suboptimal.

A notable feature, infrequently discussed among cardiologists but particularly relevant to surgeons, is the significant increase over time in the percentage of transplant patients with previous cardiac surgeries. A decade ago, this rate was 37%, and it has now risen significantly to 47%, meaning nearly half of today's transplants are reoperations, a fact of great importance. The intrinsic technical complexity of a reoperation entails higher morbidity and mortality in cardiac surgery, and heart transplants are no exception. Unfortunately, the registry does not detail information about these reoperations, which are becoming more common in heart transplant surgery, at least in Spain. Further study of this aspect would be beneficial for additional insights.

In terms of recipients, there is a trend toward more selective patient criteria. These patients present lower rates of diabetes, reduced hyperbilirubinemia, and shorter mechanical ventilation times. Additionally, progressive reductions in ischemia times reflect the outstanding coordination and dedication of organ procurement teams.

With the recent implementation of the "Criteria for Heart Transplant Distribution in Spain 2023," detailed in a recent blog post and effective April 1, 2023, the most significant change to date in prioritization criteria for heart transplants has been introduced. This change, born from a multidisciplinary consensus conference, primarily aims to prioritize patients in more critical clinical conditions, preventing them from reaching multi-organ failure thresholds and optimizing the efficient use of the scarce resource that is the donated organ. Only through continuous monitoring of clinical outcomes in the coming years can we conduct a thorough analysis to assess whether this modification has proven effective in balancing accessibility and futility in transplantation.

It is crucial to highlight initiatives aimed at expanding donor availability. First, the performance of ABO-incompatible heart transplants has increased, alleviating the shortage of pediatric donors. Furthermore, as previously discussed in blog posts, since late 2020, circulatory death donation has been implemented in nine centers in Spain, including our own. This approach is experiencing exponential growth and is set to significantly transform and expand the donor pool in our country.

Finally, it is highly likely that we have reached a peak in survival rates, slightly above 80% in the first year, as evidenced by the last decade's analysis. However, further improvements are conceivable, potentially linked to the growing experience of newly incorporated groups in ventricular assist programs, the ongoing implementation of the recent organ distribution criteria, or the expansion of circulatory death donation. Each of these advances holds the promise of a miracle, reminding us that each heart transplant is a gift of life that provides a new opportunity to dream and live fully.

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Juan Esteban de Villareal Soto

Use of Donor Hearts for Recipients Over 70: Expanding the Donor Pool Amidst Increased Life Expectancy

A retrospective analysis of the United Network for Organ Sharing (UNOS) database was conducted in the United States, comparing septuagenarians receiving donor hearts from individuals younger than 50 with those receiving from donors aged 50 and older, employing propensity score matching.

Advancements in heart failure therapies have extended patient longevity, thereby raising the age at which advanced interventions, such as heart transplantation (HTx) or durable left ventricular assist device (LVAD) implantation, may become necessary. In the United States, life expectancy stands at 73.5 years for men and 79.3 years for women, which is lower than in Spain, where life expectancy is 81.8 years for men and 87 years for women.

Daniel et al. assessed HTx recipients over 60 in the UNOS dataset from 2004 to 2013, noting reduced post-transplant survival in those receiving hearts from donors around 50. Other pre-existing studies support the benefit for HTx candidates in receiving hearts from donors over 40, rather than remaining on the waitlist. Similarly, Laks et al., in 1990, pioneered an "alternative" waitlist concept, where recipients over 65 could receive hearts from donors older than 55.

This study aims to evaluate outcomes for septuagenarian HTx recipients who received hearts from donors below and above 50. Data were sourced from the UNOS database between January 2011 and December 2021, yielding 989 HTx recipients over 70, with multiorgan recipients or re-HTx cases excluded. Propensity matching yielded 167 pairs based on 14 characteristics: age, sex, race, ABO blood group, body mass index, diabetes mellitus, hemodialysis, smoking status, ischemic or non-ischemic etiology, prior cardiac surgery, total bilirubin, ECMO support, prior intra-aortic balloon pump (IABP) or LVAD use. The median follow-up was 1288 days for donors under 50 and 1447 days for those over 50.

In the <50 donor group, mean donor age was 30 years, while it was 54 in the ≥50 group. No significant differences were observed in postoperative cerebrovascular accident (CVA), hemodialysis, or pacemaker implantation. Thirty-day mortality was 4.8% in recipients of <50 donors versus 3.6% in those with ≥50 donors ($p = 0.59$). Survival rates and graft failure were similar across groups. Post-matching, survival at 1 and 5 years was 88.0% and 79.2% for <50 donors, compared to 87.2% and 72.3% for ≥50 donors, respectively ($p = 0.41$). Infection, COVID-19 (2019), and CVA were among the primary causes of death. Waitlist mortality at 30 and 90 days was 3.0% and 6.0%, respectively, with an increase in transplants ($p < 0.001$) and a tendency towards lower waitlist mortality or delisting ($p = 0.097$). The primary cause of donor death differed by age group, with traumatic brain injury and anoxia predominant in donors <50, while cerebrovascular disease was most common in donors ≥50 ($p < 0.001$).

The study's main finding indicates that donor hearts aged ≥50 are safe for use, with comparable post-HTx survival among septuagenarians regardless of donor age. Improved outcomes over time reflect advancements in donor-recipient matching and understanding of the physiological versus chronological age of recipients.

COMMENTARY:

This study provides insight into the future of HTx, highlighting changes already made in the U.S. waitlist system; a 70-year-old patient with heart failure and shock requiring IABP support may now receive urgent priority on the waitlist (UNOS Status 2), whereas the previous protocol would have limited them to LVAD destination therapy.

Thus, this study offers a potential approach to an issue of particular importance in HTx: expanding the donor pool without compromising medium- and long-term outcomes. Accepting older donor hearts for older recipients expands the donor pool without affecting HTx outcomes, while also reducing waitlist time. Furthermore, it decreases the rejection rate of hearts that may be suboptimal for younger recipients but suitable for older candidates.

Comparable survival at 1 and 5 years with hearts from donors under and over 50 aligns with similar findings in Spain, where older donor organs are accepted. Additionally, non-cardiac causes, such as infections and malignancies, are primary causes of mortality among elderly HTx recipients, supporting the notion that using older donor hearts does not compromise HTx outcomes.

This study has limitations associated with retrospective analyses of national databases. Early post-HTx outcomes, such as primary graft dysfunction, mechanical circulatory support requirements, respiratory failure, or acute kidney injury not requiring dialysis, are unavailable for analysis. Additionally, national database studies are susceptible to errors in variable coding and data entry, a limitation inherent to this study type.

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Carlota Hernández Díez

Acute Heart Failure and Valvular Disease: A Glimmer of Hope

A position paper by the European Society of Heart Failure, the Association of Acute Cardiovascular Care, and the European Association for Percutaneous Cardiovascular Interventions addresses the challenges in managing acute heart failure (AHF) with associated valvular heart disease (VHD).

Acute heart failure (AHF) encompasses a wide spectrum of conditions resulting from the interplay between pre-existing cardiac disease and various precipitating factors. VHD often coexists with AHF, either due to chronic valvular disease exacerbated by one or more triggers or due to newly acquired valvular dysfunction. Clinical presentations vary widely, ranging from mild heart failure decompensation to acute pulmonary edema or cardiogenic shock. Despite the prevalence of this overlap in clinical practice, current heart failure guidelines lack specific recommendations for these patients. They are frequently excluded from clinical trials, and much of the evidence available stems from observational studies. This position paper attempts to clarify this area, reviewing the epidemiology, pathophysiology, diagnosis, and management of VHD in AHF.

Valvular disease accounts for approximately 10-20% of AHF admissions, with aortic stenosis and mitral regurgitation (both primary and secondary) being the most common. The presence of moderate-to-severe VHD and pulmonary hypertension portends a worse prognosis, characterized by higher rates of rehospitalization and mortality. While valvular disease generally progresses gradually, acute decompensation can be triggered by factors such as anemia, renal failure, arrhythmias, or acute coronary syndrome. These precipitating factors may also cause functional valvular conditions, such as secondary mitral and tricuspid regurgitation. Newly acquired valvular diseases, particularly valvular endocarditis and aortic dissection, demand prompt diagnosis and specific management. In some cases, the typical murmur may be absent due to rapid intracardiac pressure equalization, underscoring the importance of transthoracic and especially transesophageal echocardiography for diagnosis. In specific cases, such as prosthetic valve thrombosis, endocarditis, or aortic dissection, computed tomography (CT) plays a key role in diagnosis. Among patients with prosthetic valves, dysfunction due to thrombosis, endocarditis, or degeneration often leads to significant clinical intolerance. Multivalvular involvement, seen in approximately 20% of cases, complicates both diagnosis and prognosis, especially in assessing the severity of individual valve lesions.

Regarding treatment, this position paper reviews the use of medications such as diuretics, vasodilators, inotropes, vasopressors, and antiarrhythmics tailored to each type of valvular lesion. It emphasizes the importance of airway management, oxygenation, and the use of invasive and non-invasive mechanical ventilation when indicated. In patients with refractory heart failure or cardiogenic shock, short-term mechanical circulatory support is preferred to reduce reliance on inotropes and vasopressors, minimizing their adverse effects. However, these devices are contraindicated in patients with significant aortic insufficiency. Finally, the authors discuss invasive treatment options, including surgery versus transcatheter interventions, specific to each valvular pathology. Certain clinical scenarios require surgery as the sole option, sometimes emergently (e.g., aortic dissection, papillary muscle rupture, or endocarditis with AHF). Conversely, transcatheter techniques, especially transcatheter aortic valve implantation (TAVI) and edge-to-edge percutaneous valve repair (mitral and tricuspid), are gaining prominence in acute cases, though supporting evidence remains limited but growing. The authors recommend a multidisciplinary Heart Team approach to evaluate these complex cases.

COMMENTARY:

This document is particularly timely, given the lack of guidance in the 2021 heart failure guidelines regarding VHD in acute heart failure, with current recommendations more suited to chronic scenarios. Until the anticipated update to these guidelines is published, this position paper provides valuable insights. However, while the discussion on pathophysiology is comprehensive, more specific guidelines on the role of various diagnostic techniques would have been beneficial. Additionally, evidence on treatment approaches, both pharmacologic and invasive, remains scarce, especially concerning percutaneous interventions in AHF with VHD. It is hoped that forthcoming studies will provide the foundation for stronger recommendations in future guideline editions. Meanwhile, the article by Chioncel, et al., serves as a useful reference in our clinical practice.

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José Manuel Martínez Comendador

Systematic Assessment of Postoperative Shock in Cardiac Surgery: Does It Offer Insights?

This pioneering retrospective study examines the association between the Society for Cardiovascular Angiography and Interventions (SCAI) Shock Classification and morbidity-mortality rates in cardiac surgery patients.

Despite recent advancements in patient care, cardiogenic shock (CS) remains a condition with high mortality rates, reaching up to 50%. Given the diverse presentation and variable severity of CS, achieving effective communication regarding disease progression and patient risk poses a considerable challenge when managing this medical condition. Additionally, variations in the severity of this condition have impacted clinical trials aiming to assess advanced therapies such as temporary mechanical circulatory support (tMCS). To address these complexities, the SCAI introduced a CS Classification in 2019, endorsed by several medical societies, unifying staging and risk prediction in cardiovascular patients. Over the following years, numerous retrospective and some prospective studies evaluated this classification across various cardiovascular patient cohorts, leading to refinements announced in the 2022 SCAI Classification update. Although widely applied in cardiology, it had yet to be assessed in cardiac surgery patients.

This study focused on evaluating the utility of the SCAI Shock Classification for postoperative cardiac surgery intensive care unit (ICU) patients, assessing both hospital mortality and associations with postoperative complications and organ dysfunction.

A retrospective analysis encompassed 26792 ICU admissions after cardiac surgery at Charité German Heart Center (DHZC) in Berlin from 2012 to 2022. Patients were categorized into SCAI Shock stages A through E, based on clinical, physiological, and laboratory data from the first 24 hours post-surgery, using electronic health record data. The impact of late deterioration (defined as increased vasopressors or lactate levels in the following 24 hours) was also explored as an additional risk factor.

The patient proportions across SCAI Shock stages A through E were 24.4%, 18.8%, 8.4%, 35.5%, and 12.9%, respectively, with corresponding crude hospital mortality rates of 0.4%, 0.6%, 3.3%, 4.9%, and 30.2%. Postoperative complications and multi-organ failure prevalence also increased with higher SCAI Shock categorization. Multivariable analysis showed that each advanced SCAI Shock stage was associated with increased hospital mortality (adjusted OR: 1.26-16.59) compared with SCAI Shock stage A, as was late deterioration (adjusted OR: 8.2). The SCAI Shock Classification demonstrated strong diagnostic performance for hospital mortality prediction (AUROC: 0.84), which increased significantly when late deterioration was included in the model (AUROC: 0.90).

In conclusion, the authors argue that the SCAI Shock Classification is an effective tool for mortality risk stratification and evaluating postoperative complications and organ dysfunction in ICU patients after cardiac surgery. Thus, its application could be extended to cardiac surgery as a triage tool in postoperative care and as a selection criterion in clinical research.

COMMENTARY:

Preoperative risk scales, such as EuroSCORE or STS score, are widely used in numerous cardiac interventions worldwide, helping evaluate prognosis and, in many cases, identify patients unsuitable for surgery. However, these preoperative scores are

imperfect and carry significant limitations. A critical limitation is that they do not account for intraoperative events or the patient's postoperative status. These factors can greatly influence clinical evolution and outcomes for many patients.

It is well known that low cardiac output and, to a lesser extent, vasoplegia post-cardiac surgery are associated with increased mortality. For instance, patients experiencing refractory postoperative cardiogenic shock (PCS) that requires tMCS may face in-hospital mortality rates up to 50%. Although numerous studies have evaluated prognosis in such situations, uncertainty persists regarding risk stratification and outcomes across the shock spectrum in cardiac surgery patients.

The SCAI Shock Classification offers a simple way to assess shock severity across a five-stage scale, covering the entire spectrum of patients with or at risk of CS. Hence, the demonstrated utility of this scale in risk stratification for medically induced CS should also apply to patients undergoing cardiac surgery, which this study aimed to confirm.

From my perspective, this study holds considerable significance for several reasons:

It contributes significantly to understanding the epidemiology and outcomes related to shock post-cardiac surgery.

It stands out as the most extensive published study to date on the association between the SCAI Shock Classification and mortality in critically ill patients.

It marks a milestone as the first study to validate this classification in a population of patients undergoing cardiac surgery.

The SCAI Shock Classification demonstrated excellent discrimination and adequate calibration for mortality prediction, as detailed below. More than 56.8% of patients met the SCAI criteria for shock, exhibiting hypoperfusion, defined as SCAI Shock stages C/D/E. As SCAI Shock stage increased, disease severity, multi-organ failure, and the need for rescue therapies also rose. Additionally, patients with more severe shock (SCAI Shock stages D/E) underwent prolonged and complex surgeries, as evidenced by extended extracorporeal circulation times. Expectedly, hospital mortality increased across SCAI Shock stages, with nearly a 75-fold increase in crude mortality from SCAI Shock stage A to stage E. This incremental increase in mortality across SCAI Shock stages remained after adjusting for intergroup differences, including preoperative and intraoperative variables.

On the other hand, it is worth noting that patients without hypoperfusion (SCAI Shock stages A/B) had very low hospital mortality rates of only 0.5%, even though most received vasoactive medications (not directly used to define shock). In these low-risk patients, an early discharge protocol could be justified. Furthermore, patients with mild or moderate shock (SCAI Shock stages C/D) experienced mortality below 5%, which are still relatively low figures.

Patients who experienced late deterioration, defined as increased vasopressor usage or elevated lactate levels after 24 hours, showed additional increases in subsequent mortality. This association between late deterioration and increased mortality aligns with previous observations in cardiac ICU patients, underscoring the importance of dynamic shock assessment over time.

Comparing these results to studies analyzing non-surgical ICU populations, such as the study by Jentzer et al., shows significantly higher shock prevalence and severity per SCAI Classification in cardiac surgery patients. However, paradoxically, in-hospital

mortality at each SCAI Shock stage was higher in medical ICU patients with cardiac conditions. Mortality differences were substantial, for example, 40% vs. 4.9% in SCAI Shock stage D and 67% vs. 30.2% in stage E. This highlights a fundamental distinction between medical and surgical critical illness: post-surgical patients are selected as suitable surgical candidates without life-limiting non-cardiac comorbidities, with a correctable condition expected to improve postoperatively.

Additional plausible explanations exist for why PCS appears to have a more favorable prognosis than CS in non-surgical patients. These include the higher prevalence and severity of vasoplegia and hypovolemia in cardiac surgery, leading to mixed shock states often resolving rapidly. Also, post-cardiac surgery patients commonly require inotropic agents, such as epinephrine, and experience lactic acidosis upon ICU admission, which typically resolves quickly with volume resuscitation, resolution of vasoplegia, and abatement of initial myocardial stunning.

Incorporating the SCAI Shock Classification into early postoperative evaluation alongside preoperative scores we commonly use will likely provide more accurate risk stratification for hospital events. One of the most notable contributions of this analysis could be its potential to predict the elevated risk of severe PCS, particularly in SCAI Shock stage E, allowing for better preparation and, hopefully, prevention of subsequent complications.

In general, this study further supports the validity of the SCAI Shock Classification, providing incremental mortality risk stratification for patients undergoing cardiac surgery. SCAI Shock severity assessment demonstrates a robust prognostic framework in both medical ICU and surgical cardiac ICU populations, even with expectedly lower mortality in post-cardiac surgery patients. Therefore, this pioneering study represents a crucial step toward establishing the SCAI Shock Classification as the international standard for assessing and communicating shock severity.

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Elio Martín Gutiérrez

Embolism and Infection. Dangerous Liaisons in Long-Term Mechanical Circulatory Support Device Carriers

An analysis of the EUROMACS registry assessing the relationship between thromboembolic events and preceding infectious phenomena in patients with long-term left ventricular assist devices (LVADs).

In patients with durable LVAD support, infections are an adverse event frequently contributing to significant morbidity and mortality. According to the International Society for Heart and Lung Transplantation, infections in these patients can be classified as:

Non-LVAD-related infections: Infections not promoted by the presence of the device and unlikely to be associated with it, such as respiratory and urinary tract infections.

LVAD-related infections: Infections that can also occur in patients without an LVAD; however, unique considerations arise due to the LVAD system, including endocarditis, mediastinitis, and bacteremia.

LVAD-specific infections: Infections unique to LVAD carriers, linked to the device's physical components and unlikely to occur in non-LVAD patients, such as driveline infections and infections involving any of the device's components or the implantation space.

The study's objective was to investigate the possible association between infections and thromboembolic events, particularly cerebrovascular accidents (CVAs), in long-term LVAD-supported patients.

The data analyzed were obtained from the European Registry for Patients Assisted with Mechanical Circulatory Support (EUROMACS). A Kaplan-Meier survival analysis was conducted to assess the risk of CVA in patients who developed infectious processes while supported by an LVAD, alongside a multivariable Cox regression model.

A total of 3282 patients were included, of whom 1262 (38%) experienced some form of infection, and 457 (14%) suffered a CVA episode. Cox regression analysis revealed that a history of infection nearly doubled the risk of CVA (HR 1.9; 95% CI: 1.5–2.3; $p < 0.001$). When infections were categorized as previously mentioned, only LVAD-related and LVAD-specific infections reached statistical significance, increasing the risk of CVA by 50% (HR 1.5; 95% CI: 1.1–2.0; $p = 0.002$) and almost doubling it (HR 1.9; 95% CI: 1.4–2.8; $p < 0.001$), respectively.

COMMENTARY:

This study indicates that infections in LVAD patients constitute a significant risk factor for the development of both ischemic and hemorrhagic CVAs, either synchronously or metachronously. Several insights emerge from this research:

The clinical temporal association between infections leading to CVAs is often unclear in the literature. Kaplan-Meier follow-up analysis suggests that some embolic episodes likely arise from a hypercoagulable state during active infection, while others may occur later due to biofilms and microthrombi formation on the system, following previous bacteremia episodes.

Continuous-flow LVADs also contribute to endothelial dysfunction, which can exacerbate existing acquired von Willebrand disease and thus increase hemorrhagic events. The septic nature of some emboli and the hemorrhagic tendency in the context of anticoagulation predispose to hemorrhagic transformation of initially asymptomatic microemboli, leading to secondary hemorrhagic CVA.

Although infection and CVA association may be primarily linked to previous bacteremia episodes, intriguingly, the analysis suggests an equal or greater influence of LVAD-specific infections compared to LVAD-related infections regarding CVA risk. This may be due to a higher-than-expected rate of subclinical bacteremia episodes.

Therefore, prompt and aggressive treatment of infections in LVAD patients is essential, coupled with proactive anticoagulation management. Radical infection treatment remains challenging, and to date, there are no evidence-based antimicrobial guidelines for these patients. Further studies are needed to develop a standardized diagnostic and therapeutic approach, targeting both infection treatment and CVA risk reduction, as these events are more interconnected than initially presumed.

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Elio Martín Gutiérrez

Mechanical Ventricular Assist Devices: Universal Access?

A Canadian center conducted a study to assess the learning curve evolution in HeartMate II® device implantation.

The increasing number of patients with end-stage heart failure in our setting, coupled with a progressive reduction in organ donors, has created a need for alternative therapeutic options to sustain and extend life expectancy in these patients. Continuous-flow ventricular assist devices (CF-VADs) therapy is recommended for selected patients with end-stage heart failure, serving as a bridge to transplant, bridge to candidacy, or destination therapy.

In our country, CF-VAD programs have primarily been concentrated in tertiary centers affiliated with cardiac transplant programs. As destination therapy becomes more common—often due to a lack of compatible donors or failure to achieve transplant candidacy—some secondary centers (without cardiac transplant programs) have incorporated these device implants into their therapeutic arsenal for patients ineligible for referral to a tertiary center.

Several studies indicate that implantation outcomes are related to the annual volume of each center. Although optimal activity volume thresholds remain controversial, some authors suggest an ideal range of 20 to 50 annual implants per center. Medicare® and Medicaid® programs require surgeons to perform at least 10 procedures, prioritizing individual experience over total center volume. Nevertheless, optimal results combine appropriate patient selection, surgical procedure, postoperative care, and long-term medical follow-up.

The study includes data from a Canadian center with 51 consecutive patients who underwent HeartMate II® implantation between January 2009 and December 2017. The results of two time series, early (2009-2014; n=25) and late (2015-2017; n=26), were compared. The median follow-up time was 51 months. Early-era patients had higher rates of diabetes, prior stroke, and inotropic support before HeartMate II® implantation. The 90-day mortality rate was not significantly higher in the early era (24% vs. 15%, p=0.43). However, the incidence of the composite outcome—isolated mortality, new stroke, reoperation for bleeding, need for temporary right ventricular mechanical support, and pump thrombosis at 90 days—was significantly higher in the early era (76% vs. 42%, p=0.01). The need for temporary right ventricular support and bleeding complications were major contributors to the composite outcome, reflecting limited team experience. Cumulative survival (CUSUM) analysis established a threshold of 23 operations after which composite outcome results optimized.

The authors concluded that low-volume centers could achieve good outcomes in HeartMate II® implantation with an acceptable learning curve. Significant changes in patient selection, surgical techniques, and patient management could lead to improved outcomes after CF-VAD implantation.

COMMENTARY:

The experience of this Canadian team is both pioneering and courageous. It provides evidence on the potential success of establishing a mechanical ventricular assist program outside major transplant centers. Similarly to other advanced heart failure therapies (resynchronization therapy, mitral clip…), now available in secondary-level centers with only the requirement of cardiac surgery capabilities on site, coordinated liberalization of these programs with the transplant reference center could extend and

enhance the care network for end-stage heart failure patients, avoiding the bottleneck effect fostered by a centralized system. This notion is reinforced by the recent publication of the "Code Shock" consensus document, which seeks to structure short-term mechanical circulatory support for patients experiencing decompensation. Following stabilization, some may become candidates for these devices. Thus, multidisciplinary collaboration, even across institutional borders, effective communication beyond fax, email, and phone, and a responsible approach to device indication and associated healthcare costs can open a new care paradigm better aligned with the needs of our population.

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José Manuel Martínez Comendador

Less-Invasive Left Ventricular Assist Device Implantation: Should We Start Considering It?

This multicenter observational study evaluates morbidity and mortality following left ventricular assist device (LVAD) implantation, comparing the outcomes of conventional median sternotomy (CS) to minimally invasive (MI) approaches.

Minimally invasive approaches for LVAD implantation have the potential to improve outcomes for patients requiring mechanical circulatory support, particularly those with severe comorbidities. While CS remains the standard, LVAD implantation through MI techniques, including hemisternotomy and minithoracotomy, has demonstrated safety and feasibility, enabled by miniaturized devices such as the HeartMate 3® and the now-discontinued HeartWare®. Nevertheless, limited evidence exists on the impact of the chosen approach on postoperative morbidity and mortality.

The study's objective was to compare LVAD implantation using CS versus MI in two high-volume cardiac surgery centers. From January 2014 to December 2018, LVAD devices were implanted in 342 consecutive patients. Patient characteristics were prospectively collected, and a propensity score analysis created two comparable groups in a 1:1 match. The unmatched cohort included 241 patients who received LVAD implants via CS and 101 who underwent MI surgery. The re-sampled cohort yielded two groups, each comprising 73 patients. In the matched groups, the reoperation rate due to bleeding was 4.1% (3/73) in the MI group, compared to 17.9% (12/67) in the CS group ($p = 0.018$). The ICU stay was significantly shorter in the MI group than in the CS group (10.5 days vs. 4 days, $p = 0.008$), as was hospital stay (37 days vs. 25.5 days, $p = 0.007$). Cumulative mortality incidence for the CS group was 24% at 1 year and 26% at 2 years among non-transplanted patients, while it was 22.5% at 1 year and 25.2% at 2 years for the MI group.

The authors conclude that the minimally invasive surgical approach is a safe technique for LVAD implantation. MI surgery was associated with a significant reduction in postoperative bleeding complications and hospital stay duration, with no significant differences in mortality incidence.

COMMENTARY:

This observational study represents the largest series to date explicitly comparing LVAD implantation via minimally invasive approaches (left thoracotomy and hemisternotomy) to the conventional sternotomy approach. Jawad et al. associate the MI approach with reduced postoperative bleeding and shorter hospital stays. The uniformity in the anticoagulation protocol and balanced distribution of device types across both groups stand out as positive aspects of the study design.

An increasing interest exists in promoting LVAD implants that preserve the sternum as much as possible using MI approaches. The primary and most evident reason for this interest is the potential of MI approaches to enhance perioperative outcomes by minimizing bleeding and optimizing immediate postoperative mobility. Another potential benefit could be the enhanced feasibility of heart transplantation in patients who had LVAD implants as a bridge to transplant or candidacy, as the avoidance of the full midline incision reduces pericardial adhesions. A less discussed but pertinent factor is the belief among professionals that MI approaches reduce the incidence of right ventricular (RV) dysfunction. Theoretically, the wide pericardial opening required for CS can cause RV distention, which MI approaches might avoid. Indeed, this study observed a trend, though not statistically significant, toward lower incidence and severity of RV dysfunction in the

MI group. This study, like many others, associates MI approaches with reduced bleeding and shorter hospital stays but, in my view, does not fully address the critical question of whether RV function (both postoperative and long-term) improves due to the preservation of the pericardium and sternum in MI approaches.

The results of this study should be interpreted with caution. It is well-known that the validity of propensity score analysis heavily depends on appropriate variable selection. A limitation of this study was the exclusion of patients requiring concomitant valve procedures, and extracorporeal circulation time data from one center was missing. There is no information on pain control, a crucial factor when evaluating outcomes involving different surgical approaches, especially when including one via thoracotomy. Additionally, the authors missed the opportunity to assess RV function more rigorously. Furthermore, before matching, the MI group had a higher INTERMACS score and a greater incidence of pump-free LVAD implants, suggesting a lower surgical risk. Lastly, most cases were performed by two highly experienced MI surgeons, limiting the generalizability of the findings. Nevertheless, this study serves as a valuable reference for future prospective studies in this field.

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José Manuel Martínez Comendador

Long-Term Ventricular Assist in Spain (REGALAD Registry): Consolidation of an Unstoppable and Rising Reality

This study offers the first detailed analysis of the Spanish registry for long-term ventricular assist devices (REGALAD), encompassing all patients who received these devices in Spain from 2007 to 2020.

Despite substantial advances in heart failure (HF) management, a significant number of patients progress to advanced HF, where medical therapy alone cannot prevent functional decline, multi-organ failure, or death. Although heart transplantation (HTx) is the treatment of choice for these cases, limited donor availability, comorbidities, or other contraindications restrict access for many patients. Fortunately, long-term ventricular assist devices (dVADs) have rapidly advanced in recent years, providing circulatory support to advanced HF patients in various situations. Eligible candidates for these devices may include those on the HTx waiting list (bridge to transplant [BTT]), patients requiring time to overcome a potentially reversible contraindication to HTx (bridge to candidacy), patients with the potential for myocardial recovery (bridge to recovery), or as destination therapy for those ineligible for HTx.

The objective of this study was to analyze the clinical characteristics, outcomes, and complications of all patients who received a dVAD in Spain from 2007 to 2020, utilizing data from the Spanish Registry of dVADs (REGALAD). During this period, a total of 263 dVADs were implanted across 22 Spanish hospitals with ventricular assist programs. Of these devices, 69% were continuous-flow left ventricular assists, while 30% were pulsatile-flow devices (58 left and 21 biventricular). Additionally, two cases involved a total artificial heart (1%). Regarding assist strategies, BTT was used in 78 patients (30%), bridge to candidacy in 110 patients (42%), bridge to recovery in 3 patients (1%), and destination therapy in 72 patients (27%). Overall survival at 6, 12, and 24 months was 79%, 74%, and 69%, respectively, with the best outcomes seen in patients with continuous-flow left ventricular assists (84%, 80%, and 75%, respectively). The main complications included infections (37% of patients), bleeding (35%), neurological events (29%), and device malfunction (17%).

The authors conclude that dVADs have become established in Spain as a valuable treatment for advanced HF, with a clear trend toward intracorporeal left continuous-flow devices, which are associated with better outcomes.

COMMENTARY:

This study is unique and highly relevant for Spain as it presents, for the first time, the characteristics and outcomes of each dVAD procedure performed in the country since the devices' introduction.

Similar to other international registries, the total number of devices has progressively increased, though with a notable difference: our annual figures are significantly lower than those of other countries. For instance, if compared with 2019 INTERMACS registry data, Spain records 10 times fewer dVAD implants than the United States. Potential reasons for this disparity could include the relatively rapid access to HTx in Spain and differences in healthcare funding and budget allocations. Additionally, a high percentage of these transplants are conducted urgently under short-term mechanical circulatory support, reducing the use of dVADs as BTT. A further reason for the limited adoption of dVADs in Spain may be the lack of awareness about this treatment and its outcomes, resulting in fewer candidate referrals to specialized centers. Finally, the absence of

favorable cost-effectiveness results also hinders dVAD expansion as a destination therapy within Spain's public healthcare system.

Another striking difference between the REGALAD registry and others is the low incidence of severe INTERMACS profiles 1 or 2, at just 21% compared to 51% in the U.S. registry. In Spain, as recommended by the European Society of Cardiology's latest HF guidelines, there appears to be an initial preference for short-term ventricular support in these critical patients as a bridge to dVADs (bridge-to-bridge strategy). Indeed, 8% of our registry patients had temporary mechanical support, with outcomes equally favorable to other registry patients.

Over the years, another significant change is the shift from pulsatile paracorporeal devices to smaller, continuous-flow intracorporeal devices, which have a lower complication rate, lower energy consumption, and greater durability. The HeartMate 3 has been predominant in recent years and will likely remain so, as the other market alternative (HVAD, HeartWare) ceased distribution in June 2021 due to higher adverse event rates.

Overall survival, at 74% and 69% at 1 and 2 years, respectively, is similar to that reported in other international registries. However, these outcomes are partially hindered by a high percentage of pulsatile-flow and biventricular assists, as well as the participation of centers with limited experience. Nonetheless, the strong survival rates of isolated continuous-flow left ventricular dVADs, at 80% at 1 year and 75% at 2 years, are almost identical to those in the INTERMACS registry.

Notably, we found no significant differences in survival across implantation objectives, unlike other registries, where BTT or bridge to candidacy patients, who are generally younger with fewer comorbidities, show better outcomes than destination therapy patients. Although the proportion of destination therapy patients in the REGALAD registry is increasing, it remains significantly lower than in the INTERMACS registry, which reached 78% in 2020.

Complications remain frequent and serious, representing the primary barrier to broader treatment adoption. Stroke, both ischemic and hemorrhagic, is the leading cause of death, accounting for 38% of cases. Strict control of risk factors, especially blood pressure, as well as the development of more hemocompatible dVADs, is expected to reduce the incidence of this severe complication. Device dysfunction, particularly pump thrombosis, more common in pulsatile paracorporeal pumps, has fortunately decreased over time. Preventing thromboembolic events with dual antithrombotic therapy partly contributes to bleeding events, particularly gastrointestinal hemorrhage (19% in this series). Infections are another common complication, particularly those related to the percutaneous drive cable in intracorporeal devices. These infections are challenging to eradicate and necessitate prolonged antibiotic therapy, adversely affecting patients' quality of life. Fortunately, newer devices show a downward trend in these complications.

The main limitation of this registry, compared with others, is the small sample size and relatively short follow-up duration.

Technological advancements in increasingly effective and safer mechanical devices promise a bright future in the field of dVADs, likely revolutionizing advanced HF therapy in the near term. So far, as demonstrated by the REGALAD registry, dVADs have established themselves as a viable treatment for selected advanced HF cases in Spain, with continuous-flow intracorporeal left ventricular devices proving highly effective for this devastating condition. Although there is still much progress to be made before reaching the dVAD usage rates seen in other developed countries, the excellent outcomes

presented in the REGALAD registry, comparable to those in other international registries, highlight the capabilities of mechanical circulatory assist programs in Spain. Without a doubt, this paves the way for the expected expansion of these devices within the Spanish National Health System in the coming years.

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José Manuel Martínez Comendador

Axillary or Femoral Arterial Cannulation in Postcardiotomy Extracorporeal Life Support: Unresolved Dilemma?

This study aimed to evaluate the type and incidence of complications based on the selected peripheral cannulation site (femoral or axillary) in patients requiring postcardiotomy extracorporeal life support (PC-ECLS).

The application of PC-ECLS in contemporary cardiac surgery has been progressively increasing. Its primary indication is the inability to discontinue cardiopulmonary bypass intraoperatively or the presence of cardiopulmonary failure of various etiologies during the early postoperative period.

Despite medical and technological advances, PC-ECLS mortality remains high, with in-hospital survival ranging from 25% to 46%. Beyond the feared and devastating cerebrovascular complications, multiple potential issues are related to the cannulation site. Central cannulation in PC-ECLS is associated with a high rate of early reoperation for bleeding. Peripheral cannulation mitigates this issue but is not without other complications that should be considered. The primary advantage of femoral cannulation lies in its rapid implementation in emergency circumstances, though disadvantages include the likelihood of lower limb ischemia, differential hypoxia (Harlequin syndrome), and limited patient mobilization. Axillary cannulation, which is more technically demanding and typically performed in the operating room, often has a higher rate of bleeding and arm hyperperfusion syndrome. However, its fundamental advantage is that it provides antegrade flow, reducing the risk of Harlequin syndrome. Due to its proximity to cerebral arteries, axillary cannulation may pose a potential source of cerebral embolism.

The objective of this study was to compare axillary and femoral cannulation in terms of cannulation site-related complications and the incidence and type of cerebrovascular events.

Of 573 consecutive patients requiring PC-ECLS between 2000 and 2019 at a single center, 436 were included in a retrospective analysis and grouped according to the primary peripheral arterial access chosen for PC-ECLS. In 250 patients (57.3%), indirect cannulation with a side graft anastomosed end-to-side to the axillary artery was performed, whereas the femoral artery was used as the primary arterial access in 186 patients (42.6%). No significant differences were observed in 30-day survival (axillary: 62% vs femoral: 64.7%; $p = 0.561$) or 1-year survival (42.5% vs 44.8%; $p = 0.657$). Cerebral computed tomography confirmed a significantly higher incidence of stroke with a modified Rankin Scale (MRS) ≥4 (moderate to severe disability) in the axillary group (axillary: $n = 28$, 11.2% vs femoral: $n = 4$, 2.2%; $p = 0.0003$). Stroke localization included right hemisphere ($n = 20$; 62.5%), left hemisphere ($n = 5$; 15.6%), bilateral ($n = 5$; 15.6%), or infratentorial ($n = 2$; 6.25%). Although no differences were found in the incidence of severe bleeding secondary to cannulation, the need for cannulation site change due to bleeding was more frequent in the axillary group (axillary: $n = 13$, 5.2%; femoral: $n = 2$, 1.1%; $p = 0.03$). Clinically evident limb ischemia was significantly more frequent in the femoral group (axillary: $n = 12$, 4.8%; femoral: $n = 31$, 16.7%; $p < 0.0001$).

The authors conclude that while survival was similar with both procedures, surgeons should be highly aware of the specific complications associated with each peripheral access when choosing PC-ECLS cannulation sites. Although axillary cannulation has a low arm ischemia rate and the apparent advantage of providing antegrade flow, the high incidence of right hemispheric strokes should be considered.

COMMENTARY:

The Achilles' heel of ECLS is well-known to be its vascular and cerebral complications. This study is particularly relevant as it constitutes the largest series comparing the two most common types of ECLS cannulation (axillary vs. femoral artery) and establishes a strong association between axillary cannulation and stroke for the first time. The most notable findings include similar mortality when comparing both techniques, a significantly higher rate of stroke (odds ratio 4.5) with axillary cannulation, and a greater incidence of vascular complications with femoral cannulation.

The most innovative contribution of this study was the clinical and statistically significant association between axillary cannulation and stroke. Previous smaller studies had suggested this, while others did not conclude such an association. A clear methodological limitation was the use of an MRS ≥4 (moderate to severe disability) to classify stroke instead of the typically used MRS ≥2 (mild disability) in clinical trials on TAVI, potentially underestimating the actual incidence of this complication. The retrospective nature of the study may explain the lack of data regarding the timing of strokes and the absence of a specific anticoagulation protocol, leaving unanswered whether a significant portion of these strokes occurred during device explant or were caused by improper anticoagulation levels.

The rate of limb ischemia in femoral cannulation was notably high (16.7%). In several recently published series, the incidence of vascular complications has decreased to 5% with the use of distal perfusion catheters. The author does not provide information on the percentage of distal cannula use, but it is likely that its usage was minimal, especially in the first ten years. Given that limb ischemia rates may now be lower and considering the high incidence of strokes with axillary cannulation, it could be argued that femoral cannulation may be the preferred technique in most cases. However, to reach a similar conclusion, multicenter randomized studies comparing different cannulation strategies in ECLS would be necessary.

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José Manuel Martínez Comendador

Veno-arterial ECMO in Cardiogenic Shock: Is There a Preferred Method for Left Ventricular Unloading?

This retrospective study on patients with veno-arterial ECMO compares the clinical and hemodynamic efficacy of intra-aortic balloon pump (IABP) versus the Impella® device as left ventricular (LV) unloading techniques.

There is no doubt that veno-arterial extracorporeal membrane oxygenation (VA ECMO) in cardiogenic shock (CS) has saved thousands of lives over the last decade. A feared complication, occasionally difficult to manage, is LV distention due to lack of unloading. Protocolized measures for loss of pulsatile wave in arterial pressure monitoring—a patient emergency under ECMO support—are well known and effective (arrhythmia correction, flow reduction, blood pressure lowering, inotropy increase). However, when these are insufficient, indirect LV unloading methods, like IABP, or more direct ones, such as the Impella® device (Abiomed®, Danvers, Massachusetts, USA), are available. This study sought to evaluate the clinical and hemodynamic effects of IABP and Impella® devices in patients on VA ECMO support.

A retrospective review was conducted on VA ECMO patients at Columbia Hospital (New York) from January 2015 to June 2020. Patients were classified as receiving isolated ECMO or ECMO with LV unloading via IABP or Impella®. Clinical pre-ECMO characteristics, survival, complications, and hemodynamic changes associated with each device initiation were recorded. A total of 143 patients received isolated ECMO, while 140 received ECMO with LV unloading (68 ECMO with IABP, 72 ECMO with Impella®). Patients on ECMO with Impella® had a higher incidence of bleeding events compared with isolated ECMO or ECMO with IABP (52.8% vs. 37.1% vs. 17.7%; $p < 0.0001$). Compared with isolated ECMO, ECMO with IABP showed better survival at 180 days ($p = 0.005$), while there were no significant survival differences when compared to ECMO with Impella®. In a multivariable Cox hazard analysis, age (HR = 1.02; $p = 0.015$), pre-ECMO lactate levels (HR = 1.06; $p = 0.004$), pre-ECMO creatinine (HR = 1.06; $p = 0.032$), and need for ECMO in cardiopulmonary resuscitation settings (HR = 2.09; $p = 0.001$) were independent risk factors for mortality, whereas male sex (HR = 0.54; $p = 0.002$) and pre-ECMO IABP presence (HR = 0.45; $p = 0.010$) acted as independent protective factors. There were no significant hemodynamic differences between ECMO with IABP and ECMO with Impella® cohorts.

The authors concluded that concomitant IABP support may help reduce morbidity and improve 180-day survival in VA ECMO patients with cardiogenic shock.

COMMENTARY:

Despite advancements in CS pathophysiology and management, mortality remains excessively high. Devices such as IABP, ECMO, or Impella® have revolutionized shock treatment, particularly at severe stages (D and E). While peripheral VA ECMO can be life-saving in CS as a bridge to recovery or other long-term therapies, LV unloading is essential to prevent LV distention (LVD) and its potential sequelae like acute pulmonary edema, thrombosis/embolism, and lack of ventricular recovery. Depending on clinical circumstances, LVD patients may require postload reduction, increased native contractility, or additional mechanical support, such as IABP or left ventricular assist devices (LVAD) (e.g., Impella®). Determining the best approach in such scenarios remains a scarcely debated challenge. The diversity in CS etiology, severity, and duration before initiating therapy makes comparing unloading strategies difficult, especially in a study like Char et al.'s, with a limited sample size. Moreover, the inclusion

of ECMO patients due to cardiopulmonary resuscitation (extracorporeal cardiopulmonary resuscitation, ECPR) further complicates evaluation, as these patients are at a particularly high risk of death, anoxic brain injury, multi-organ failure, and LVD. The 2021 AHA ECPR expert consensus guidelines recommend IABP, direct LV drainage cannula, Impella®, or atrial septostomy for LV unloading; however, they do not detail specific diagnostic criteria for LVD or optimal timing for intervention.

Given the urgency and clinical variability in CS presentations, it is understandable why prospective randomized trials are nearly impossible. Consequently, studies like this, though retrospective with limited sample sizes, provide essential evidence in a field with many uncertainties, especially when they include hemodynamic data on the impact of different support devices.

Following the analysis of 300 VA ECMO patients, the main finding of Char et al.'s study was that LV unloading did not improve discharge survival or 180-day outcomes, despite improved hemodynamic status in ECMO patients. When the two unloading methods were analyzed separately, patients with IABP showed better survival, particularly when IABP was implanted preventively before LVD onset. On the other hand, Impella® patients had a higher incidence of bleeding complications. Survival differences must be interpreted cautiously due to inherent selection bias, as device choice was not randomized, a limitation that multivariable analysis cannot mitigate in a retrospective study.

These results suggest that, as both procedures are equally effective for hemodynamic stabilization in ECMO patients with LVD, IABP may be preferable for initial LV unloading due to its bedside implantability and removal, even without fluoroscopy, and lower bleeding risk compared to Impella®. The authors advocate for systematic early IABP use in patients who may eventually require ECMO. In our daily practice, patients without ventricular function recovery after a few days often end up on urgent transplant waiting lists, requiring not only IABP but also additional LV unloading systems, frequently Impella® in our hospital, or other techniques, depending on variables such as LV dysfunction severity, thrombus presence in the ventricular wall, aortic insufficiency, concomitant pathologies, and transplant center experience. LV unloading method selection is complex, and while this study does not provide definitive information, it is a step forward in this area. This work adds valuable nuances to the discussion of LV unloading approaches in VA ECMO patients.

Finally, it is crucial to recognize that within a short period, many patients who would have succumbed to cardiopulmonary collapse a decade ago can now be rescued by VA ECMO (pre-hospital ECMO, regional/provincial "Shock Code" programs) and even transitioned to longer-term therapies. We must acknowledge the profound impact this therapy can have on patients previously facing certain death. Every decision and detail that can improve the management of this condition is vital and contributes exponentially to knowledge expansion in this promising field of medicine.

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José Manuel Martínez Comendador

Early Extracorporeal CPR for Refractory Out-of-Hospital Cardiac Arrest: Is It Really the Solution?

A recent randomized, multicenter trial published in the New England Journal of Medicine assesses the effectiveness of early extracorporeal CPR compared with conventional CPR in patients experiencing refractory out-of-hospital cardiac arrest (OHCA).

Currently, despite significant advancements in understanding cardiac diseases over the past four decades, only 1 in 10 patients with OHCA survive. In Spain, approximately 50000 cases of cardiac arrest (CA) occur annually, with about 3/5 taking place outside hospitals, ultimately resulting in a high number of deaths, around 45000. Patients with the highest survival probability are those with ventricular fibrillation (VF), which can potentially be reversed through electrical cardioversion (ECV); however, even among these, up to half may experience refractory VF, which foretells an unfavorable prognosis due to rapid multi-organ failure onset if cardiopulmonary resuscitation (CPR) maneuvers fail to reverse this state early.

CPR supplemented with veno-arterial ECMO, also known as extracorporeal CPR, has been proposed as an option for patients with VF refractory to conventional CPR. Naturally, the feasibility of this approach largely depends on the medical emergency system available within a specific geographic region. However, the efficacy and safety of extracorporeal CPR remain inconclusive, as most available data comes from single-center study series. In fact, the latest European resuscitation guideline assigns a very low level of evidence to extracorporeal CPR.

In this multicenter, randomized controlled trial conducted in the Netherlands, patients with OHCA were assigned to receive extracorporeal CPR or conventional CPR (standard advanced cardiac life support). Eligible patients were aged between 18 and 70, had received bystander CPR, presented with an initial ventricular arrhythmia, and had not achieved return of spontaneous circulation within 15 minutes after CPR initiation. The primary outcome was survival with a favorable neurological outcome, defined as a Cerebral Performance Category score of 1 or 2 (range 1–5, with higher scores indicating more severe disability) at 30 days. Analyses were performed on an intention-to-treat basis. Of the 160 randomized patients, 70 were assigned to receive extracorporeal CPR and 64 to receive conventional CPR. Twenty-six patients were excluded for not meeting inclusion criteria at hospital admission. At 30 days, 14 patients (20%) in the extracorporeal CPR group were alive with a favorable neurological outcome, compared to 10 patients (16%) in the conventional CPR group (OR = 1.4; $p = 0.52$). The number of serious adverse events per patient was similar in both groups.

The authors concluded that, in patients with refractory OHCA, extracorporeal CPR and conventional CPR yielded similar effects on survival with a favorable neurological outcome.

COMMENTARY:

The INCEPTION study under review concluded that extracorporeal CPR offers no significant advantage over conventional CPR in terms of the primary outcome. Without yet delving into these apparently disappointing results, the article provides invaluable information on the use of extracorporeal CPR in OHCA settings. The study's rigorous methodology presents an unparalleled opportunity for future research with greater statistical power. The randomization involved 160 patients with "witnessed" OHCA, a

detail that may go unnoticed but is crucial for approximating the time elapsed since CA onset. For inclusion in the study, patients had to present a shockable rhythm (e.g., VF) and a lack of return of spontaneous circulation after 15 minutes of CPR initiation. Another noteworthy aspect is that the study was conducted in the Netherlands, where emergency response teams arrived at the patient's side in approximately 8 minutes, with hospital arrival occurring an average of 35 minutes after CA onset—figures that are difficult to exceed in most countries. Additionally, the median time from CA onset to initiation of VA-ECMO was 74 minutes; while also brief, this timeframe may be insufficient to yield substantial benefits after over an hour of CPR. Finally, I would emphasize that the trial's primary endpoint was survival with a favorable neurological outcome, referring to adequate brain function that enables at least minimal independence in daily activities; analyzing survival alone would be uninformative if neurological sequelae preclude a normal life.

Before the INCEPTION study, the efficacy of extracorporeal CPR compared to conventional CPR had only been assessed in two randomized controlled trials (RCTs) with contradictory results. The ARREST trial was prematurely terminated due to favorable outcomes in patients receiving ECMO (a 36% increase in survival rate compared to conventional CPR). Although the inclusion criteria in the ARREST study were similar to those in INCEPTION, there are notable differences. The ARREST study included only 30 patients before its premature termination, thus increasing the probability that any findings might have resulted from chance due to the small sample size. Unlike ARREST, the INCEPTION trial involved multiple centers, making it more representative of real-world conditions if extracorporeal CPR were to become more accessible. Belohlavek et al., in another RCT conducted in Prague analyzing extracorporeal CPR, concluded that it did not improve outcomes compared to conventional CPR. This study was also terminated early due to the lack of significant differences in its primary endpoint of survival with a favorable neurological outcome at 180 days (32% vs. 22% in favor of extracorporeal CPR among 256 evaluated patients). Unlike ARREST, this study was conducted in a single center but with a much larger sample size (264 patients). Furthermore, like INCEPTION, it was conducted in a setting with a well-developed emergency response system, and ECMO was implemented within reasonable, short times.

The results from the three RCTs seem contradictory and may be disappointing. However, this does not necessarily imply that extracorporeal CPR is ineffective in certain cases. Overall, data from the three RCTs indicate a numerical advantage in the primary outcome of increased survival without severe neurological disability, favoring the use of extracorporeal CPR. I believe most medical professionals would agree that VA-ECMO is an effective tool in managing patients in refractory CA, as long as it is implemented promptly in a hospital setting with trained personnel, potentially significantly improving survival odds compared to conventional CPR. Nevertheless, despite its availability in hospitals with the best medical resources, the actual times from the onset of OHCA to VA-ECMO initiation in these hospitals are, in most cases, too long to demonstrate plausible benefits, possibly due to irreversible multi-organ damage.

The newly published 2023 Spanish Cardiogenic Shock (CS) code aims to implement early mechanical circulatory support (MCS) nationwide for patients with CS. However, the actual implementation of an effective protocol faces challenges due to non-uniform assistance, action heterogeneity, and the lack of a standardized approach in our country. If favorable clinical evidence for extracorporeal CPR were to be established in the future, implementing a real and effective extracorporeal CPR code would likely be an immensely complex challenge.

Thus, based on currently available data, generalized use of extracorporeal CPR in patients suffering refractory OHCA cannot be recommended. Larger-scale studies with strong statistical power are needed to appropriately evaluate the impact of extracorporeal CPR in this specific clinical context.

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José Manuel Martínez Comendador

ECMO-CS Study: Does It Clarify When to Implant VA-ECMO in Cardiogenic Shock?

This was the first multicenter randomized clinical trial assessing the outcomes of immediate VA-ECMO implantation compared to an initially conservative strategy (allowing subsequent VA-ECMO if hemodynamic deterioration occurs) in patients with severe or rapidly deteriorating cardiogenic shock.

Despite significant advances in cardiology, the high early mortality in cardiogenic shock (CS) remains a significant challenge in clinical practice. Although various mechanical circulatory support (MCS) devices that enable hemodynamic stabilization in CS have emerged over the last decade, their impact on survival remains inconclusive. Among available MCS options, venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the most widely utilized due to its capacity to rapidly and effectively provide circulatory and respiratory support in cases of right, left, or biventricular failure.

Both the ESC and AHA current guidelines consider MCS for CS patients, particularly when hypoperfusion and hemodynamic deterioration persist despite inotropic and vasopressor treatment. However, they lack specificity on timing, target populations, or particularly beneficial cases, as most recommendations rely on retrospective studies, registries, and expert opinions. To date, no randomized clinical trial (RCT) had specifically examined VA-ECMO use in CS patients.

The ECMO-CS study under analysis today is a multicenter RCT including 117 patients with severe CS or rapidly deteriorating hemodynamics, randomly allocated to two groups: 58 patients received immediate VA-ECMO, while 59 initially received conservative therapy. The primary outcome was a composite of 30-day mortality, need for any MCS device, and cardiac arrest. No significant differences were found between the groups, with a 63.8% incidence in the ECMO group and 71.2% in the conservative group. Notably, 39% of the conservative group patients ultimately required VA-ECMO. There were no significant differences in complications, including 30-day cardiac arrest incidence (10.3% vs. 13.6%), all-cause mortality (50% vs. 47.5%), and serious adverse events (60.3% vs. 61%).

The authors concluded that immediate VA-ECMO in patients with severe or rapidly deteriorating CS did not improve clinical outcomes compared to an initial conservative approach with later VA-ECMO implantation in cases of hemodynamic deterioration.

COMMENTARY:

It is striking that, despite CS being the leading cause of death in patients with acute myocardial infarction (AMI), fewer than 20 RCTs, including fewer than 3000 patients in total, have been conducted since the first SHOCK trial in 1999. Almost all of these studies face repeated limitations. First, patient recruitment has proven challenging; second, there is vast design variability across studies. Another constant limitation is the lack of critical variables such as cause of death, right-heart catheterization data, details on inotropic and vasoactive drugs, or basic cardiac arrest information. In 2019, the Society for Cardiovascular Angiography and Intervention (SCAI) proposed a new CS classification to unify criteria, establishing five stages (A to E) to stratify mortality risk by severity.

This multicenter study presented by Ostadal et al. is noteworthy as the largest VA-ECMO RCT in CS patients to date. At first glance, its findings suggest limited benefit from early VA-ECMO implantation, but there are nuances to consider. Conducting this study required 8 years and collaboration among 4 centers to recruit just 117 patients,

reinforcing the recruitment difficulty for RCTs in CS and underscoring the need for new research strategies. Registries could potentially offer valuable data. The baseline characteristics of both groups were comparable, with STEMI (50.4%) and heart failure exacerbation (23.1%) as the most common underlying causes, aligning with registered CS series data. Although this study did not use the new SCAI shock classification, the patients included roughly correspond to SCAI stages D (hypoperfusion with deterioration) and E (extreme, hypoperfusion with deterioration and refractory shock) of this classification. These are the most severe but least prevalent stages, with expected mortalities of 40% and 67%, respectively—figures in line with the final mortality rates in both study groups.

Notably, and perhaps most critically, in the conservative group, crossover to other MCS devices (including VA-ECMO) was permitted for patients with worsening hemodynamics, defined as a lactate increase ≥3 mmol/L in 24 hours. This led to 39% of this group eventually receiving VA-ECMO. Given the high crossover rate, results should be interpreted with caution. The study does not imply that MCS is ineffective in CS; rather, early VA-ECMO implantation does not impact outcomes if later MCS use is allowed in cases of deterioration. Another takeaway is that early, unnecessary VA-ECMO implantation may lead to avoidable complications, while delayed or excessively late implantation fails to improve outcomes and patient prognosis. This underscores the need for clear, standardized criteria to determine the optimal timing for MCS implantation in CS.

The study has limitations to consider when interpreting results. First, it lacks precise data on the definition and timing of resuscitated cardiac arrest, complicating interpretation of ECMO group results. Furthermore, no information is provided on the incidence and duration of cardiac arrest prior to randomization—a recognized independent risk factor in CS mortality. Importantly, out-of-hospital comatose patients were excluded from the study, limiting the generalizability of results to this high-risk population. Additionally, the median patient age exceeded 65 years, surpassing the inflection point indicating a poorer CS prognosis by 5 years. Other considerations, such as deciding on left ventricular drain cannulation or limb perfusion to prevent ischemia in ECMO patients, were left to the clinicians' discretion and may reflect non-uniform criteria. Lastly, the study did not establish formal criteria for transitioning to more advanced destination therapies, weaning from other devices, or limiting life-support treatments.

Ultimately, the ECMO-CS study has highlighted certain limitations that future CS treatment research with VA-ECMO should consider. Nevertheless, there are still unanswered questions and advancements to be made in this complex and challenging field. Fortunately, two ongoing RCTs promise to shed more light on VA-ECMO use in AMI-CS patients. These are the ECLS-SHOCK trial, randomizing 420 AMI-CS patients to ECMO versus standard treatment, and the ANCHOR trial, in which 400 AMI-CS patients will be randomized to ECMO with intra-aortic balloon pump versus conventional treatment. We await their results, hoping to inch closer to the long-awaited solution for improving CS patient prognosis.

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José Manuel Martínez Comendador

Unloading the Left Ventricle in Venoarterial ECMO: Methods, Timing, and Candidates

A review of the various methods and indications for left ventricle (LV) unloading in patients supported with venoarterial extracorporeal membrane oxygenation (VA-ECMO).

VA-ECMO is a type of mechanical circulatory support that provides systemic flow of 4-6 L/min in cases of severe cardiorespiratory failure. However, its retrograde flow configuration through femoral cannulation can lead to LV overload, causing distension, blood stasis, thrombosis, and pulmonary congestion. Although LV unloading modalities are used to prevent these complications, their effectiveness and timing of implementation are still unclear, as they may add additional morbidity to an already critically ill patient.

This review is divided into three parts to address different questions. The first part focuses on identifying patients who could benefit from LV unloading, using reliable clinical, hemodynamic, and echocardiographic predictors. The second part analyzes the various unloading methods available, offering practical recommendations based on the latest scientific evidence. Pharmacological and non-invasive options, the insertion of decompression catheters, and a wide variety of unloading devices are examined. The third part discusses the optimal timing for deploying an unloading device, comparing preventive versus reactive unloading according to certain criteria. Finally, goals are presented to follow once the unloading method is implemented, providing guidelines for managing the patient in various circumstances. The purpose of this article in our blog is to simplify and summarize the most relevant points of this comprehensive review.

Indications for LV unloading

Established complications caused by increased afterload, such as pulmonary edema or heart failure due to lack of aortic valve opening, clearly indicate the need for LV unloading. However, the timing for primary unloading in the absence of obvious complications to facilitate LV recovery remains unclear. The use of unloading devices is not without cost and carries potential risks of vascular and hemorrhagic complications, and also adds practical complexity to device setup, anticoagulation management, monitoring of vascular access sites, and difficulty in mobilizing the patient.

To identify patients at higher risk of complications due to increased afterload, several predictors must be considered. Hemodynamic predictors include reduced arterial pulsatility and elevated pulmonary capillary wedge pressure (PCWP), which reflects high LV filling pressure. Echocardiographic predictors include increased LV dimensions, blood stasis and thrombi in the LV, absence of aortic valve opening, or a left ventricular outflow tract (LVOT) velocity-time integral (VTI) <10 cm. Clinical predictors include the development of pulmonary edema or refractory ventricular arrhythmias.

LV unloading has been shown to improve survival in patients with cardiogenic shock (CS) secondary to myocardial infarction, with an absolute risk reduction of 6.6%, due to improved subendocardial perfusion. Prophylactic LV unloading has also shown clear benefit in patients with chronic heart failure and elevated PCWP, who are especially vulnerable to increased afterload.

Unloading strategies

- Pharmacological and Non-Invasive Approaches

Before considering invasive approaches, it is important to reduce afterload in patients. To achieve this, the goal is to optimize VA-ECMO flow to provide adequate systemic perfusion with the lowest possible afterload. Reduction/withdrawal of vasoconstrictor support can be an initial step to maintain mean arterial pressures of 60 mmHg and systolic pressures of 80-90 mmHg. Low flow reduction, below 2.2 L/min/m², may be sufficient to maintain adequate perfusion and decrease ventricular distension. However, very low flows below 1.5 L/min/m² increase the risk of thromboembolic complications in the ECMO circuit.

Preload correction may be another strategy. Fluid therapy optimization is an option, but it is not suitable for all patients due to frequent increases in capillary permeability and third spacing. Increasing diuresis with diuretics or hemofiltration may be attempted, especially in those patients who have not yet developed complications related to high afterload.

Inotropes can be used to improve ventricular contractility. This strategy is employed as an initial measure to counteract increased afterload or as a bridge to more invasive unloading approaches in patients who have developed or are at risk of developing complications. However, it is important to apply it temporarily since inotropes increase myocardial oxygen demand, and increased mortality has been observed in observational studies.

- LV Decompression by Catheters

Catheter insertion into the LV, left atrium (LA), or pulmonary artery is performed, and these are connected to the venous cannula of the VA-ECMO circuit. Some groups use transesophageal echocardiography and 7Fr Pigtail catheters for this insertion. Others have achieved similar results with even smaller 5F and 6F catheters. However, due to limited flow and a higher risk of hemolysis, routine use of these smaller catheters is not recommended.

- Percutaneous Atrial Septostomy

This technique is performed using a balloon guided by fluoroscopy or echocardiography. Although common in pediatric populations, there is limited evidence available for its use in adults. There is a risk of developing thrombi in the LV or aortic root, as well as the risk of stroke after removing the venous cannula (paradoxical embolism). Another possibility is left-sided VA-ECMO with transseptal puncture, placing a multi-perforated venous cannula in the LA. This allows for simultaneous biatrial drainage. This approach is particularly useful in patients with LV thrombi or unilateral peripheral vascular disease, where implanting a large-caliber femoral cannula is contraindicated. It may also be an alternative in patients in whom a transaortic device cannot be used (e.g., aortic stenosis or mechanical prosthesis). The ultimate evolution of this modification is the conversion to TandemHeart®, a centrifugal pump that uses a 21F transseptal cannula located in the LA for drainage and maintains the same output as the original ECMO via arterial cannulation. An oxygenator can be added to the TandemHeart® system, or, as mentioned before, the LA cannula can be connected to the VA-ECMO drainage cannula via a Y-connector, allowing for biatrial drainage and unloading of both ventricles.

- Pulmonary Artery Drainage

Pulmonary artery drainage is a technique used in VA-ECMO to reduce LV pressure and volume by inserting a single- or multi-perforated cannula. Among the available cannulas, the Protek Duo® stands out. This bilumen cannula was initially conceived to create a percutaneous right ventricular support system, with drainage from atrial perforations and infusion into the distal pulmonary artery, limiting recirculation present in other systems like the Avalon® cannula. When used for unloading, both lumens would be connected to the ECMO inflow. It is available in sizes of 29F and 31F and can be inserted via the jugular vein with good navigability, allowing flows of up to 4.5 L. The results are promising and it is particularly useful when converting the system to right or biventricular support.

- Intra-Aortic Balloon Pump (IABP)

This is the most widely used device for LV unloading, as it reduces afterload and improves coronary flow. Although it has demonstrated benefit in patients with CS secondary to AMI, there are no randomized studies justifying its use as an LV unloading method. The results of observational studies evaluating its efficacy are heterogeneous and inconclusive.

- Percutaneous Left Ventricular Assist Devices (pLVAD)

The combination of pLVAD and VA-ECMO is increasingly used to treat CS. pLVADs are microaxial flow pumps that continuously move blood from the LV to the aortic root, reducing workload, pressure-volume area, and myocardial oxygen consumption. The Impella CP® is the most commonly used device for LV unloading in this configuration, often referred to as "ECMELLA" or "ECPELLA." The pLVAD is generally inserted percutaneously through the femoral artery contralateral to the ECMO perfusion cannula, although it can also be surgically implanted via the axillary artery. Contraindications for its use include having a mechanical prosthesis in the aortic position, severe aortic insufficiency, LV thrombus, and peripheral arterial disease.

The combination of pLVAD and VA-ECMO has been shown to reduce PCWP, improve pulmonary flow, and reduce LV size. However, as with IABP, there are no randomized studies to support its use for LV unloading. Recent registries suggest that "ECPELLA" reduces mortality compared to VA-ECMO alone, although this benefit may be offset by an increased risk of bleeding and ischemic complications in the lower extremities.

A critical aspect in managing "ECPELLA" is to adequately balance the flows of both devices. This must be dynamic, with a higher VA-ECMO flow prioritized initially to ensure adequate systemic perfusion. Then, a gradual transition is made to pLVAD support to promote cardiac recovery, and in a final phase, VA-ECMO weaning is considered. To avoid Harlequin syndrome in patients with hypoxemic respiratory failure, a lower pLVAD flow is recommended until pulmonary function improves, after which flows can be adjusted again, although conversion of the system to V-VA ECMO alongside pLVAD may still be necessary.

The initial flow of the Impella® should generally be lower than the maximum achieved by these devices. The Impella 5.5® can provide anterograde flows of up to 6 L/min, which is usually sufficient for adequate systemic perfusion in most cases. Its use as an unloading method has been associated with earlier VA-ECMO weaning and lower VA-ECMO flow to improve RV function and oxygenation before decannulation. Axillary insertion of the Impella® requires a surgical approach, but allows for high flows over significantly longer periods than the Impella CP® (cases of up to 83 days have been reported) and greater positional stability to ensure

proper functioning. Although its license in Europe is for 30 days and in the United States for 14 days, it presents potential advantages such as the possibility of patient mobilization and a lower incidence of hemolysis and thrombosis, making it an ideal option as a bridge to transplantation or long-term LVAD implantation after VA-ECMO decannulation. This strategy may be beneficial in cases of decompensated heart failure, patients with poor recovery prospects, or when prolonged mechanical circulatory support is anticipated.

- Surgical Approaches

Central VA-ECMO is used in postcardiotomy shock or graft failure following heart transplantation, where a sternotomy has already been performed. Although cannulation of the ascending aorta avoids the retrograde flow characteristic of peripheral VA-ECMO, ventricular distension can still occur when the LV is compromised, leading many centers to routinely perform LV unloading. This can be achieved by surgical insertion of a 16-20F cannula through the LV apex, pulmonary vein, or pulmonary artery, connected to the VA-ECMO drainage system via a Y-connector. Some minimally invasive approaches, such as subxiphoid or anterolateral thoracotomy, have also been described for cannula insertion with the same function in situations with an intact chest or when the sternotomy has already been closed. In this regard, inserting an apical unloading cannula allows conversion of the ECMO system to a paracorporeal left ventricular assist system (Levitronix®).

- Selection of the Strategy

The chosen strategy largely depends on the degree of increased afterload. IABP is suitable for slightly increased afterload, while for a distended LV with little contractility and high filling pressures, active unloading with pLVAD or a surgical decompression cannula is more appropriate. We are awaiting the results of the HERACLES study, the first clinical trial comparing these unloading strategies.

Timing of unloading

Unloading devices can be implanted before, during, or after the initiation of VA-ECMO, either prophylactically or in response to clinical, echocardiographic, or hemodynamic manifestations of increased afterload. Observational studies suggest that prophylactic unloading, performed within 2 hours of VA-ECMO initiation, may improve mortality compared to reactive unloading. However, randomized trials are needed to confirm these findings, and we await the results of the EARLY-UNLOAD and REVERSE trials, which will evaluate the benefits of early unloading with LA septostomy and Impella CP®, respectively. The ECLS-SHOCK trial evaluates the benefit of ECMO in patients with refractory shock secondary to AMI, and the results from the subgroup using unloading methods will provide relevant information.

Goals of unloading

Once unloading is initiated, continuous monitoring of ECMO flow is essential, as well as optimizing device parameters to achieve an adequate mean arterial pressure that ensures optimal systemic perfusion and PCWP < 15 mmHg. Aortic valve opening should also be assessed using echocardiography. Echocardiography plays a crucial role in evaluating RV function and LV contraction recovery, which will be reflected in an improvement in the arterial pulse wave. As hemodynamics improve, efforts should be made to gradually reduce inotropic drug doses. If evidence of cardiac recovery is observed, such as a pulse pressure > 10 mmHg, mean arterial pressure > 60 mmHg with low doses of inotropes, and EF > 30%, VA-ECMO weaning may be considered.

If an additional device, such as pLVAD or IABP, is used, VA-ECMO weaning should be attempted first, if feasible, to reduce afterload and myocardial oxygen consumption, potentially improving cardiac recovery. This is particularly relevant if an improvement in RV function and oxygenation is observed, allowing a transition to exclusive LV support. If cardiac recovery is deemed possible but VA-ECMO weaning is not yet feasible, another long-term support device, such as the Impella 5.5® or a long-term LVAD, may be considered. In cases where cardiac recovery seems unlikely, VA-ECMO can be maintained as a bridge to transplantation. Finally, in patients who do not improve despite LV unloading or develop multiorgan failure, palliative measures may be the only option.

In conclusion, the choice of unloading method largely depends on local expertise, although there is still a lack of data to guide selection among different strategies. The algorithm presented in this review provides guidance in this regard. In any case, ongoing and future randomized clinical trials will help determine when, for whom, and how LV unloading should be performed in patients supported with VA-ECMO.

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Mireya Beatriz Castro Verdes

Prognostic Echocardiographic Findings in Patients on Veno-Arterial ECMO for Cardiogenic Shock

This retrospective study analyzes critical echocardiographic findings associated with poor prognosis in patients on veno-arterial extracorporeal membrane oxygenation (VA ECMO) for cardiogenic shock.

Echocardiography plays a pivotal role in various stages of managing critically ill patients on VA ECMO, providing essential information for therapeutic decisions, evaluating responses, and early detection of complications. However, despite its widespread and increasing use, there remains a lack of standardization for necessary parameters and their cutoff values, as well as their potential prognostic value. This study aimed to evaluate the presence and timing of specific “critical” echocardiographic findings and analyze their correlation with in-hospital mortality.

This retrospective study collected clinical, hemodynamic, and echocardiographic data from 130 patients receiving VA ECMO support for cardiogenic shock from diverse etiologies between 2011 and 2018 at Toronto General Hospital, Canada. Data included causes of cardiogenic shock, patient baseline characteristics, validated "survival after veno-arterial ECMO (SAVE)" score, need for left ventricular decompression, survival, and cause of death. Transthoracic (TTE) and transesophageal (TEE) echocardiograms were reviewed, categorized temporally into three groups: the first (within 36 hours post-cannulation), the last (pre-decannulation), and the intermediate. Critical echocardiographic findings were defined as minimal or absent ejection, intracavitary thrombus, pericardial effusion, and cannula malposition.

A total of 236 TTEs and 296 TEEs were analyzed in 126 patients, with a mean support duration of 6.8 ± 4.8 days. The initial echocardiogram showed the highest incidence of critical findings (34.7%): minimal or absent left ventricular (LV) ejection was observed in 23.1% of cases, intracavitary thrombus in 6.6%, tamponade in 4.1%, and cannula malposition in 0.8%. Presence of these parameters was associated with an increased in-hospital mortality with an OR of 2.32 ($p = 0.037$). In patients without these findings on the first echocardiogram, critical findings appeared in 2.4% of intermediate and 11.3% of final studies. Additionally, the presence of any critical echocardiographic parameter was linked to increased mortality (OR 2.72; $p = 0.011$).

The authors conclude that echocardiographic monitoring is vital in managing VA ECMO patients, with those at higher risk potentially benefiting from more frequent evaluations to identify prognostic findings.

COMMENTARY:

VA ECMO provides short-term circulatory and respiratory support for patients in cardiogenic shock unresponsive to conventional medical management. However, a notable proportion of patients fail to recover or continue to deteriorate despite its use, partially due to delayed initiation in cases presented or transferred late to ECMO-capable centers, or when the decision is made after advanced multi-organ failure onset. Additionally, potential complications from ECMO use may have drastic consequences for the patient, alongside common critical care complications like infections. Consequently, in-hospital mortality for cardiogenic shock in contemporary series remains high despite VA ECMO support, reported around 56%. In this study, a similar in-hospital mortality rate of 58.5% was observed, with ECMO-related mortality at 3.9%. The mean age of patients was 48 years (range: 19–75), with higher mortality in older patients ($p =$

0.004). The authors examined the SAVE score as a prognostic clinical parameter. SAVE, a tool for predicting in-hospital survival for VA ECMO patients based on clinical data, was validated with data from the international ELSO registry and externally in an Australian cohort. A lower SAVE score also correlated with mortality in this study ($p < 0.001$).

Patients with various etiologies of cardiogenic shock were included, including some associated with lower VA ECMO survival rates, such as post-cardiotomy (39.2%), congenital heart disease (8.5%) (both part of SAVE score), and post-cardiac arrest (20.8%); however, critical echocardiographic findings were not associated with shock etiology in this study. The mode of VA ECMO (peripheral vs. central) was not specified, precluding conclusions on this aspect. No differences were found in patients with new prostheses (OR 1.06; $p = 0.93$), though the type was unspecified. Nearly half of the deaths (47.4%) occurred due to irreversible multi-organ failure post-decannulation. No cases or reasons were given for potential progression to long-term support or heart transplant. Other non-cardiac deaths included 17.1% from neurological complications and 19.7% from sepsis.

Echocardiography's low cost, wide availability, and bedside utility make it the primary imaging choice for VA ECMO patients, complementing hemodynamic data on myocardial recovery and helping to address situations where anticipated improvements do not occur. The authors previously published a review of their relevant contributions in this context. Several prior studies have described echocardiographic parameters related to successful VA ECMO weaning, though a direct link between weaning parameters and discharge survival has yet to be established. In the current study, the authors went further by validating the prognostic use of echocardiography, correlating specific critical parameters with mortality, a previously unproven link.

Selected echocardiographic parameters reflect adverse hemodynamic conditions in VA ECMO patients:

1. Minimal or absent ventricular ejection (without specific cutoff): In patients with VA ECMO, the LV has decreased systolic function, preload, and myocardial reserve, potentially hindering forward ejection. This may worsen due to increased LV afterload from ECMO return flow, which in severe cases, may prevent aortic valve opening.

2. Intracavitary thrombus: Resulting from increased myocardial oxygen consumption, subendocardial ischemia, and functional impairment, this can create a stasis leading to thrombus formation despite systemic anticoagulation.

3. Pericardial effusion: Diagnosing tamponade in VA ECMO is challenging due to altered hemodynamics; thus, any pericardial effusion should be monitored closely with clinical and hemodynamic deterioration in mind.

4. Cannula malposition or vascular injury: While the centrally or peripherally placed arterial return cannula is often inaccessible for echocardiography, the venous cannula extracting blood from the right atrium is usually visible. Malposition can cause serious complications, including thrombus formation in the cannula lumen, linked to increased mortality in pediatric VA ECMO patients.

In this study, the presence of any of these findings in the initial echocardiogram correlated with in-hospital mortality, with higher prevalence among patients with low

pulse pressure (OR 5.58; $p < 0.001$) and those requiring LV decompression (PR 7.00; $p < 0.001$). This supports early or even prophylactic decompression measures based on echocardiographic findings to prevent early mortality in VA ECMO patients.

Regarding the modality, though direct comparisons between TTE and TEE in VA ECMO are lacking, TEE generally offers superior spatial resolution, critical in patients with limited acoustic windows. However, its invasive nature entails risks in anticoagulated patients. In this study, TTE and TEE use was nearly equal, with contrast echocardiography applied in 17.5% of cases to enhance TTE resolution. Contrast effect duration is reduced in VA ECMO due to microbubble destruction in the circuit, necessitating focused, brief evaluations. Notably, no complications were reported from contrast use, enhancing its safety in this context. All consoles used were Centrimagä, without bubble detection systems. Other consoles might integrate ultrasound sensors that detect bubble or thrombus-associated flow changes. Although contrast bubble size is generally small, high-sensitivity consoles might trigger alarms, causing ECMO flow cessation with potentially catastrophic consequences. Therefore, checking the console's detection systems and disabling them before using contrast, or opting for TEE over TTE with contrast, is recommended.

In summary, mortality in cardiogenic shock remains high despite short-term circulatory support systems. Echocardiography is invaluable for these patients, and early identification of critical echocardiographic parameters can aid in recognizing patients at higher risk who may benefit from early interventions or closer monitoring. Contrast echocardiography has proven safe with consoles lacking bubble detection.

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Mario Castaño Ruiz

Results of ECMO Support in COVID-19 Patients: Expert Commentary

Expert analysis by Dr. Mario Castaño, coordinator of our society's ECMO-COVID registry, on the temporal evolution of in-hospital survival of COVID-19 patients requiring ECMO support in the United States.

This study examines the temporal evolution of in-hospital survival among 594 consecutive COVID-19 patients treated with extracorporeal membrane oxygenation (ECMO) at 49 hospitals across 21 states in the United States, using data from a prospective database extracted from the Specialty Care Operative Procedural rEgistry (SCOPE). Patients were divided into four groups according to the treatment period: Group A, March to June 2020; Group B, July to December 2020; Group C, January to June 2021; and Group D, July to December 2021.

The average number of cases per hospital was 12.1 (median 6 cases, range 1-73 cases, interquartile range 2-11 cases). ECMO indications and periprocedural management were determined by each center's protocols and treatment guidelines. No ECMO implant was performed during cardiopulmonary arrest/cardiopulmonary resuscitation.

The overall in-hospital survival was 37.2% (n = 221), 38.6% for VV-ECMO patients and 21.3% for VA-ECMO. Survivors were younger (43 vs. 49 years, $p < 0.001$), more frequently female, and had fewer days between diagnosis and orotracheal intubation (IOT; 7 vs. 10 days, $p < 0.001$). Mean age significantly decreased over time, whereas the time elapsed between COVID-19 diagnosis and intubation increased. All adjunct treatments (steroids, convalescent plasma, antivirals, anti-IL6, prostaglandins, and hydroxychloroquine) exhibited significant temporal variations across study periods.

Survival decreased between April and November 2020, improved from November 2020 to May 2021, and declined again between May and December 2021. Treatment timing throughout the pandemic contributed 18.4% to survival variability, with other significant factors contributing over 2%, including age (58.5%), days elapsed from diagnosis to IOT (8.1%), and circuit changes (5.5%). The center's influence accounted for only 2.7%.

The authors conclude that ECMO is a reasonable strategy for critically ill patients and that minimizing variability in indications and management could maximize survival.

COMMENTARY:

As observed in other series, patients included during the second COVID-19 wave had higher mortality than those in the first. In this and other studies, the most commonly cited reasons include the broadening of indications and an increase in implementing centers, leading to ECMO implantation in higher-risk patients in poorer condition and at centers with less experience. Notably, the influence of the treating center on mortality variation was only 2.7%, despite intense heterogeneity in experience among the participating centers (median 6 cases, range 1-73 cases, interquartile range 2-11 cases). This lack of influence from the center's experience has been observed in other registries, including one conducted by our Society.

Age is a decisive survival factor (58.5% contribution) as in all prior series. Mean ages and survival cutoff points hover around 40-45 years in the series that have analyzed this, underscoring the need for candidate selection regarding this parameter. Indeed, this series shows that, in the second period, the mean age of treated patients increased, subsequently decreasing as patient selection improved. However, other morbidity

markers (diabetes mellitus, renal failure, hypertension, presence of multiple comorbidities) did not worsen in the second period relative to the first.

The observed curves for concomitant therapy management reveal that corticosteroid use, a drug that has significantly contributed to survival in patients with severe COVID-19, was considerably lower in the early study periods than later, which does not explain the lower mortality in the initial phase except through the initial stringent patient selection.

The influence of days between diagnosis and ECMO initiation, especially from diagnosis to IOT, is also a consistent factor across series, potentially carrying critical importance, similar to age. Lung damage from the disease itself worsens with non-protective high-pressure mechanical ventilation (ventilator-induced lung injury) and “self-inflicted” lung injury in spontaneously breathing patients requiring high oxygen, with substantial respiratory effort and consequent significant airway pressure variations.

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José Manuel Martínez Comendador

EARLY-UNLOAD Study: Conventional Management vs. Early Ventricular Unloading in VA-ECMO Patients

The EARLY-UNLOAD study is a single-center, prospective clinical trial comparing early initiation of routine LV unloading in cardiogenic shock (CS) patients supported by venoarterial extracorporeal membrane oxygenation (VA-ECMO) against conventional management.

VA-ECMO is the most widely used form of mechanical circulatory support, providing rapid systemic flow of 4-6 L/min in cases of severe CS. However, its typical configuration with retrograde flow through femoral access frequently results in left ventricular (LV) overload, potentially leading to distention, blood stasis, thrombosis, and pulmonary congestion. Various methods of LV unloading to mitigate these complications have been widely discussed this year in a prior commentary on this blog.

The present study evaluated transseptal left atrial (LA) cannulation as a modality for LV mechanical unloading (LV-MU), contrasting it with more common options such as intra-aortic balloon pump (IABP) or peripherally inserted ventricular assist devices like the Impella CP® (commonly known as “ECMELLA” or “ECPELLA”). The EARLY-UNLOAD trial represents a prospective, single-center clinical trial conducted in CS patients requiring peripheral VA-ECMO. Its primary objective was to assess the efficacy of early routine LV-MU through transseptal LA cannulation within 12 hours of VA-ECMO initiation compared with conventional management.

A total of 116 patients, with a mean age of 67.6 years and 29.3% women, were included and placed on VA-ECMO for CS treatment. Of these, 58 (50%) were randomized to receive early routine LV-MU, while the other 58 (50%) followed conventional management. Primary outcomes showed no statistically significant difference in 30-day mortality (primary endpoint), with a rate of 46.6% in the early LV-MU group and 44.8% in the conventional management group (hazard ratio [HR] 1.02). However, 50% of the conventional group required rescue LV-MU due to refractory LV overload (distention with blood stasis, minimal aortic valve opening, and refractory pulmonary congestion). The average time to transseptal LA cannulation in the early LV-MU group was 1.1 hours, versus 21.8 hours in the conventional group who switched to rescue LV-MU.

Regarding the primary secondary endpoint, which included all-cause mortality or need for rescue transseptal LA cannulation, a statistically significant benefit was observed in the early LV-MU group (HR 0.44; 95% CI: 0.27-0.72; $p = 0.001$), largely driven by the need for rescue LV-MU. However, most secondary endpoints, such as in-hospital mortality, lactate levels, ECMO weaning, mechanical ventilation duration, renal replacement therapy, strokes, bleeding, or limb ischemia, showed no statistically significant differences between groups, with the exception of a shorter time to pulmonary congestion resolution in the experimental group.

In summary, the study’s findings suggest that routine early LV-MU through transseptal LA cannulation does not reduce 30-day mortality compared to conventional management in VA-ECMO-supported CS patients.

COMMENTARY:

This study is a milestone as the first randomized trial addressing early LV-MU therapy (using transseptal LA cannulation) compared to conventional management in CS patients requiring VA-ECMO. While awaiting further trials like the REVERSE study (using

Impella CP® for LV-MU), these results suggest against the routine early application of an LV-MU method.

In CS secondary to complicated acute myocardial infarction (AMI), at least as indicated by the single weighty trial to date (ECLS-SHOCK, discussed in a recent commentary here), early VA-ECMO initiation versus standard medical therapy does not appear to benefit 30-day survival. However, our clinical experience and the results from multiple retrospective studies indicate that the rising use of these devices is crucial in certain CS cases to save lives. Notably, most VA-ECMO-supported CS cases in this study also involved AMI patients (66.4%), followed by decompensated heart failure (13.8%), fulminant myocarditis (8.6%), and other causes comprising the remaining 11.2%. Therefore, the most common VA-ECMO use in CS cases here aligned with the complicated AMI context observed in routine clinical practice and the ECLS-SHOCK study.

It's worth noting that nearly all study patients were in severely critical states of CS, specifically in SCAI stages D or E, with 77.6% in stage D and 22.4% in stage E. They presented mean arterial lactate levels of 7.1 mmol/L, an average LV ejection fraction of 16%, and 45% had experienced cardiopulmonary arrest (CPA), though only those with witnessed CPA and responsive to commands were included. In Kim MC et al., the indication and need for ECMO are clear, enhancing the study's value and applicability.

At first glance, transseptal cannulation might appear less invasive than other LV-MU methods like the Impella CP®, as it utilizes venous access rather than arterial. However, this approach is not without risks. Challenges include potential cardiac perforation and tamponade, as seen in two cases in the experimental group. Furthermore, this method requires an additional cannula in the VA-ECMO drainage circuit and iatrogenic interatrial communication with its hemodynamic implications. The feasibility of percutaneous atrial septostomy as a valid technique hinges on operator expertise, institutional infrastructure, and interdisciplinary collaboration in patient management.

No significant differences were found regarding 30-day mortality or other secondary endpoints, including weaning, ECMO duration, mechanical ventilation duration, or renal replacement therapy. In other words, results were comparable across both groups, with the only significant difference being a shorter time to resolve pulmonary congestion in the early decompression group (3 days vs. 5 days). These results alone hardly justify routine early LV-MU.

Nevertheless, the observed 50% crossover rate (with conventional management patients eventually requiring rescue LV-MU) underscores that, on average, half of the patients require some form of LV-MU within 24 hours. Therefore, at least half of VA-ECMO patients initially deemed unnecessary for LV-MU meet criteria for its initiation within 24 hours.

These findings suggest avoiding routine LV-MU in all patients receiving peripheral VA-ECMO from the outset. Instead, it seems prudent to conclude that individualized evaluation of LV unloading is warranted, especially during the initial 24-48 hours, paying particular attention to signs of refractory congestion and LV overload.

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Section V A:

Aortic valve disease

Elio Martín Gutiérrez

Combined Aortic Valve Replacement and Revascularization Surgery: Do Rapid-Deployment Prostheses Offer Any Advantage?

A retrospective study from two European centers with extensive experience using Edwards Intuity® bioprostheses compares their perioperative and five-year outcomes with the Carpentier Edwards Magna Ease® bioprosthesis in combined aortic valve replacement and coronary artery bypass grafting (CABG).

The Edwards Intuity® prosthesis belongs to a recent generation of devices designed for aortic stenosis treatment. It is a rapid-deployment prosthesis, similar to other devices like the Livanova Perceval S® and the now-defunct Medtronic 3F®, which are collectively known as sutureless or rapid-deployment prostheses. These devices have found their therapeutic niche, especially in promoting minimally invasive approaches and reducing surgical times in complex combined procedures.

While any of these devices may appear suitable for similar indications, specific design characteristics render the Edwards Intuity® prosthesis better suited for combined procedures involving coronary artery revascularization or ascending aorta replacement, as it does not interfere with the proximal anastomoses of grafts or vascular conduits due to its supra-annular profile. When combined aortic and mitral valve surgeries are required, particularly with mitral valve replacement, other sutureless prostheses, such as the Livanova Perceval S®, are preferred due to their subannular profile, which minimizes interference during the procedure.

Bottio et al.'s study assesses the mid-term performance of the Edwards Intuity® bioprosthesis compared to the Carpentier Edwards Magna Ease® prosthesis, which is considered the gold standard for design and pericardium treatment. The Edwards Intuity® has been in use for around ten years, with the longest series reporting outcomes up to seven years, incorporating the initial learning curve, which included a paravalvular leak rate between 5–12% and an atrioventricular block incidence of approximately 10%. In contrast, the Carpentier Edwards Magna Ease® has the longest follow-up, with series extending over 20 years and reintervention rates below 15% in patients over 65 years.

A total of 285 patients were recruited from two European centers (Padua, Italy, and Lugano, Switzerland) and divided into two groups based on the aortic bioprosthesis used: 50.5% received the Edwards Intuity® and 49.5% the Carpentier Edwards Magna Ease®. A propensity score adjustment and Cox regression analysis were applied. No significant differences were observed in 30-day mortality (2.8% vs 5%) or at the five-year follow-up (7% vs 9%). Significantly shorter aortic cross-clamping and cardiopulmonary bypass times were achieved with the Edwards Intuity® (94 vs 120 min, $p<0.001$; 128 vs 160 min, $p<0.001$), and its hemodynamic performance was superior, mainly due to a greater left ventricular outflow tract clearance by eliminating suture material and native ring interference.

COMMENTARY:

Although this study does not follow a non-inferiority design, it demonstrates comparable outcomes for the new-generation Edwards Intuity® prosthesis compared to its reference, with potential advantages in simplifying the surgical technique and achieving better hemodynamic outcomes for the implanted prosthesis. As seen in other studies, the immediate impact derived from this technical simplification does not translate into “hard” clinical outcomes like survival, likely due to procedural equivalency or the need for larger samples to find statistically significant differences. Additionally, longer follow-ups are

needed in such studies to assess long-term degeneration rates compared to the Carpentier Magna Ease® prosthesis and to evaluate the potential impact of lower gradients, with consequent myocardial mass regression and potential survival benefit. Finally, given that rapid-deployment prostheses allow for a larger post-implant valve area, their role as a platform for valve-in-valve procedures compared to conventional sutured prostheses remains to be determined, particularly in patients with small aortic annuli, where experience remains limited.

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Elio Martín Gutiérrez

Second Chances: Rescue of Patients Rejected for Transcatheter Aortic Valve Implantation with Aortic Valve Replacement

This study presents the surgical outcomes of a British center, where selected high-surgical-risk patients initially rejected for TAVI were reconsidered for Aortic Valve Replacement (AVR).

The evolution of scientific evidence over the past decade in comparative studies on transcatheter aortic valve implantation (TAVI) and aortic valve replacement (AVR) has been directed towards reducing surgical risk for patients included in such studies. Early on, the PARTNER IB study, comparing TAVI in inoperable patients due to prohibitive surgical risk with medical treatment, established the clinical benefit of the interventional strategy over conservative management. The PARTNER IA study, which compared TAVI to AVR in high-surgical-risk patients, demonstrated TAVI's non-inferiority in terms of survival when compared to the, at that time, gold-standard technique.

The positive outcomes and technological advancements have supported a gradual expansion of TAVI indications, resulting in an increased number of candidates for the procedure. Consequently, Heart Team practices have shifted to selecting candidates with progressively lower surgical risk profiles than those for whom the procedure was originally intended. Given the high cost associated with the procedure, there is a need to optimize aspects such as efficiency, cost-effectiveness, and the avoidance of futility. This "TAVI phenomenon" has led to a significant reduction in AVR procedures, which has prompted surgical teams to re-evaluate patients whose intervention would have previously been deemed questionable due to their high theoretical risk, according to conventional scores (EuroSCORE II and STS-PROM score).

This paper reports a single-center case-control study (Southampton, UK), which retrospectively compared outcomes of high-surgical-risk patients for AVR, evaluated and rejected in a multidisciplinary session for TAVI between 2009 and 2019. Among 1095 high-surgical-risk patients assessed, TAVI was denied to 519. Of these, 114 (10.4%) were re-evaluated and selected for AVR, while the remaining 405 (37%) were managed conservatively.

Upon referral of candidate cases to the reference center, initial assessment was performed by a surgeon who determined the surgical risk. High/prohibitive risk patients were then evaluated in a multidisciplinary session for TAVI. Reasons for rejection included technical aspects that made the procedure prohibitive (vascular access, dilated roots, large annulus, low coronary ostia, calcified mitral annulus, and severe ventricular hypertrophy) and patient-related clinical factors (significant comorbidities being the primary cause for rejection; lack of consent; or minimal/absence of symptoms). Although the authors did not detail morbidities among patients rescued with AVR versus those treated conservatively, it is expected that the latter group had higher comorbidity, which may have impacted follow-up mortality. The mean age was 80 years, with an average logistic EuroSCORE of 8. Additional procedures to AVR were performed in 15.7% of cases, mainly coronary revascularization. Hospital mortality in the AVR group was 2.2% (below the predicted high surgical risk, >8-10%), and the stroke rate was 4.4%. Five-year survival was 12.6% for the conservative management group versus 59.5% in the AVR group ($p < 0.001$). AVR acted as an independent protective factor (HR = 0.37; $p < 0.001$), with fewer hospital readmissions compared to the conservative management group (13.6 episodes/patient-year vs. 6.9 episodes/patient-year; $p = 0.002$).

The authors conclude that AVR can be considered in elderly, high-surgical-risk patients rejected for TAVI in centers with low operative mortality, as AVR may outperform conservative treatment in well-selected patients.

COMMENTARY:

Despite the study's limitations, an important message emerges: the selection criteria for candidates with severe aortic stenosis for AVR or TAVI remain imprecise, preventing perfect procedure matching for each patient. In daily practice, this is exemplified by cases like a patient indicated for multiple combined procedures who is accepted for surgery, while another over 75 years old with isolated severe aortic stenosis and low surgical risk is selected for TAVI, or multiple successful cases of TAVI explants subjected to AVR initially denied.

The outcomes in this surgical group, despite consisting of highly comorbid octogenarians, are noteworthy for their success in both the perioperative phase and follow-up. The superiority of the surgical group over conservative management, while reminiscent of the "table-turning" in PARTNER IB, should not be viewed as such since these patients are likely not comparable. However, the high mortality in the conservative management group reinforces the need to continue focusing on these patients as, with appropriate selection, a two-thirds reduction in mortality and a significant improvement in quality of life can be achieved.

The evidence supporting current and future clinical guideline recommendations remains biased by selection criteria in sample populations, operators, and participating centers, which diverges from real-world practice. Hence, attention to registry-reported outcomes may offer a more practical strategy for managing severe aortic stenosis patients. Furthermore, beyond registry data, the active participation of surgical teams in Heart Team decision-making, tailored for each patient, remains the best assurance for assigning the optimal treatment option, suited to each phase of the disease and each center's capabilities, under the necessary outcome audit by teams conducting each procedure. Neither age (a reference parameter in recent clinical guidelines, albeit arbitrary) nor predicted surgical risk (often overestimated in available scores; risk factors not considered in these scores; lack of generalization in using TAVI-specific risk scores that could be compared with surgical-specific ones) continue to serve as adequate criteria for assigning patients to one alternative or another. Therefore, multidisciplinary assessment remains essential, as does the active participation of the cardiac surgeon. With the need to incorporate surgeons into transcatheter techniques, as they possess the full technical arsenal to offer the best therapeutic option for each patient, their opinion must be considered.

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Elio Martín Gutiérrez

By Their Calcium You Shall Know Them: Differences in Calcification Patterns of Bicuspid and Tricuspid Aortic Valves, Technical and Clinical Implications

Translational research on calcification patterns of bicuspid and tricuspid aortic valves and their implications in surgical and interventional treatment of aortic stenosis.

The increasing interest in treating aortic stenosis, coupled with the growing number of cases in an aging Western population (3% of individuals over 75, 10% over 80), has led to studies aimed at expanding knowledge of its pathophysiology, which has implications for different treatment techniques—both surgical and interventional—and their clinical outcomes. This article delves into various concepts related to calcification patterns of bicuspid and tricuspid aortic valves, their pathophysiology, and their relationship with patient survival following intervention.

Cardiac valve structure, from a histological perspective, comprises two well-differentiated regions. One is the endocardium, which produces nitric oxide, like the rest of the vascular endothelium; the other is the extracellular matrix that forms the valve structure and is populated by mesenchymal cells. Pathophysiologically, both regions are affected differently. The endocardium's function is primarily compromised by the process known as atherosclerosis, where various cardiovascular risk factors play a role. The loss of functional cells reduces nitric oxide production and the hydrophilic coating of its glycocalyx, increasing the risk of atheroembolic events and bacterial endocarditis. On the other hand, stress forces, though also responsible for endothelial dysfunction, predominantly impact the extracellular matrix, transforming mesenchymal cells into osteoblastic cells and initiating the formation of calcification nuclei that lead to aortic stenosis. The growth of these nuclei without adequate vascularization can lead to central necrosis, also providing a substrate for infectious endocarditis.

Differences in stress and shear forces between bicuspid and tricuspid aortic valves lead to notable differences in degeneration and calcification patterns. In all valves, the highest stress area during the cardiac cycle is at the commissures, which is particularly significant at the raphe in bicuspid valves. Additionally, cardiac ejection through the outflow tract behaves more laminarily over the left and right coronary leaflets, causing greater vibration on the non-coronary leaflet. In bicuspid valves, due to their dome-shaped opening, this vibration is more common over the free edge of the effective valvular area, with the annulus being more protected as the leaflets lack the same degree of mobility as in tricuspid valves. In the annular region, the endocardium's proximity to the aortic endothelium also subjects it to atherosclerotic processes.

The authors assigned 101 patients with severe aortic stenosis to surgical and interventional treatments. Fifty patients had bicuspid aortic valves, and fifty-one had tricuspid valves. Calcification patterns were rigorously analyzed in all patients via angio-CT. There were no differences in preoperative variables. Survival outcomes were analyzed based on calcification patterns, comparing both types of valves. Although the surgical and interventional options were not separately reported, the therapeutic choice did not significantly impact postoperative results. Regarding calcification patterns, the non-coronary leaflet exhibited the highest calcification degree across all valve types. Bicuspid valves showed a higher calcification volume, more concentrated on the non-coronary leaflet and the free edge, compared to tricuspid valves. Tricuspid valves showed a greater degree of annular involvement. Five-year survival was similar for patients with bicuspid or tricuspid valves after treatment. However, patients with annular

calcification above the median showed lower survival. Calcification levels above the median in the leaflet body or free edge involvement did not significantly affect survival.

COMMENTARY:

This is an original study that investigates the pathophysiology of aortic stenosis and its clinical implications. Little is still known about the mechanisms underlying degenerative valve disease. However, this study confirms the osteoblastic activity's preference for areas of highest mechanical stress.

The calcification pattern's implications for treating aortic stenosis are critical and often overlooked in treatment planning. While surgical technique involves a complete replacement, where the calcified leaflets are entirely removed, and the annulus is adapted to the prosthesis, TAVI involves an implant where the persistence of the valvular structure can interfere with the newly deployed prosthesis and the structures in the aortic root. This fact results in complications such as paravalvular leaks, more commonly occurring in the non-coronary leaflet region, as it has the highest degree of calcification. Severe degrees of annular calcification have also been associated with paravalvular leaks, especially when distributed asymmetrically, and they favor annular rupture in balloon-expandable prostheses. In bicuspid valves, calcification pattern variations in the free edge and raphe lead to poor implant adaptation, resulting in suboptimal stent positioning with paravalvular leaks in the commissures and greater stress on calcium deposits, which can cause embolism. Calcium masses are laterally displaced, occupying the Valsalva sinus space, altering its diastolic hemodynamics and potentially compromising coronary flow in specific aortic root configurations (coronary ostium height <10 mm, prominent calcium masses on the aortic face of coronary leaflets). Along these lines, different studies, with limited impact on current clinical guidelines, have associated adverse events during TAVI with the valve's calcium score measured in Hounsfield units. In the future, various computational systems with individualized flow dynamics analysis, mechanical stress, augmented reality, and 3D technology will allow more accurate implant outcome predictions and not only patient assignment to the surgical or interventional option at equal predicted risk but also the most suitable device to use according to adaptability, radial strength, stent cell size, release mechanism, etc.

Finally, another relevant factor has been the association of extensive annular calcification with higher mortality during follow-up. Despite balanced group characteristics, including age and cardiovascular risk factors, patients with more annular calcification may likely have a higher atherosclerotic burden, another mechanism underlying degenerative valve disease. This increased morbidity has likely been responsible for differences in survival during follow-up, regardless of the treatment technique applied.

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Daniel Martínez López

Outcomes of Aortic Valve Repair in Tricuspid Valves: Do We Know Why They Fail?

A retrospective analysis by a high-volume aortic valve repair center examines short- and mid-term outcomes of various isolated valve repair techniques on tricuspid aortic valves.

Aortic valve repair has emerged as an appealing alternative to prosthetic replacement in younger patients by avoiding the need for anticoagulation that mechanical prostheses necessitate. Although a safe procedure, repair failure remains the most common complication. Understanding the mechanisms associated with valve insufficiency during follow-up or reintervention is critical for accurate patient selection and optimal surgical indication, aiming for the most durable repair possible. Potential failure mechanisms have been studied in bicuspid aortic valves and in aortic root remodeling or reimplantation, including cusp prolapse, leaflet retraction, and annular dilation. However, these mechanisms have not been analyzed in isolated repairs on tricuspid aortic valves.

This retrospective study aimed to evaluate mid-term results of isolated aortic valve repair in tricuspid valves at one of the world's largest centers for aortic valve repair. A total of 264 patients were analyzed from a registry over 17 years, with a median echocardiographic follow-up of nearly six years (5.9 ± 3.6 years) and a clinical follow-up of almost seven years (6.8 ± 3.6 years). A noteworthy aspect of the study was the introduction of a classification based on cusp prolapse or retraction as a cause of aortic insufficiency. However, retraction in this context was not defined as fibrosis and/or free margin traction causing residual insufficiency but rather as any cusp with a geometric height under 19 mm. Survival, reintervention, and the incidence of significant aortic insufficiency during follow-up were analyzed. Ten-year survival was 76.7% ± 3.5%, significantly lower in patients who underwent concomitant coronary or mitral repair with the aortic valve procedure. Among those with isolated repair, ten-year survival was much higher (92.3% ± 2.7%). In subgroup analysis, the use of subcommissural plication was associated with worse survival ($p = 0.044$). Conversely, the use of pericardial patches in repair did not significantly impact survival ($p = 0.088$). Intraoperative effective height measurement correlated with improved survival ($p < 0.001$). Regarding reintervention-free outcomes, the authors recorded a ten-year rate of 73.3% ± 4.2%, with 41 (16%) patients requiring reintervention. Causes of reintervention included prolapse in 10 cases, retraction in 22, both phenomena in 4, and endocarditis in 5 patients. In these patients, various techniques—including subcommissural plication, annuloplasty, or pericardial patch—showed no significant differences in reintervention risk. Among the cohort, 48 (18%) developed significant aortic insufficiency (grades 3 or 4+) during follow-up. Analysis showed a ten-year residual insufficiency-free rate of 66.9% ± 5.2%. Subgroup analysis revealed that patients whose repair mechanism was prolapse had lower rates of aortic insufficiency during follow-up compared to those with cusp retraction as the cause (log rank = 0.036). Again, none of the techniques showed an improvement in prognosis in these patients.

The authors conclude that aortic valve repair in tricuspid valves offers good long-term survival. Repair of cusp retraction had lower durability than prolapse repair. Intraoperative measurement of effective height was associated with improved survival in tricuspid aortic valve repair.

COMMENTARY:

Despite efforts in recent years by Schäfers' group in Homburg to standardize aortic valve repair, little is known about short- and mid-term outcomes of this technique in tricuspid aortic valves. Unlike bicuspid valves, tricuspid valves have less associated annular ectasia, often leaving diseased cusps as the main cause of valve insufficiency, making success highly dependent on the surgeon's expertise.

The heterogeneity of the sample presented in this study may dilute the results. In this case, the high number of concomitant surgeries might adversely affect survival. Isolated aortic valve repair yields nearly 93% ten-year survival, superior to many series of aortic prosthetic valve replacements, which typically show around 80% survival at ten years.

Regarding residual aortic insufficiency, results indicate a nearly 67% ten-year freedom from residual insufficiency. The mean aortic annulus diameter is high (26 mm), including two patients with Marfan syndrome. Some cases might have benefited from root reimplantation or remodeling, though aortic root measurements are not provided for confirmation. The residual insufficiency rates could be partially explained by the cohort's patient characteristics. Tables reveal a high number of repairs deemed complex, with 110 patients receiving pericardial patches and 49 showing leaflet retraction defined as geometric height under 19 mm. In many published series, these patients would not be candidates for valve repair.

The most relevant information arises from the surgical findings in reintervened patients. The repairs that failed most frequently were those with retracted cusps, and annuloplasty showed no effect on residual insufficiency. Most repair failures were due to cusp retraction. Notably, the use of pericardial patch or subcommissural plication was not associated with higher reintervention rates in these valves. Longer follow-up is required to determine if both curves significantly diverge over time.

Aortic valve repair in complex scenarios, such as retraction or combined prolapse and retraction, yields poorer outcomes. In such cases, aortic valve replacement is likely the best option. Findings like those published by the SPAVALVE group reinforce the feasibility of offering biological prostheses at younger ages, thereby avoiding anticoagulation risks in young patients. Despite advances in aortic valve repair, tricuspid aortic valves remain surgically challenging even in specialized centers.

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Carlos Merino Argos

Cardiorespiratory Fitness As A Protective Factor Against The Need For Aortic Valve Replacement And Mortality After Aortic Valve Replacement Surgery

A prospective registry of a large cohort investigating the correlation between the need for aortic valve replacement and cardiorespiratory fitness along with physical activity.

For several decades, aortic stenosis (AS) has been the most prevalent valvular disease in developed countries, contributing significantly to morbidity, mortality, and a high healthcare burden. Various studies and registries have associated classic cardiovascular risk factors with the development of AS. However, the pathogenesis of degenerative aortic stenosis (DAS) is not yet fully understood, and there is still debate regarding the role of physical exercise and cardiorespiratory fitness (CRF) in its progression. Below, we present a study conducted by the group led by BTS Smenes et al., which, through a prospective registry of a large cohort in Trøndelag County (Norway), explores the association between the need for invasive therapies, such as surgical valve replacement (AVR), CRF, and physical exercise.

Over recent decades, degenerative aortic valve disease has become the most common valvular pathology in our region. This is primarily due to the drastic reduction in the incidence of rheumatic mitral and aortic valvulopathies, along with the progressive aging of the population. Although various factors have been associated with DAS, no treatment exists to halt its progression. The only effective interventions are invasive procedures such as AVR or TAVI. The authors of this study hypothesize an inverse relationship between the need for AVR and both physical training and CRF. Additionally, they will evaluate the association of postoperative mortality with these two variables.

To conduct this analysis, a prospective study was carried out using data collected from the HUNT cohort in Trøndelag since 1984, in which over half of the county's population participated. Participants were divided into three groups based on weekly physical activity reported in questionnaires: low activity (less than one hour of high-intensity exercise or less than three hours of low-intensity exercise per week), moderate activity (1-3 hours of high-intensity or more than three hours of low-intensity exercise per week), and high activity (more than three hours of high-intensity exercise per week). CRF was also estimated using clinical variables and exercise questionnaires, based on a model developed with over 4,500 patients from the same population who underwent cardiopulmonary exercise testing (HUNT3 Fitness Study). This allowed the population to be divided into quintiles according to estimated CRF. During the prospective follow-up, the relationship between these groups and the need for isolated AVR due to severe AS (defined as a mean echocardiographic gradient greater than 40 mmHg) was analyzed, along with AVR combined with other procedures in a sensitivity analysis. Patients who had undergone other types of cardiac surgery (including AVR due to aortic insufficiency) and those who underwent TAVI were excluded.

A total of 57,214 participants (52.6% women) were included and followed for an average of 17.6 years, with 102 isolated AVRs for AS recorded. The average age at inclusion was 45.6 ± 16 years, and the average age at intervention was 70.1 ± 9.8 years. While no statistically significant association was found between higher reported physical activity and the need for AVR, the authors did observe a 15% reduction in the need for isolated AVR for each estimated MET increment in CRF (HR 0.85; 95% CI 0.73-0.99). Additionally, a lower incidence of this surgery was observed in the groups with higher

CRF, with the reduction being statistically significant only in the fifth quintile (HR 0.44; 95% CI 0.23-0.86). Results did not vary when considering the sensitivity analysis that included combined procedures during the surgical act. Similarly, while no differences in survival post-AVR were found based on physical activity groups, a 37% reduction in mortality was observed for each estimated MET increment in CRF, in a statistically significant manner (HR 0.63; 95% CI 0.47-0.83); with a lower risk of mortality post-AVR in the fifth CRF quintile compared to the first (HR 0.06; 95% CI 0.01-0.47).

The authors conclude that the main finding of this study is that estimated CRF is strongly and inversely associated with the risk of AS requiring AVR, and that higher estimated CRF is associated with better postoperative survival.

COMMENTARY:

This is a prospective, observational registry with a very large sample size and extended follow-up, demonstrating a reduced risk of requiring AVR for AS among patients with higher estimated CRF, as well as improved survival in this population when intervention is needed. These data align with other studies that have also associated lower incidence of DAS in subpopulations with greater physical capacity, such as the study published by Laukkanen et al. in a Finnish population. Additionally, within the same “HUNT” cohort analyzed, the same group had already demonstrated lower incidence of coronary artery bypass surgery and improved survival in patients with higher estimated CRF, a pathology that shares several risk factors with DAS.

Conversely, despite the strong association between physical exercise and CRF, no inverse relationship was found between surgery and the subgroup of participants reporting higher activity levels. The authors hypothesize that this could be due, on one hand, to potential overestimation in self-reported physical activity, and on the other, to the possibility that excessive physical exercise may accelerate the progression of DAS, without properly distinguishing this subpopulation within those with more than three hours per week of vigorous activity.

The main limitations of the study are that, as a prospective observational registry, there is no comparator group; physical activity was self-reported rather than measured; and CRF was estimated based on a model developed with a subgroup of the same population rather than measured directly by cardiopulmonary exercise testing. Additionally, aortic valve status at inclusion was unknown, and patients who underwent TAVI were excluded.

Regardless, we can conclude by reinforcing the idea that there is an association between patients' physical capacity and reduced incidence of AVR as well as improved postoperative survival. Therefore, this aspect, along with the numerous benefits already demonstrated in other areas of cardiovascular disease and beyond, should encourage us to promote physical activity within the general population.

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José Manuel Martínez Comendador

Mid-term follow-up meta-analysis of the sutureless Livanova® Perceval® aortic valve prosthesis: adaptation to real-world scenarios

This systematic review and meta-analysis is the first study to independently evaluate the mid-term outcomes (5 years) of isolated aortic valve replacement using the Perceval sutureless prosthesis.

New technologies aimed at treating aortic stenosis are constantly evolving to reduce risks and address an increasingly comorbid population. Within this context, the sutureless Livanova® Perceval® prosthesis has emerged as a promising alternative. While short-term data has been highly favorable, evidence on mid-term outcomes remains limited. Therefore, this systematic review and meta-analysis represents the first study to specifically assess the isolated mid-term results of the Livanova® Perceval® prosthesis.

In this study, a systematic literature review was conducted across five databases. The selected articles evaluated echocardiographic and mortality outcomes beyond 5 years in patients who underwent aortic valve replacement (AVR) with the Livanova® Perceval® prosthesis. Two reviewers extracted and reviewed the articles. Weighted estimates were made for all postoperative and mid-term data. Aggregated Kaplan-Meier survival curves were reconstructed from digitized images to assess long-term survival. Seven observational studies were identified, analyzing a total of 3,196 patients. Thirty-day mortality was 2.5%. Aggregate survival at 1, 2, 3, 4, and 5 years was 93.4%, 89.4%, 84.9%, 82%, and 79.5%, respectively. The incidence of permanent pacemaker implantation (7.9%), severe paravalvular leak (1.6%), structural valve deterioration (1.5%), stroke (4.4%), endocarditis (1.6%), and valve explantation (2.3%) were within acceptable ranges during the follow-up period. The hemodynamics of this prosthesis also showed favorable mid-term results, with a mean transprosthetic gradient (range 9 to 13.6 mmHg), peak transprosthetic gradient (17.8 to 22.3 mmHg), and effective orifice area (1.5 to 1.8 cm^2) across all prosthetic sizes. Cardiopulmonary bypass (78 minutes) and aortic cross-clamp times (52 minutes) were also favorable.

The authors conclude that this is the first meta-analysis to date to evaluate the mid-term outcomes of the Perceval prosthesis independently, demonstrating good mortality, hemodynamic, and morbidity outcomes beyond 5 years.

COMMENTARY:

The importance of this study lies in it being the first meta-analysis evaluating mid-term outcomes (more than 5 years of follow-up) of the sutureless Livanova® Perceval® prosthesis, highlighting its efficacy and safety.

Regarding the primary objective, a 5-year survival rate of 79% was observed, a figure comparable to that found in current literature for conventional prostheses (75%-86%). Another notable finding was the excellent long-term mean transvalvular gradient with this sutureless prosthesis (9-13.6 mmHg), lower than that of conventional prostheses, and comparable to or even better than stentless bioprostheses and transcatheter aortic valve replacements (TAVR).

In terms of complications, the rates of severe periprosthetic leakage (1.6%) and structural valve deterioration (1.5%) were low at mid-term. This suggests that the mid-term

performance of this prosthesis is at least comparable to that of conventional prostheses. The incidence of paravalvular leakage was also low (3.6%), slightly worse than that of conventional bioprostheses but better than the reported rates for TAVR (3-25%). Additionally, the reintervention rate due to periprosthetic leaks in this meta-analysis was less than 1%, which is lower than the 3.3% reported in a recent meta-analysis evaluating the Edwards® Intuity® prosthesis. The incidence of stroke and prosthetic endocarditis at mid-term follow-up does not differ significantly from conventional prostheses. However, in this study, the incidence of stroke at 5 years (4%) is lower than that reported in other TAVR studies (10-15%). With respect to the need for permanent pacemaker implantation, an incidence of 7.9% was observed, which, although not very high, is still higher than that of conventional bioprostheses. Potential contributing risk factors include annular oversizing, intra-annular implantation, and preoperative findings such as right bundle branch block or prolonged QRS. Another advantage of this sutureless prosthesis was the reduction in ischemia and cardiopulmonary bypass times compared to conventional aortic valve prostheses. Although clinical benefits in shorter procedures, such as isolated AVR, are harder to demonstrate, greater benefits are likely to be found in combined surgeries involving multiple procedures. Additionally, the implant system design promotes the feasibility of minimally invasive approaches where conventional or stentless prostheses might present greater technical challenges. Meta-analyses comparing transcatheter bioprostheses with the Livanova® Perceval® have already shown a significant advantage of the latter at 5 years in terms of mortality and adverse events. However, these studies rely on observational data adjusted by propensity analysis, and there is a scarcity of studies evaluating TAVR beyond 5 years.

It is important to consider some limitations of this meta-analysis. First, five of the seven included studies were not randomized, which may introduce bias in the results. Additionally, unclear recruitment strategies were observed in some cases, and outcome definitions varied among studies. Furthermore, the sample size at mid-term follow-up was relatively small, potentially limiting the generalizability of the findings.

In this regard, our experience with the Livanova® Perceval® prosthesis at the University Hospital of A Coruña since 2013, with over 1,400 implants, provides a comprehensive view of the use of sutureless prostheses. We can affirm that our results largely align with previously published data. Noteworthy features and peculiarities include: 1) Significantly reduced ischemia and cardiopulmonary bypass times compared to conventional AVR. Notably, our figures are even lower than those mentioned in this review (32 min vs. 52 min in this study). 2) Larger-sized Livanova® Perceval® prostheses compared to conventional prostheses, resulting in lower peak and mean gradients in echocardiographic follow-ups (similar to those found in this review) that remain stable over time. 3) Earlier extubation and shorter ICU and hospital stays compared to conventional prostheses. 4) A lower incidence of atrioventricular blocks (AVB) currently below 4%, nearly half of that reported in this review. Although we initially had a higher AVB rate, since 2015, modifications in implantation technique and more precise prosthesis sizing, thus avoiding annular oversizing, have significantly reduced this complication. 5) Low incidence of structural deterioration and bioprosthetic dysfunction, following standardized definitions from the European consensus. With more than 7 years of clinical follow-up and an average echocardiographic follow-up of over 3 years, we found 0% severe structural deterioration, 8.8% moderate deterioration, and 2.9% bioprosthetic dysfunction, figures still lower than those in recent studies comparing conventional bioprostheses with TAVR, such as NOTION. 6) Feasible and effective “TAVI-in-Perceval” option thanks to the flexible nitinol stent of the Livanova® Perceval® prosthesis, which allows slight TAVR oversizing and has a “protective” effect to prevent coronary ostial obstruction through metal components that keep the Valsalva sinuses open. 7) Versatility of use in combined surgeries, not only coronary but also mitral

surgery (series of over 50 patients with good outcomes). In summary, our more than 10 years of experience with this prosthesis support the results of this study in many aspects.

As TAVR has gained ground in recent years as the preferred option for patients over 75 years or those with high surgical risk, as cardiac surgeons, we must highlight AVR as an attractive, effective, durable, and safe option, especially in patients within a “gray zone” for therapeutic decision-making due to their clinical and anatomical characteristics. In this sense, the sutureless Livanova® Perceval® prosthesis stands out for its ease of implantation in diverse scenarios. The widely demonstrated short-term and now mid-term benefits discussed in this study (even surpassing TAVR in several aspects) further support the utility of the Livanova® Perceval® prosthesis in a wide variety of clinical and anatomical contexts, making it an increasingly relevant and growing alternative to conventional bioprosthetic AVR and TAVR.

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Elio Martín Gutiérrez

Sutureless Perceval Aortic Valve Prosthesis: Outstanding Performance with Real-World Data

Mid-term results of the SURE-AVR international registry: a decade of Perceval sutureless bioprosthesis implantation.

Nearly 20 years have passed since the adoption of minimally invasive approaches gained traction in our country, approximately the same period we incorporated sutureless bioprosthesis implantation into our technical arsenal (including the now-discontinued ATS/Medtronic 3F). Upholding the principle imparted by our mentors—"neither be the first to adopt a technique nor the last to abandon it"—sufficient time has passed to solidify data on this type of prosthesis. Since its inception, the Perceval prosthesis has attracted equal support and criticism, suggesting that, as in many aspects of our field and life, virtue lies at the center.

Regardless, aortic valve replacement (AVR) remains a relevant technique with excellent outcomes for managing primary aortic valve disease, whether in the form of stenosis, regurgitation of degenerative or rheumatic origin, or various forms of dual lesions. According to the STS registry, AVR mortality has improved from 4.3% to 2.6%. Nonetheless, the patient profile undergoing surgery has evolved with the advent of TAVI, though enhanced surgical teams, perfusion techniques, and postoperative care have also played an essential role.

This study presents real-world results from the international SURE-AVR registry, encompassing 73 centers across 18 countries in Europe, Canada, the USA, and Australia, sponsored by Corcym S.r.l. (Vercelli, Italy). This registry compiles data for all the sponsor's products for aortic valve disease treatment, with a focus on the Perceval prosthesis, a division recently acquired.

Between 2011 and 2021, 1,652 patients received AVR with the Perceval bioprosthesis in 55 centers worldwide. Given the period covered, various stages in the prosthesis evolution were included, from anticalcification treatments to modifications in implant techniques. The patient population closely mirrors that of our region, with an average age of 75 years; 82.4% were symptomatic; and morbidities such as diabetes mellitus (31%), COPD (14%), renal insufficiency (11%), prior stroke (6.5%), or preoperative AF >20% contributed to an intermediate surgical risk level (EuroSCORE II 4.1±6.3%). Notably, 16.3% had undergone previous cardiac surgery. Early implant indications for the Perceval bioprosthesis deviated from initial recommendations for sutureless prostheses, including endocarditis (2.1%) and bicuspid aortic valve (8%). The only contraindications for implantation were aneurysmal dilation and/or aortic root dissection (the classic UST/annulus ratio >1.3 is no longer considered contraindicated) and known hypersensitivity to nickel alloys.

In 45.3% of cases, patients underwent minimally invasive approaches, with over one-third involving concomitant procedures. Of these, 26% were myocardial revascularization, while combined valve surgeries such as mitral valve (5.8%) or tricuspid valve (2.8%) procedures were less common. The Perceval prosthesis was successfully implanted on the first attempt in 98.5% of cases, with mean aortic clamp and extracorporeal circulation times of 61 minutes and 77 minutes, respectively; isolated valve procedures averaged 51 and 77.4 minutes, respectively. These times were consistent across minimally invasive and median sternotomy approaches. With a maximum follow-up of 8 years, reaching 5 years in 87.3% of patients, postoperative

mortality was 0.3% in the immediate perioperative period, with cardiovascular mortality at 1.9%/patient-years and all-cause mortality at 4.5%/patient-years. Overall 5-year survival reached 78.8%.

An essential aspect of prosthesis performance is valve-related complications. Grade 2+ paravalvular leakage occurred in only 0.1%, and grade 2+ intraprosthetic leakage in 0.2%. No patient experienced both intraprosthetic and paravalvular leaks. Permanent pacemaker implantation was necessary in just 5.7% of cases. Prosthesis-related reintervention was required in 0.8%/patient-years, due to endocarditis (7 cases, 0.4%), structural valve deterioration (10 cases, 0.6%), and non-structural dysfunction (6 cases, 0.3%). Of the 16 cases of structural and non-structural deterioration, 12 were resolved through TAVI-in-Perceval procedures, with only 4 requiring open surgery. As typical for this prosthesis, gradients remained stable throughout follow-up, with excellent mean values of 13 mmHg and peak values of 24 mmHg, yielding a residual mean aortic valve area of 1.8 cm^2.

The authors conclude that the prospective real-world data from the SURE-AVR registry demonstrates that the Perceval bioprosthesis is a safe and effective surgical option for aortic valve disease, providing excellent clinical and hemodynamic outcomes over the mid-term follow-up.

COMMENTARY:

The SURE-AVR registry offers one of the largest published experiences with the Perceval bioprosthesis, featuring data from a wide range of centers, collected prospectively over a decade. Rather than a limitation, the introduced heterogeneity should be seen as democratizing this prosthesis type, accessible to any surgical team across different settings. While this is a sponsored registry, it stands out for its transparency and a proper declaration of conflict of interest, with independent clinical data. Several results warrant separate discussion due to their relevance.

First, the patient profile is of intermediate surgical risk, still minimally impacted by the TAVI phenomenon. Also notable is the use of the prosthesis in selected cases of infectious endocarditis (without annular destruction) and bicuspid valve disease (Sievers type 1 or 2). From a technical perspective, favorable mortality results align with technical aspects that show no marked superiority compared to standard practice in our region: limited minimally invasive approaches and conventional surgical times, even for isolated AVR. This likely reflects real-world data rather than selected-center results, offering an authentic perspective on international surgical practice without any sense of inferiority.

The evolving patient profile is also evident, with AVR frequently combined with other procedures, making isolated AVR in moderate-to-low risk patients under 75 increasingly rare. While over one-third were combined procedures, most involved myocardial revascularization (despite an initial perception that its suprannular profile was unsuitable for proximal anastomoses). Surprisingly, there was a low rate of combined valve procedures in the registry, one scenario where this prosthesis might offer technical advantages. Currently, the Perceval bioprosthesis is indicated for:

- Minimizing surgical times in AVR combined with other valve and/or revascularization procedures.

- Promoting minimally invasive approaches, whether in initial procedures or reoperations requiring limited dissection.

- Challenging small or hostile aortic roots, where it achieves superior hemodynamic results compared to sutured prostheses.

The low rate of combined valve surgeries may reflect the limited experience of some teams with the prosthesis in combined procedures.

Finally, the hemodynamic performance of the prosthesis is exceptional, with a higher rate of L and XL sizes (54%) than in typical practice. Paravalvular and intraprosthetic leak rates were minimal, with very low permanent pacemaker requirement rates, largely influenced by an updated implant technique applied to most registry cases. Structural deterioration rates are comparable to benchmarks like the Carpentier-Edwards Perimount, with 1.99% and 15% degeneration at 10 and 20 years, respectively. The registry lacks long-term data beyond 10–15 years when bioprostheses tend to experience structural failure. The initial version of Perceval accounted for most cases, with only 233 Perceval Plus implants, anticipated to improve durability due to its new anticalcification treatment and aldehyde-free storage medium (FREE). Structural dysfunction was resolved via valve-in-valve procedures, offering advantages over sutured prostheses:

- Nitinol's superelastic stent allows for larger TAVI prosthesis implantation without high-risk ring fracture and avoids patient-prosthesis mismatch, enhancing hemodynamic outcomes.

- The stent extends the sinuses of Valsalva, distancing them from prosthetic leaflets and preventing their sequestering and coronary occlusion.

In conclusion, the SURE-AVR registry supports the Perceval bioprosthesis's mid-term benefits, its accessible use, and its place as a viable alternative to sutured bioprostheses with unique design and implantation advantages. It is hoped that the Perceval Plus modifications will enhance durability, enabling it to compete effectively with sutured counterparts and TAVI.

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José Manuel Martínez Comendador

Technique for aortic valve replacement with Perceval prosthesis plus mitral surgery: 7 essential steps

This editorial article thoroughly details the perioperative guidelines and surgical technique for aortic valve replacement with a Perceval sutureless prosthesis in patients undergoing concomitant mitral surgery.

Combined aortic and mitral valve surgery accounts for approximately 10-15% of all valve surgical procedures, with significantly increased mortality and perioperative risk compared to surgeries involving only one valve. Sutureless prostheses used in aortic valve replacement have demonstrated remarkable short- and long-term advantages. Among the most notable benefits are their ease of implantation and reduction in surgical times. Although the use of these sutureless prostheses in combined aortic and mitral valve surgeries has not been widely adopted or thoroughly described, there is potential that reducing ischemia and cardiopulmonary bypass times may mark a milestone in improving outcomes. In this original article, Zaheer et al. share their experience in this type of intervention and provide a detailed, step-by-step description of the most critical aspects to successfully perform this surgical technique.

1. Proper planning

Aortic annular measurements using computed tomography or echocardiography are extremely beneficial and highly recommended to anticipate the optimal size of the Perceval prosthesis. In this context, it is important to note that both mitral repairs and replacements with prostheses are viable in combination with the Perceval prosthesis, with no conclusive evidence supporting one technique over the other.

2. Accurate assessment of the mitral-aortic distance

Early clinical experience raised concerns that implanting a Perceval prosthesis could be counterproductive due to fears that the mitral prosthesis might interfere with the lower portion of the Perceval prosthetic ring, increasing the risk of displacement. However, lessons learned from early experience with transcatheter aortic valve implantation (TAVI) have provided a new perspective, suggesting that the mitral-aortic junction size is a critical factor. It has been established that if the distance between these structures, measured by echocardiography, is less than 9 mm, the risk of procedural failure increases. In the context of a Perceval prosthesis procedure, the article's authors propose that to ensure procedural success, this distance should be 4 mm in the case of mitral repairs and 8-10 mm in the case of mitral replacements.

3. “Measure twice, implant once”

In most mitral-aortic surgeries, surgeons commonly perform the complete excision of the aortic valve and the decalcification of the aortic annulus before implanting the mitral prosthesis, with an initial measurement taken at this stage. However, the final prosthesis size is likely to be smaller after the mitral prosthesis is implanted. This first measurement is the only opportunity for the sizer to freely pass through the left ventricle (LV) via the aortic annulus, allowing for a more precise and realistic measurement of the aortic annulus. After the mitral prosthesis is implanted, a second measurement of the aortic annulus is essential. At this point, it is crucial to ensure the sizer properly fits at the level of the aortic annulus. It is not useful to measure at a lower level, as the mitral prosthesis

will obstruct the sizer's passage into the LV, potentially giving the impression that a smaller prosthesis is required. Apart from this, the technique does not differ from conventional implantation.

4. Mitral first

A fundamental principle is to avoid oversizing the mitral prosthesis, as this could reduce the size of the aortic annulus, necessitating a smaller Perceval prosthesis. Additionally, oversizing could deform the aortic annulus, increasing the risk of paravalvular or intravalvular leaks, as well as the possibility of the Perceval being deployed in a supra-annular position. When dealing with a bioprosthetic mitral valve, it is essential to ensure that none of the mitral prosthesis posts align with the left ventricular outflow tract (LVOT), as this could increase the gradient and more frequently cause insufficiency and malposition of the Perceval prosthesis. The trend toward lower-profile posts in current mitral prostheses has significantly reduced this complication. Finally, using everted sutures in the mitral prosthesis implantation (patches on the atrial side) can help preserve the length of the mitral-aortic junction, preventing its shortening and thus facilitating the subsequent release of the Perceval prosthesis.

5. Balloon catheter inflation: option and considerations

Controlled balloon catheter inflation is a critical step allowing the Perceval bioprosthesis to expand fully, ensuring the proper positioning of the infrannular prosthetic ring within the native aortic annulus. However, some surgeons prefer to avoid this step to prevent potential prosthesis dislocation if the balloon is positioned too low, coinciding with the mitral prosthesis plane. This could result in an upward dislocation of the Perceval prosthesis into a distal position. In this context, the article does not clearly specify the technique recommended.

6. Assessment of correct release and deployment of the Perceval prosthesis
It is crucial to verify that the prosthesis expands fully and without visible deformities upon complete deployment. It is also essential to ensure the correct orientation of the prosthetic leaflets, with each one aligning with the respective aortic sinuses. Similar to the conventional technique, there should be no visible annulus above or below the prosthetic ring. Additionally, in this particular case, after deployment, the typical clearance between the Perceval prosthesis and the mitral prosthesis is generally 1 to 3 mm, which should also be verified to confirm proper positioning.

7. Decision-making in various circumstances

Firstly, if a problem is detected with the Perceval prosthesis, there are several solution options. If it is suspected that the aortic prosthesis is distorted due to the mitral prosthesis, this problem can be carefully addressed by applying gentle upward traction along the non-coronary sinus. In the case of an abnormal deployment and clear malposition of the prosthesis, it can be relatively easily removed using the so-called "X-movement" technique, always ensuring not to damage the aortic root during this process.

Secondly, if the problem is related to the mitral prosthesis and requires revision, it can usually be performed safely without removing the Perceval prosthesis. Unlike sutured aortic prostheses, the Perceval is flexible, facilitating visualization of the mitral area. However, in situations where additional sutures need to be placed in the anterior mitral annulus, it may sometimes be preferable to remove the Perceval prosthesis for convenience and to perform the intervention more safely.

COMMENTARY:

Double valve replacement surgery is a common procedure in our daily practice. According to databases like the STS, it represents approximately 11% of all valve operations, with the aortic and mitral valves being by far the most frequently addressed. However, it is important to highlight that the mortality associated with combined aortic and mitral valve surgery is significant, reaching around 10% as reported by the same database.

On the other hand, evidence strongly supports that shorter cross-clamp and cardiopulmonary bypass times lead to better outcomes, particularly in elderly patients or those at higher surgical risk. Registries such as SURE-AVR, along with review articles and meta-analyses we have recently discussed on this blog, have clearly demonstrated the short- and mid-term benefits of Perceval sutureless prostheses. One of the most notable and well-supported advantages of these sutureless prostheses is their ability to reduce ischemic and bypass times. This feature has garnered increasing interest among many professionals, especially in the context of multivalve surgeries, where optimizing surgical time could be of critical importance.

The literature on the use of Perceval prostheses in combined aortic and mitral valve surgery is scarce. In the most recent study with the largest sample size, Zubarevich et al. compared 46 patients who underwent surgery with conventional prostheses to 23 patients who received Perceval prostheses, with data stratification applied. The mean age was 70 years, with an average EuroSCORE of 6 points. Although surgical times were significantly reduced with the use of Perceval prostheses, this benefit did not translate into a significant reduction in morbidity and mortality.

At our hospital, CHUAC (A Coruña), we have performed a total of 64 combined aortic and mitral valve procedures since the implementation of this prosthesis. Although we have not conducted a direct comparative study with the conventional prostheses used in our center, we have observed that our ischemia and cross-clamp times remain shorter compared to the Perceval group results reported in the Zubarevich et al. study. Despite these differences in timing, it is important to note that the outcomes in terms of morbidity and mortality were very similar.

From our experience in A Coruña, we generally agree with the findings presented in the article; however, we would like to make some clarifications regarding certain steps:

- In terms of proper planning, if we anticipate that the aortic root and annulus are significantly dilated (annuli exceeding 27–29 mm), especially as determined by intraoperative transesophageal echocardiography, it may be the best decision to initially refrain from attempting to implant a Perceval prosthesis. This approach avoids the need for a high-level aortotomy, which could complicate the surgical technique required for implanting a conventional sutured prosthesis.

- Regarding the necessary distance in the aorto-mitral junction to safely implant the Perceval, we follow two fundamental criteria. First, we emphasize the importance of having an aorto-mitral "curtain" of at least 5 mm, as measured via echocardiography. Second, and even more critical, is the intraoperative visual confirmation of this distance after the mitral prosthesis has been implanted. To effectively preserve this distance after mitral valve replacement, we consider it beneficial to implant the prosthesis in an intra-annular position. Additionally, we recommend placing the sutures for the

anterior mitral annulus, whenever possible, not in the true mitral annulus but in a 5-mm recess in the anterior mitral leaflet, which is prepared in advance for this purpose.

- In our department, we follow the balloon inflation procedure but emphasize two critical aspects. First, we meticulously avoid lowering the balloon catheter excessively, which prevents prosthesis dislocation toward the aorta. Second, we limit the inflation to a pressure of 4 atmospheres for a duration of less than 5 seconds, aiming to reduce the likelihood of atrioventricular blocks, as corroborated by previous publications.

Despite the need for further studies to more conclusively support the clinical benefits of the Perceval prosthesis in combined mitral valve surgery, this procedure offers a clear advantage of shorter surgical times compared to conventional prostheses. Additionally, it remains a straightforward and safe option. The article by Zaheer et al. provides valuable insights and recommendations on this surgical technique, which will undoubtedly benefit many surgeons.

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José Manuel Martínez Comendador

Impact of prosthesis-patient mismatch in the Asian population following transcatheter aortic valve implantation

This article examines for the first time the incidence of prosthesis-patient mismatch (PPM) and its midterm clinical impact on an Asian patient cohort undergoing transcatheter aortic valve implantation (TAVI).

The indications for TAVI are rapidly expanding to include patients at lower surgical risk with extended life expectancy, making valvular hemodynamics increasingly relevant for this group.

PPM arises when the effective orifice area (EOA) of the prosthesis is insufficient relative to the patient's body surface area (BSA). The adverse outcomes of PPM after surgical aortic valve replacement (SAVR) have been well-documented and were confirmed in a recent meta-analysis, indicating a significant 34% increase in mortality. PPM following TAVI, however, has been less studied, and existing data are inconsistent. The 2018 STS/ACC TAVR registry reported severe PPM in 12% of cases, associating it with increased one-year mortality and heart failure-related rehospitalizations. It is well-known that the Asian population generally has a significantly smaller aortic annulus than European counterparts, yet the incidence and clinical impact of PPM post-TAVI in this population remain largely unknown.

The objective of this study was to evaluate the EOA following TAVI using standardized assessment methods and to determine the midterm clinical impact of PPM post-TAVI with self-expanding CoreValve® or Evolut R® prostheses (Medtronic®) in an Asian population.

In a cohort of 201 consecutive patients who underwent TAVI, PPM incidence was assessed at 30 days, defined by indexed EOA as severe (<0.65 cm^2/m^2) or moderate (0.65–0.85 cm^2/m^2). Multivariable regression models examined predictors of PPM as well as mortality and heart failure rehospitalizations at midterm follow-up. Moderate and severe PPM were observed post-TAVI in 37 patients (18.4%) and 3 patients (1.5%), respectively, with these 40 patients comprising the PPM group. Predictors of PPM included female sex, larger BSA, and reduced left ventricular ejection fraction (LVEF). Over a midterm follow-up (median, 30.4 months), patients with PPM exhibited higher risks of all-cause mortality (HR, 1.95; $p = 0.027$), cardiovascular mortality (HR, 3.38; $p = 0.043$), and heart failure rehospitalization (HR, 2.40; $p = 0.025$).

The authors conclude that PPM is associated with increased mortality and rehospitalization rates for heart failure in the Asian population at midterm follow-up.

COMMENTARY:

This article, although a retrospective study, holds significance not only by demonstrating worse clinical outcomes in the PPM group post-TAVI but also as it does so for the first time in an Asian cohort with longer midterm follow-up than previous studies (30.4 months). Patients with larger BSA, reduced LVEF, and elevated transvalvular gradients were more likely to experience PPM. Notably, beyond the first year post-TAVI, PPM's clinical impact on these patients subsides, suggesting that the repercussions of this condition are relatively early post-implantation.

Multiple studies and meta-analyses have shown a high incidence of PPM after SAVR, with a 30% increase in mortality. The STS/ACC TAVR registry, which includes over 60,000 patients, reported a PPM incidence of 37%, markedly higher than that observed in this study by Chen et al. This study reveals that PPM has a substantial clinical impact (mortality and rehospitalizations) on a TAVI patient cohort with a mean age of 80, raising concerns over its potential effect on patients 10–20 years younger.

Surgeons have tools available to reduce PPM risk by calculating the expected EOA for a prosthesis using various tables and/or applications, selecting the most appropriate prosthesis type and size for the patient. Although these industry-generated EOA tables are not flawless and have faced criticism, they may be indispensable for minimizing PPM incidence in certain patient subgroups. With the current evidence, largely supported by studies like Chen et al., there is a clear need for similar tables tailored for TAVI prostheses. Any clinician involved in TAVI should have access to such information, particularly as trials are underway to assess TAVI in younger, lower-risk patients.

It is time for multidisciplinary teams, especially when managing younger patients, to consider expected postprocedural EOA for each valve type and size to guide patient management decisions. Depending on individual cases, consideration must be given to TAVI and surgical prosthesis options, types and sizes (including mechanical valves that are less prone to PPM), and even potential aortic root enlargement techniques (such as Nicks or Manouguian procedures).

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Elio Martín Gutiérrez

Polish AVALON Registry of Low-Surgical-Risk Patients Undergoing Transcatheter Aortic Valve Implantation vs. Surgical Aortic Valve Replacement

Short-term outcomes and mid-term survival analysis of the polish AVALON registry in low-risk patients undergoing TAVI vs. SAVR.

With ongoing follow-up from comparative TAVI vs. SAVR clinical trials in low-risk patients, the release of new evidence and its impact on future clinical guidelines, occasionally, studies like the one presented here help challenge pre-existing, potentially biased trends. This sub-analysis from the Polish AVALON registry, conducted across three major national centers, contradicts the well-established body of evidence favoring TAVI's non-inferiority, or even superiority in secondary outcomes, often elevated by aggregation into composite outcomes widely observed in comparative analyses of both techniques for treating severe aortic stenosis.

The evidence comparing TAVI and SAVR in low-surgical-risk patients largely derives from PARTNER 3 with the Edwards Sapien 3® prosthesis (showing a benefit for TAVI at 1-2 years in the composite endpoint of death + stroke + rehospitalization, with the latter primarily influencing the outcome) and the Evolut-Low Risk study with the Medtronic CoreValve® prosthesis (demonstrating TAVI's non-inferiority in the composite endpoint of mortality + disabling stroke). These studies supported the FDA and CE approvals of the respective prostheses. Extended follow-up in this cohort is available from the 5-year NOTION study.

The AVALON analysis initially included 2393 patients treated between 2015 and 2019, thereby avoiding older TAVI devices. Primary prostheses used were Edwards Sapien 3®, Medtronic CoreValve Evolut®, Boston Symetis®, and Abbott Portico® for TAVI, while SAVR patients received bioprostheses with proven durability (unlike PARTNER 3 and Evolut-Low Risk, where these aspects were not specified, or NOTION, where high usage of Mitroflow/Crown® or St. Jude Trifecta® was reported, known for early structural degeneration). In total, 629 patients received TAVI exclusively via transfemoral access, and 1764 underwent SAVR, predominantly through median sternotomy, with 4% receiving minimally invasive approaches. Although both groups were broadly comparable (all low-risk patients), a propensity-matching analysis was conducted on 13 clinical variables, including age, insulin-dependent or non-insulin-dependent diabetes, renal dysfunction grades, LVEF, and NYHA, with low tolerance for intergroup differences. Patients requiring interventions beyond aortic valve replacement were excluded, controlling for the higher rate of associated procedures commonly penalizing SAVR in randomized studies. Ultimately, 329 TAVI and 593 SAVR patients comprised the final analytical set.

With comparable low-risk patient groups, procedural mortality and survival up to 2 years were similar. However, SAVR demonstrated 30% lower mortality at 6 years ($p = 0.13$). Subgroup analysis revealed that men, those under 75 years, smokers, those with an EuroSCORE II <2, hypertensives, patients with AF, and those with CKD, benefited more from SAVR in terms of survival.

These results may partially be attributable to post-procedural morbidity. Nevertheless, the rate of pacemaker implantation during post-procedural hospitalization was low (SAVR 1.4% vs. TAVI 3.3%; $p = 0.002$), as were bleeding complications (SAVR 5.2% vs. TAVI 2.7%; $p = 0.08$), renal failure (SAVR 4.7% vs. TAVI 2.4%; $p = 0.9$), and stroke

(SAVR 1.9% vs. TAVI 0.3%; p = 0.1). The study did not assess echocardiographic parameters such as paravalvular leakage or residual gradients, nor the incidence of new LBBB, which could explain the survival impact during follow-up. Additionally, factors such as porcelain aorta, prior thoracic radiation, aortic valve calcification patterns, and femoral access restrictions were not considered, potentially introducing selection bias inherent to retrospective studies.

The authors conclude that, while there is no demonstrated survival difference between TAVI and SAVR in the first two post-procedural years, beyond this period, SAVR is associated with improved survival. Extended follow-up of randomized studies in low-surgical-risk patients is needed to confirm these findings and draw definitive conclusions.

COMMENTARY:

This study, published in a prestigious journal, is grounded in real-world outcomes, as captured in a registry setting, and though retrospective, benefits from a careful design focused on producing accurate and conclusive results as opposed to potentially biased studies (e.g., isolated all-cause mortality analysis, 6-year follow-up, exclusion of procedures beyond aortic valve intervention, selection of proven prostheses, and manageable rates of perioperative complications, reflecting the expertise of operators and care teams). It shows better mid-term survival for SAVR compared to TAVI, aligning with meta-analyses like that of Barili et al., which indicated that TAVI offers survival benefits only within the first few months, with outcomes equalizing at two years and SAVR outperforming TAVI beyond this period, particularly in low-surgical-risk patients.

The registry's findings again highlight the limitations of randomized evidence in establishing reliable recommendations and guiding clinical practice. Although clinical trials continue to shape treatment standards, they are subject to a rigorous selection process that limits real-world applicability. For instance, 80% of candidates in the NOTION study were excluded, and >40% in the AVALON registry had dual aortic lesions—the most common presentation of aortic valve disease—compared to only 4% in NOTION. It is known that dual-lesion patients face worse outcomes due to more extensive myocardial remodeling resulting from both pressure overload from stenosis and some degree of volume overload from insufficiency, unlike pure stenosis cases. Consequently, real-world data, though prone to selection bias, can be a valuable resource for illuminating patient outcomes with severe aortic stenosis and aiding in better treatment allocation.

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José Manuel Martínez Comendador

Reflections and Clarifications on the Risk of Bias in Trials Comparing Percutaneous vs. Surgical Aortic Valve Replacement

A systematic review and meta-analysis aimed at quantifying and analyzing biases in clinical trials comparing transcatheter aortic valve implantation and surgical aortic valve replacement.

Evidence comparing transcatheter aortic valve implantation (TAVI) with surgical aortic valve replacement (SAVR) for treating aortic stenosis (AS) is based primarily on seven randomized clinical trials (RCTs). Since the first RCT was conducted in 2007, patient inclusion criteria have gradually expanded to include those with lower surgical risk profiles. These studies have demonstrated not only the non-inferiority but, in some cases, the superiority of TAVI compared to conventional treatment, shaping the guidelines for managing severe symptomatic AS in the 2021 ESC/EACTS Guidelines on Valvular Heart Disease.

Randomization helps control various biases, such as confounding factors in assigning treatment options. However, certain limitations persist, including selection criteria that do not accurately represent the target population, deviations from assigned treatment (DAT) post-randomization (crossover, intention-to-treat vs. as-treated analyses, etc.), protocol deviations in relation to additional procedures besides AS treatment, and patient loss during follow-up. These unresolved issues introduce biases that may affect the validity of RCTs. Quantifying these biases in TAVI vs. SAVR RCTs had not been adequately addressed until now.

The aim of this study was to determine whether randomization effectively protects TAVI vs. SAVR RCTs from other biases that may arise at different stages of study design. To this end, a systematic literature review was conducted from January 1, 2007, to June 6, 2022, across MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials. Two independent researchers extracted data following PRISMA guidelines. A random-effects meta-analysis was conducted, including eight eligible RCTs with a total of 8,849 participants, who were randomized to TAVI (n = 4,458) or SAVR (n = 4,391) with a maximum follow-up of five years. An analysis of the impact of various biases on the aggregate outcomes of the selected studies was conducted:

The pooled DAT rate was 4.2%, favoring TAVI (pooled relative risk [RR] vs. SAVR = 0.16; $p < 0.001$), indicating a higher rate of continued treatment for patients initially assigned to TAVI than vice versa.

The pooled loss-to-follow-up rate was 4.8%. Meta-regression showed a significant association between the rate of follow-up loss and the length of follow-up, although there was an imbalance in favor of TAVI (RR = 0.39; $p < 0.001$), with a lower rate of patient attrition compared to the SAVR group.

The pooled average rate of patients receiving additional procedures besides AS treatment was 10.4%: 4.6% in the TAVI group and 16.5% in the SAVR group (RR = 0.27; $p < 0.001$). The most frequent associated procedure was myocardial revascularization, which was also less common in the TAVI group (RR = 0.40; $p < 0.001$).

The authors conclude that a significant proportion of DAT, follow-up loss, and additional concomitant procedures skew results in favor of TAVI, posing a systematic, selective imbalance that may affect the validity of comparative TAVI vs. SAVR RCTs.

COMMENTARY:

This review is based on eight RCTs: PARTNER 1A, 2A, and 3; the US CoreValve Pivotal High Risk Trial; SURTAVI; the Evolut Low Risk Trial; NOTION; and UK TAVI. It originates from suspicions that early RCTs comparing TAVI with SAVR outcomes in high-risk surgical patients exhibited potential methodological errors. In subsequent trials conducted with intermediate- and low-risk surgical patients, these biases appeared to persist. Barili, the lead author of this meta-analysis and a strong proponent of TAVI, demonstrated with this meta-analysis something that had only previously been suggested: a systematic, selective imbalance, with a lower rate of DAT, patient loss to follow-up, and additional procedures performed in the TAVI group.

The first issue involved DAT. After randomization, most patients assigned to TAVI continued with the assigned treatment, while a higher proportion of patients in the SAVR group deviated from their assigned treatment. The cause of this phenomenon is unknown, but one hypothesis could be how this type of clinical trial is “presented” to potential participants. Patient expectations generated before randomization toward the experimental treatment (in this case, TAVI) may have been frustrated upon learning they were assigned to conventional (surgical) treatment, potentially leading to voluntary study withdrawal in greater numbers due to the apparent disadvantage of conventional surgery versus a less invasive option.

The second relevant finding concerns the significant imbalance in patients undergoing additional associated procedures between the TAVI and SAVR groups (4.6% vs. 16.5%, respectively). Although multiple associated procedures have been enumerated, the most common was myocardial revascularization, affecting 4.5% of patients in the TAVI group compared to 10.8% in the SAVR group. The 2021 ESC/EACTS Guidelines on Valvular Heart Disease state that this higher incidence of myocardial revascularization in the surgical group should ultimately be seen as a protective factor. This assumption is not entirely accurate, as an additional procedure increases perioperative risk (as demonstrated by various surgical risk scales) and, while it may reduce the risk of future clinical events, this has not yet been proven. The most plausible explanation for the higher proportion of concomitant procedures in the SAVR group could be the significant flexibility that surgeons have to modify the surgical technique when encountering other concurrent conditions, as well as the learned tendency to address all surgical issues once the patient is on the operating table.

Finally, and no less important, is the finding of significantly lower patient loss to follow-up in the TAVI arm. Follow-up losses reached as high as 20% at five years in the SAVR group and consistently increased over time (1.4% at one year vs. 8.9% at five years). These dropout biases, particularly when follow-up loss is high, can compromise study validity, especially if clinical events contributing to the primary endpoint (such as death and stroke) are infrequent. The cause of this phenomenon remains unclear. Perhaps again, the fact that patients are receiving conventional surgery rather than the experimental treatment could be a reason, especially if their recovery is uneventful, leading them to skip follow-up visits. The same ESC/EACTS 2021 Guidelines on Valvular Heart Disease adopted an age-based intervention approach, recommending TAVI for patients over 75 years old (class IA). Prosthesis durability is a highly relevant topic, and many RCTs are extending follow-up to assess long-term outcomes. However, due to limited survival or lack of follow-up continuity, most trials will lack the statistical power to detect ten-year differences, which would prevent clarifying this issue. Therefore,

regardless of their results, these studies should not be used to further lower the age threshold for TAVI.

We all agree that RCTs provide the best evidence available, but they are not infallible sources of all answers. Even the highest-quality research studies have limitations, and the key lies precisely in those “details.” This meta-analysis serves as a reminder for clinicians that, even with RCT-based information, caution is needed in interpretation, and sound clinical judgment and common sense should prevail.

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Elio Martín Gutiérrez

Residual Paravalvular Insufficiency after TAVI: Mild Leakage Matters

Results from a Japanese and a Swedish center, sourced from the international TAVI Registry, compare 1-year post-TAVI survival and morbidity among patients with mild residual paravalvular leakage and those with no residual/trivial leakage post-implantation.

Discussing paravalvular leakage after transcatheter aortic valve implantation (TAVI) requires an overview of the procedural evolution and outcomes over its 21-year history. Because TAVI involves implanting a device while the native aortic valve remains in place, there is an increased risk of incomplete remodeling of calcifications around the annulus and leaflets, potentially leading to paravalvular leaks from gaps between native tissue and the prosthetic stent. In response, successive generations of these prostheses have incorporated technical modifications tailored to different implantation approaches: balloon-expandable, self-expanding, or mechanically-expandable.

In balloon-expandable models, like the Edwards® Sapien®, the primary advantage is greater radial force during implantation, which enables more effective remodeling of calcified tissue. Additionally, the inclusion of skirt-like adaptors that adjust the stent to irregular tissue contours has been the proposed solution to reduce paravalvular leakage. Self-expanding valves, such as the Medtronic® Evolut®, Boston® ACURATE neo®, Abbott® Portico®, and Navitor®, exert less radial force initially but offer greater adaptability, improving fit over subsequent days through the martensitic phase of the nitinol stent. These devices also feature skirts, albeit with a lower profile than balloon-expandable options. The most effective enhancement, however, has been dynamic sealing, achieved through a reverse valve mechanism in the Abbott® Navitor® prosthesis, which effectively blocks regurgitant flow. Lastly, mechanically-expandable valves like the Boston® LOTUS Edge® use high-density mesh stents to replicate the radial force of balloon-expandable models. This stent structure provides tissue remodeling, a feature termed "adaptive seal," within which the valvular mechanism is anchored, bypassing the tissue remodeling phase seen in balloon-expandable models and reducing structural damage risk to the leaflets.

The emphasis on and clinical significance of paravalvular leakage has evolved over time, increasingly considering a risk-benefit assessment of the procedure. Initially, even moderate leaks were deemed acceptable, given that most TAVI patients were inoperable or at high surgical risk, with priority given to resolving stenosis (PARTNER I). It was also argued that, given that aortic valve disease often presents as mixed lesions, patients would better tolerate some regurgitation. However, as TAVI has been extended to younger, lower-risk patients, tolerance for complications, including paravalvular leakage, has declined. In intermediate-risk populations (SURTAVI, PARTNER 2), a slight reduction in survival due to mild paravalvular leakage was observed in medium-term follow-up (5 years, Makkar et al., PARTNER 2).

This finding accelerated the establishment of assessment and grading criteria, culminating in the current VARC-2 guidelines based on three echocardiographic levels (none/trivial, mild, moderate, severe), which are employed in this study. It remains to be seen how paravalvular leakage will impact future studies on low-risk groups (PARTNER 3, Evolut Low-Risk), particularly with the inclusion of newer prosthetic designs. However, the trend now favors real-world registries over extended clinical trial follow-ups due to the excessive biases and follow-up losses highlighted by Barili, previously discussed on this blog.

To this end, this study reviews outcomes from the TAVI Registry, drawing data from two centers, one in Japan and the other in Sweden, covering the years 2008 to 2019. Various prosthesis models were used, with balloon-expandable valves being the most prevalent (58%) and transfemoral approach the most common (94%). Post-dilatation was performed in 6% of patients without residual leakage and in 14% of those with mild leakage (p = 0.004, adjusted groups). The analysis included patient characteristics, morbidity and mortality rates at follow-up, and 5-year survival among patients with absent/trivial paravalvular leakage versus those with mild leakage. Higher grades of leakage were excluded from analysis due to their known impact on short- to medium-term survival. Raw data from 1,404 patients were adjusted using propensity score matching, resulting in two homogenous groups of 332 patients each. Only patients with complete follow-up were included. In the unadjusted analysis, patients with mild residual paravalvular leakage were older, had more comorbidities, a lower body mass index, and more severe stenosis. These differences were mitigated by the adjustment, with findings indicating that patients with mild paravalvular leakage had a 41% higher mortality rate at 5 years, independent of periprocedural mortality or complications.

The authors conclude that patients with mild residual paravalvular leakage after TAVI experience increased mortality at medium-term follow-up compared to those without residual leakage, underscoring the prognostic significance of even mild leakage.

COMMENTARY:

Divergent findings on the impact of mild paravalvular leakage observed across clinical trials have led to it being viewed as an acceptable complication, sometimes considered a satisfactory technical outcome. However, this study confirms the reduction in survival over follow-up, as suggested in prior studies. Therefore, mild paravalvular leakage, along with new-onset left bundle branch block, the need for permanent pacemaker implantation, subclinical vascular injuries, asymptomatic thrombosis, or limitations in percutaneous access to the coronary tree, should no longer be considered minor complications. These factors must be weighed in patient selection for surgery versus intervention by the Heart Team, especially in low-risk and asymptomatic cases.

Several hypotheses have been proposed to explain the association between mild paravalvular leakage and increased mortality. First, in patients with aortic stenosis, left ventricular compliance is often low, meaning volume overload might persist despite mild residual regurgitation. Indeed, this adverse effect has been described with mild mitral regurgitation post-repair and the poorer prognosis in patients with combined aortic stenosis and regurgitation versus those with pure stenosis. Second, mild paravalvular leakage may lead to gastrointestinal bleeding episodes due to an acquired von Willebrand factor deficiency caused by the mechanical stress from regurgitant flow, resembling Heyde syndrome pathophysiology. Third, it is hypothesized that mild leakage might gradually worsen over time, exacerbating these adverse effects.

In summary, after 21 years of development, TAVI continues its pursuit of technical perfection through advancements in device technology and procedural aspects. Meanwhile, patient selection will continue to rely on the discernment of the Heart Team, particularly in intermediate- to low-risk and asymptomatic cases. Further research is needed to determine which preprocedural factors can predict the development of these so-called minor complications that significantly impact patient survival. Assessment will need to be increasingly thorough, moving beyond evaluations based solely on age, surgical risk, vascular access diameters, and predictors of major complications.

Comprehensive assessment of the burden and distribution of calcification in aortic root structures, potentially through simulation and modeling, may help better align patients with the most appropriate therapeutic option, including the specific transcatheter prosthesis. Despite the favorable outcomes observed with TAVI, there may remain a subset of patients for whom resection of calcified leaflets and implantation of a bioprosthesis on a decalcified annulus will continue to be necessary.

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José Manuel Martínez Comendador

Update on alternative access for transcatheter aortic valve implantation (TAVI)

A comparative review of different non-transfemoral alternative access options for TAVI, with the objective of providing updated information on the latest techniques, outcomes, and advances in the field.

Over the past decade, transcatheter aortic valve implantation (TAVI) has evolved from a therapeutic option limited to patients at very high surgical risk to an established alternative for low- to intermediate-risk patients. Technological advances in percutaneous prostheses, with ongoing improvements toward reducing the size of introducers and delivery systems, have allowed femoral access to remain the access of choice whenever feasible. Consequently, the proportion of non-transfemoral (TF) access has declined from 20% to 5% in recent registries. However, it is important to note that in a significant number of TF-TAVI patients, TF access is not ideal due to excessive calcification, tortuosity, or limited femoral artery diameter. Indeed, in the intermediate-risk population treated with second-generation percutaneous prostheses via TF access, the risk of major, life-threatening bleeding complications was excessively high (8-12%).

This review seeks to provide current evidence for each of the existing alternative access options, enabling well-informed decisions when choosing the most appropriate and safe access based on each patient's clinical and anatomical characteristics.

Transthoracic Access: Transapical (TA) and Transaortic (TAo)

From a technical perspective, in the early stages of TAVI procedures, transthoracic access became a preferred alternative due to the high profile of introducer sheaths that prevented safe peripheral access. TA-TAVI, first performed in 2005, offers advantages such as easy guidewire crossing through the aortic valve and comfortable maneuverability of the prosthesis due to the short distance required. However, this approach is consistently associated with a certain degree of myocardial damage, as well as with rare but technique-related complications, such as cardiac tamponade, mitral subvalvular apparatus damage, or uncontrollable bleeding from the ventricular apex. TAo-TAVI, first performed in 2010, is a more anecdotal transthoracic alternative that generally requires a partial upper sternotomy, although it can sometimes be performed via the suprasternal notch. Contraindications include previous sternotomies or severely calcified ascending aortas.

In terms of outcomes, large registries of high-risk patients indicate similar 30-day and 1-year mortality rates for both transthoracic accesses, at approximately 12% and 25%, respectively. There are also no significant differences in other complications.

Comparing transthoracic and transfemoral TAVI is challenging because the former is typically used in higher-risk patients. Some propensity score-matching studies suggest that outcomes are similar; however, in most comparative studies, transthoracic TAVI yields worse results in terms of major adverse events as well as in-hospital and late mortality. The incidence of neurological events is similar or lower with transthoracic TAVI, despite a higher incidence of postprocedural atrial fibrillation, likely due to the absence of retrograde catheter manipulation in the aortic arch. Additionally, overall costs are higher with this alternative access, owing to longer hospital stays and a higher incidence of readmissions. Consequently, there has been a progressive decline in the use of this

approach; for example, according to the French TAVI registry, it decreased from 19% in 2010 to 4% in 2015.

Peripheral Arterial Access: Transcarotid (TC) and Transsubclavian/Axillary (TS)

From a technical standpoint, the progressive reduction in introducer and delivery system diameters has promoted the use of alternative peripheral arteries other than TF access. Both TC and TS access theoretically allow the procedure to be performed under local anesthesia with sedation. TS access was first used in 2007. The primary surgical complexity lies in the variable depth of this artery depending on the patient's body habitus, the close proximity of the brachial plexus, and the relatively fragile arterial wall due to a less robust media layer compared to the femoral artery. Furthermore, achieving optimal coaxial alignment is technically challenging, especially if the right subclavian artery is used and the aortoventricular angle is <70º. Although some studies report similar outcomes for percutaneous versus surgical access, surgical access is generally preferred because managing vascular complications can be very challenging given the artery's limited accessibility and difficulty with compression. TC access, first employed in 2010, requires a surgical incision. Given that the common carotid artery typically has less atherosclerosis than the internal carotid or femoral arteries and is superficially located, surgical dissection is technically simple, even in obese patients. It is considered accessible if the minimum luminal diameter is ≥6 mm and there is no significant stenosis (≥70%) in the contralateral artery. The left side also offers better coaxial alignment between the aorta and the prosthesis delivery system.

Analyzing outcomes in intermediate- to high-risk populations, both accesses provide similar results in terms of major adverse events and 30-day and 1-year mortality (5% and 15%, respectively). Regarding vascular complications, both accesses show a low incidence; however, in some studies, such as the French TAVI registry, the incidence is significantly lower with TC access (TC: 0.2% vs. TS: 1.3%). In a significant sub-study of the STS/ACC TVT registry with propensity score matching, the incidence of stroke was significantly lower with TC access (TC: 4.2% vs. TS: 7.4%), as were fluoroscopy time, total contrast volume, and hospital stay.

Comparing peripheral arterial (non-transfemoral) TAVI to transthoracic TAVI, recent data suggest that TC/TS access yields better survival at 30 days and 2 years, with a lower rate of most major adverse events except stroke.

Comparing peripheral arterial (non-transfemoral) and TF-TAVI, the most relevant propensity score-matched study by Beurtheret et al. found no significant differences in major adverse events, except for vascular complications, which were lower with non-transfemoral TAVI (TC/TS: 0.68% vs. TF: 1.36%). In the few studies that directly compare TC-TAVI and TF-TAVI, such as Watanabe et al. (without propensity matching), there were no significant differences in clinical outcomes; in the propensity-matched study by Folliguet et al., there was no difference in 1- and 2-year mortality, though TC-TAVI had a higher incidence of stroke, bleeding, and renal failure but a lower rate of vascular complications. Overall, TS-TAVI outcomes were also very similar to those of TF-TAVI. In summary, promising results have been achieved with both TC and TS access, and previous concerns about neurological outcomes with TC-TAVI seem to be dissipating.

Transcaval (TCv) Access

The most recent approach, TCv access, is generally used when other options are not feasible. This procedure requires detailed preoperative assessment using computed tomography of the descending aorta to determine the optimal location for the caval-aortic

crossing. While it has a very high success rate (99%), it is associated with a higher incidence of bleeding complications and vascular complications near 20%, a non-negligible rate of aortocaval fistula that does not seem to affect mortality or readmission rates, and a mortality rate of 8% and 29% at 30 days and 1 year, respectively.

Lastly, this update provides a highly useful decision-making algorithm used at the Quebec Heart and Lung Institute. TF-TAVI would be the first option, with alternative access selected based on each patient's characteristics, with TC as the first alternative option, followed by TS, TAo, and TA in successive order.

COMMENTARY:

This article by Junquera et al. is an excellent, concise, yet comprehensive review that any cardiac surgeon looking to learn, improve, and expand the use of TAVI via alternative access should read and have in their collection. The most relevant meta-analysis comparing TC versus TF-TAVI, published by Abraham et al. this month in *Am J Cardiol*, reinforces this review's findings. Although TC-TAVI patients have a higher risk profile, the meta-analysis demonstrates excellent outcomes for both accesses, although with a 30-day mortality advantage for TF-TAVI (TC: 3.7% vs. TF: 2.6%, p= 0.02) and vascular complications in favor of TC-TAVI (TC: 1.5% vs. TF: 3.4%, p = 0.04).

Despite the potential advantages and satisfactory outcomes of TC and TS access, these approaches are available in only 10% and 39%, respectively, of centers performing TAVI in industrialized nations, whereas TA-TAVI continues to be offered in 70% of these centers. At our center in A Coruña (CHUAC), we have accumulated over 10 years of experience with more than 400 non-transfemoral TAVI cases, primarily TA-TAVI until two years ago, and since then, we have transitioned to TC/TS-TAVI, with over 120 cases and excellent results corroborating the findings of this review. It is essential that any hospital performing TAVI is familiar with at least one alternative access to optimize outcomes for aortic stenosis treatment.

Given the outstanding results shown in the current review by Junquera et al. regarding TC/TS access, it is advisable to consider these alternative peripheral options in cases where femoral access presents a higher risk of complications.

In our institution, we have already implemented this strategy in patients with borderline femoral access, opting for alternative peripheral access, primarily TC access, instead of TF access. It is essential that the choice of the most suitable access be personalized by a multidisciplinary Heart Team, considering each patient's specific characteristics. Lastly, it would be highly recommended to establish decision-making algorithms in each center to help determine the best therapeutic option in daily practice.

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Elio Martín Gutiérrez

Current state of aortic valve replacement surgery in 2023

This article is more than a mere review. Its creation is motivated by the commemoration of the twentieth anniversary of Dr. Alain Cribier's first TAVI implantation. Additionally, it is signed by some of the primary collaborators in the U.S. randomized clinical trials and is structured similarly to a clinical guideline or "Focus Update" document. These factors, along with its publication in one of the most prestigious cardiology journals during an "inter-guideline" period, suggest that many of its statements will not be trivial but rather shape the future direction of aortic valve disease treatment until the release of the next consensus documents.

The review begins with the well-known historical progression of the successive clinical trials conducted on Edwards® Sapien® and Medtronic® CoreValve®/Evolut® prostheses, with patients at progressively lower surgical risk. Today, age has become the most relevant factor in the decision between TAVI or surgical aortic valve replacement (SAVR). Each study's results were integrated into subsequent guideline updates, with class I or IIa recommendations, and the FDA approval of the procedure and various device generations for each risk profile. It is commendable that the authors present an update on all-cause mortality at the longest available follow-up for each of these trials, showing consistently better results for the surgical cohort in high- and intermediate-risk patients at 5 years (PARTNER IA, CoreValve US, PARTNER 2A, SURTAVI). However, there were no significant differences in low-risk trials (NOTION at 5 years; PARTNER 3 and Evolut Low Risk at 2 years). With this, it seems the authors intend to demonstrate the low utility of predicted surgical risk in assigning patients to one treatment option over another.

Consequently, the decision between TAVI and SAVR must be based on a set of clinical and technical aspects analyzed point-by-point by the authors and summarized in a table reminiscent of the 2018 European Society of Cardiology guidelines "Favours TAVR/Favours SAVR" criteria, which first introduced 75 years as a criterion for treatment allocation. Below, we will discuss the controversies surrounding each factor limiting TAVI and in which situations SAVR remains preferable.

COMMENTARY:

The main criteria for SAVR indication analyzed were:

1. Age and life expectancy: It is unsurprising that the age recommendation for TAVI has gradually decreased. This paper is the first reference document to formally suggest 70 years as the new cutoff point, leaving a gray area between 51 and 69 years and recommending surgery at 50 years. The authors argue for the use of bioprostheses in intermediate ages and present different options for patients under 50 to reduce the risk of oral anticoagulation, including low INR levels (1.5–2) and extending the application of the Ross procedure. They acknowledge that TAVI durability remains uncertain beyond 10 years and present an unconvincing argument for structural degeneration at 6–9 years. To maximize bioprosthesis implantation, they also discuss a strategy of multiple procedures in young patients, weighing the pros and cons of each:

    - SAVR-TAVI-TAVI: This is considered the optimal approach, starting with a surgical bioprosthesis, which offers better support for

subsequent percutaneous procedures. Additionally, specific supports are designed for this purpose (Edwards® Inspiris®), or root/ring enlargement techniques can be performed to prevent prosthesis mismatch or allow future valve-in-valve implants.

- TAVI-SAVR-TAVI: Here, TAVI is the initial treatment. The advantage is that the first procedure is less invasive, and in reoperation, the explant of the transcatheter prosthesis followed by surgical implantation allows for a potential fourth intervention if needed. However, the limited experience in explanting TAVI prostheses and the high complication rates reserve this strategy for cases where TAVI is justified as a bridge for patient recovery or other medical issues (e.g., awaiting cancer surgery).

- TAVI-TAVI-TAVI: This fully percutaneous option is the least favorable, as it complicates coronary access and increases the risk of complications by the third procedure. If this route is chosen, a balloon-expandable/self-expanding/balloon-expandable prosthesis sequence is recommended to minimize coronary compromise in future procedures.

Access for percutaneous coronary approach remains unresolved. In over half of the cases, there is misalignment between the TAVI prosthesis commissures and one of the coronary ostia, compromising access in approximately 10% of patients who received a balloon-expandable prosthesis, which is less prone to this complication.

Another issue to consider in these patients, especially in those starting with TAVI, is the impact of conduction disorders. Beyond the effect on survival and quality of life, these patients are likely to require multiple generator replacements over their lifetimes. Surgical options should be prioritized for patients at risk of this complication (asymmetric calcium distribution, right bundle branch block, bifascicular block).

2. Anatomical aspects: Different factors associated with the aortic valve, aortic root, ascending aorta, and vascular access limit TAVI indication. These include:

- Bicuspid and unicuspid aortic valves: Although randomized evidence is lacking due to these patients' systematic exclusion from clinical trials, observational data show higher rates of paravalvular leakage, stroke, and pacemaker implantation, with no short-term mortality impact. The association with concomitant aortopathy also establishes SAVR as the only reasonable alternative for patients with appropriate surgical risk.

- Unfavorable aortic root anatomy: The aortic annulus and root geometry can present challenges. A large annulus (area >575 mm^2 and/or perimeter >85 mm in systole) has been addressed with the

development of 29 mm Edwards® Sapien® and 34 mm Medtronic® Evolut® prostheses. SAVR, with or without root replacement, is the preferred approach for extra-large annuli (area >683 mm^2 and/or perimeter >94.2 mm) to avoid severe complications (paravalvular leakage, device embolization). Similarly, while a small annulus was vaguely defined as <21 mm, new thresholds with an area <400 mm^2 and/or perimeter <72 mm predict increased rates of severe mismatch (EOA/BSA <0.65 cm^2/m^2) following TAVI. Incidence rates of mismatch are similar in surgical cohorts, though authors point out an "unrelenting" restriction in root/annulus expansion procedures. For the aortic root, the main issue arises with small roots due to the risk of sinus of Valsalva occupation by calcified leaflets and compromised coronary perfusion. Suitable anatomy for SAVR includes ostial height <10 mm and aortic root diameter <28 mm.

- Calcification of the left ventricular outflow tract (LVOT): This asymmetric calcification pattern strongly predicts stroke, paravalvular leakage, and annular rupture, making SAVR preferable whenever surgical risk is not prohibitive.

- Porcelain aorta and chest radiation: Although the former was a classic reason for inoperability, the latter has traditionally led to TAVI recommendation as it was a PARTNER I selection criterion inherited in subsequent clinical trials. Post-radiation pericarditis rarely poses difficulties for surgical technique. However, cases of porcelain aorta caused by post-radiation sequelae (e.g., ostial coronary stenosis, calcification of the anterior mitral leaflet, aortic stenosis, and porcelain aorta) make the percutaneous option preferable.

- Limitations for vascular access: Assigning SAVR due to an unsuitable iliofemoral approach is currently considered unreasonable. The choice between TAVI and SAVR should be based on other factors, selecting the most appropriate access based on tomography after deciding on the transcatheter option. Traditionally, poor outcomes in the transapical cohort of the PARTNER I study were associated with greater morbidity among vasculopathic patients, with the approach serving as a marker rather than a risk factor. Similarly, so-called "alternative" approaches, such as transaxillary or transcarotid, can be equated to the transfemoral approach in comparable patient cohorts, as shown in a meta-analysis comparing transcarotid and transfemoral TAVI published by Abraham et al. this month in the *American Journal of Cardiology.* Notably, the authors no longer consider transaortic or transapical approaches, though they do include the unconventional transcaval approach.

3. Concomitant heart disease: Despite the expansion of transcatheter procedures for structural heart disease, concomitant procedures with TAVI remain rare and typically yield poor outcomes, often associated with patient subgroups ineligible for surgery. Among the different conditions favoring SAVR over TAVI, the authors recommend SAVR in cases of:

- Significant concomitant mitral valve disease, including mitral regurgitation and especially rheumatic mitral stenosis.
- Significant tricuspid regurgitation.
- Intracavitary thrombus, especially in the left ventricle.
- Suspected endocarditis.
- Dual aortic lesions with at least moderate regurgitation (as these patients were generally excluded from clinical trials, with only 4% represented, primarily cases of isolated aortic stenosis or aortic stenosis with mild regurgitation).
- Pure aortic regurgitation (systematically excluded from clinical trials, not only for functional “non-calcified” causes but also for pathology of the leaflets from type III mechanisms).
- Severe asymptomatic aortic stenosis with guideline indications (e.g., abnormal stress test and/or elevated proBNP levels). Lacking robust evidence to recommend TAVI in these patients, upcoming randomized clinical trials such as EARLY-TAVR, DANAVR, or EVoLVeD are awaited.
- Hypertrophic cardiomyopathy requiring septal myectomy.
- “Milking” coronary artery requiring myotomy.
- Atrial fibrillation (AF) that would benefit from concomitant surgical ablation and left atrial appndage closure.

Coronary artery disease merits special mention. The authors recommend SAVR with concomitant coronary revascularization in cases of left main disease with a SYNTAX score >32 points and/or three-vessel disease with a SYNTAX score >22 points. Left main disease with a SYNTAX score <32 and/or three-vessel disease with a SYNTAX score <22 represents a gray zone, where treatment choice should depend on additional criteria, as noted by the authors.

To conclude, I would like to highlight the title of the commentary, which offers a positive perspective on SAVR, even if it is only as a complement to the limitations of TAVI. Although SAVR is no longer the only or even the primary treatment option for aortic stenosis, it is still finding its place. Its future depends on the hands of surgeons in three key aspects:

1. Participation in medical-surgical sessions with full integration into the discussion about the best therapeutic option for each patient.
2. Active involvement in generating and reviewing evidence, both at an individual level and through scientific societies, ensuring that the published

information meets scientific rigor and responsibility. The ultimate expression of this role is reflected in future consensus documents or clinical guidelines.

3. Striving for excellence in surgical outcomes, which includes expanding minimally invasive approaches, using bioprostheses with proven durability, and incorporating concomitant procedures that can add a quality advantage to surgical techniques: left atrial appendage closure, AF ablation, septal myectomy, aortic root and annular enlargement, ascending aorta replacement, complete revascularization, etc., over TAVI.

4. Integration of surgeons into the Heart Team, mastering transcatheter techniques and achieving favorable outcomes in "alternative non-percutaneous approaches" that require a surgical approach and/or vascular control, allowing competition with percutaneous transfemoral approaches.

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Bárbara Oujo González

Conventional aortic valve replacement versus transcatheter implantation in patients with bicuspid valve: is it a good idea?

This retrospective American study evaluates short- and mid-term outcomes in a cohort of 56,331 patients with severe aortic stenosis and bicuspid aortic valve (BAV) undergoing conventional aortic valve replacement (AVR) or transcatheter implantation (TAVI).

Bicuspid aortic valve (BAV) disease is the most common congenital heart condition, with an approximate prevalence of 1% in recent studies. The bicuspid aortic valve is composed of two uneven leaflets, typically presenting a central raphe that connects the fused leaflets, leading to various morphotypes. This anatomical alteration increases hemodynamic stress, resulting in early degeneration of the valve and a higher risk of valve dysfunction, manifesting as either stenosis or aortic insufficiency. Additionally, patients frequently present with associated aortopathy, requiring surgical intervention in approximately 30% of cases.

In the era of transcatheter aortic valve implantation (TAVI), several randomized studies support the procedure's use in increasingly younger, lower-risk patients. However, for patients with BAV, TAVI remains an off-label indication due to the limited number of comparative studies in the literature assessing TAVI versus AVR in these patients, as they were excluded from major clinical trials. This study aims to evaluate the association between treatment strategy and outcomes, including hospital mortality, complications, and resource use in BAV patients.

A retrospective analysis was conducted on a multicenter cohort of 56,331 patients with severe aortic stenosis and BAV who underwent AVR (93.2%) or TAVI (6.8%) between 2012 and 2019. Over the study period, there was a gradual increase in the use of the percutaneous approach. Females constituted 31.4% of the cohort, with a higher proportion in the TAVI group (38.8% vs. 30.8%, $p < 0.001$). Consistent with other series, TAVI patients were significantly older than those in the AVR group (69 vs. 59 years, $p < 0.001$) and had a higher prevalence of comorbidities (heart failure, pulmonary, liver, or renal disease). The primary outcome assessed was in-hospital mortality during the initial stay, and secondary outcomes included periprocedural complications, such as cardiac arrest and myocardial infarction (MI), need for pacemaker implantation (PM), respiratory infection (pneumonia), hemorrhagic complications, acute kidney injury, readmission (at 30 and 90 days post-intervention), and costs. Results showed higher mortality in the TAVI group compared to the AVR group (1.6 vs. 0.8, $p < 0.001$), though these differences were resolved after risk adjustment. Periprocedural complications analysis revealed fewer hemorrhagic complications, acute renal failure, and respiratory infections in TAVI patients compared to AVR. However, the TAVI group had a higher PM implantation rate (7.6 vs. 4.4, $p< 0.001$), though this rate was lower than that observed in previous TAVI studies with tricuspid valves (around 17%). Furthermore, the TAVI group showed a higher 90-day readmission rate, mainly for cardiovascular reasons (non-significant, as with mortality when risk-adjusted), and a greater risk of reintervention (defined as angiography, valvuloplasty, or TAVI in subsequent hospitalizations) with an OR of 3.9, resulting in higher hospital costs despite a shorter initial stay (average of 3.1 days).

COMMENTARY:

Currently, TAVI is recognized as the procedure of choice in older patients (> 75 years) or those with high surgical risk for severe aortic stenosis. For intermediate-risk patients, the optimal treatment is determined individually by the Heart Team, considering the patient's clinical, anatomical, and functional characteristics. However, current clinical practice guidelines do not include recommendations for patients with severe aortic stenosis secondary to BAV.

While several studies have demonstrated TAVI's non-inferiority compared to conventional surgery in the previously mentioned groups, few comparative studies are available for patients with BAV. This study by Sanaiha et al. provides one of the largest series to date, allowing a representative number of both procedures in patients with this valvulopathy and concomitant severe aortic stenosis. However, it is important to remember that this is a non-randomized cohort study with population groups showing different baseline characteristics (evidenced by differences in mortality and readmission rates adjusted after applying risk-adjusted statistical techniques). Regarding complications, it is unsurprising that the surgical group had a higher hemorrhagic risk due to the more invasive nature of open surgery, where platelet dysfunction and coagulation factor deficiency after extracorporeal circulation are usually the norm. Additionally, the surgical group had a higher rate of respiratory infection, likely related to prolonged mechanical ventilation time, and an increased risk of renal impairment. On the other hand, the association between TAVI and a higher postoperative PM risk is well established, even in this patient subgroup. Regarding valve function, information on anatomical (valve ring size, prosthetic size) and functional aspects (short- and mid-term valve gradients or paravalvular leakage) post-procedure is lacking, which is particularly relevant in patients with presumably longer life expectancy, where valve durability is critical. Furthermore, this study did not include patients with BAV and associated aortopathy (root/aorta dilation), a common clinical finding that could increase procedural risk in TAVI or impact follow-up outcomes as it remains an untreated concomitant condition.

From an economic perspective, TAVI implantation in BAV does not appear to reduce healthcare costs, given TAVI's inherent need for specific perioperative studies (such as aortic computed tomography), the higher cost of prostheses, and the increased risk of subsequent procedures.

In conclusion, despite being one of the largest series analyzing BAV patients undergoing open surgery versus TAVI without mortality differences and with fewer periprocedural complications with TAVI, it is crucial to highlight the need for randomized and long-term studies to better define TAVI's implications for younger BAV patients. Such studies would provide stronger conclusions on the efficacy and safety of this technique in this patient subgroup.

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Mónica García Bouza

Transcatheter aortic valve implantation versus surgical aortic valve replacement in aortic insufficiency: is it justified?

Analysis of post-procedure outcomes and mid-term follow-up of TAVI vs. SVA in a U.S. healthcare insurance database for patients with pure aortic insufficiency.

Currently, surgical aortic valve replacement (SVA) has been relegated by transcatheter aortic valve implantation (TAVI), which has become the recommended approach in clinical guidelines for specific cases of aortic stenosis. Surgery has clearly lost its primary role in treating these patients. We are even at the point of considering it only when percutaneous procedures are ruled out, a topic previously discussed in blog entries (Luthra S et al., Asian Cardiovasc Thorac Ann. 2022: "Second Chances: Salvaging Patients Rejected for Transcatheter Aortic Valve Implantation with Surgical Aortic Valve Replacement").

This time, we present an article published in April of this year on the use of TAVI in a setting where surgery is still the standard of care: aortic insufficiency. The study analyzed a cohort selected from a U.S. health insurance database, aiming primarily to evaluate mid-term mortality.

According to a report from 2011–2014 by the Society of Thoracic Surgeons (STS) and the American College of Cardiology Transcatheter Valve Therapy (ACC TVT) registry, up to 40% of TAVI implants in the U.S. are indicated for patients with native aortic insufficiency. However, few studies have examined the safety and efficacy of percutaneous versus surgical treatment in this condition, and the results have been conflicting. Furthermore, the studies conducted to date suffer from numerous limitations, such as small sample sizes, retrospective designs, and short follow-up periods. Nevertheless, the study that inspires this commentary is one of the largest analyses of elective transfemoral TAVI outcomes for aortic insufficiency compared to SVA.

Patients included from January 2016 to December 2019 were identified using International Classification of Diseases (ICD) procedure codes and were enrolled in health insurance for at least one year before the intervention. Patients with a history of aortic stenosis, ventricular assist device implantation, aortic dissection, endocarditis, valve-in-valve procedures, and emergency cases were excluded. Additionally, for the TAVI group, all non-transfemoral approaches were excluded, and for the SVA group, patients with concomitant surgery on the mitral valve, aortic root, or ascending aorta were excluded. The primary endpoint was mortality at the longest available follow-up. Secondary endpoints included hospital mortality, 30-day and 1-year mortality, 30-day and 1-year stroke, and admission with a primary diagnosis of heart failure, endocarditis, stroke, or reintervention on the aortic valve. Acute kidney injury, atrial fibrillation (AF), transfusion requirements, need for permanent pacemaker implantation, and conversion to surgery in TAVI procedures were also analyzed. Mortality data was collected up to August 2020. Patients were censored upon disenrollment from insurance, upon experiencing an adverse event, or at the study's end. Overlap propensity weighting and multivariable logistic regression and Cox proportional hazard models were used to adjust for confounders in analyzing the outcomes.

The final cohort included 11,027 patients from 345 centers, with 1,147 (10.4%) undergoing TAVI and 9,889 (89.6%) SVA. In terms of baseline characteristics, patients in the TAVI group had higher frailty scores ($p < 0.001$), a greater prevalence of bicuspid

aortic valves (60.9% vs. 43.2%, p < 0.001), and 2% required concomitant percutaneous revascularization. The SVA group was younger on average (mean age: 72.9 ± 5.1 vs. 76.9 ± 7.1 years, p < 0.001), with fewer comorbidities, and underwent concurrent tricuspid valve surgery in 0.24% and coronary artery bypass grafting in 29.7% of cases.

At a median follow-up of 31 months (interquartile range: 18–44 months), the TAVI group showed higher all-cause mortality in both unadjusted and adjusted risk analyses (HR = 1.90; p < 0.001). There were no differences in in-hospital mortality (1.7% vs. 2.0%; p = 0.6) or 30-day mortality (2.2% vs. 2.7%; p = 0.5) between groups. Similarly, the TAVI group presented a comparable 30-day stroke risk (2.4% vs. 2.2%; p = 0.6) to the SVA group, but had a higher risk of aortic valve reintervention (HR = 2.13; p = 0.03). In the TAVI cohort, 1% of patients (n = 11) required conversion to SVA. There were no significant differences in the risk of heart failure within the first year of follow-up between the TAVI and SVA groups. However, the TAVI group showed a higher heart failure risk after 1 year compared to the SVA group (HR = 2.02; p = 0.04).

TAVI was associated with lower rates of in-hospital acute kidney injury (6.4% vs. 17.8%; p < 0.01), blood transfusion (3.2% vs. 18.2%; p < 0.01), and new-onset AF (2.7% vs. 28.7%; p < 0.01), as well as shorter hospital stays (median: 2 days, interquartile range: 1–3 days vs. 6 days, interquartile range: 5–8 days; p < 0.001). However, it was linked to a higher risk of permanent pacemaker implantation (11.5% vs. 6.7%; p < 0.001) and significant residual paravalvular leakage (1% vs. 0.2%; p = 0.03).

Based on these findings, the study concludes that patients with pure native aortic insufficiency treated with currently available TAVI devices experience fewer short-term complications and comparable short-term mortality, whereas SVA is associated with better clinical outcomes in the mid-term follow-up.

COMMENTARY:

The outcomes observed align with expectations, although the proportion of patients with pure aortic insufficiency assigned to TAVI in the U.S. is noteworthy. Additionally, the authors attempted to improve post-procedure results through confounding control using weighted propensity score analysis. However, residual confounding persists, as the TAVI group remains older and with more comorbidities prior to adjustment. Furthermore, certain factors, such as prior thoracic radiation, fragility indicators, and degree of left ventricular remodeling, were not considered despite potentially influencing treatment decisions. Additionally, the impact of concomitant myocardial revascularization, performed in 30% of surgical patients but only 2% of TAVI patients, remains unclear and may affect patient outcomes due to possible residual ischemia.

These aspects, along with factors such as residual paravalvular leakage or pacemaker implantation, could significantly impact survival, with a potentially more pronounced effect as follow-up time extends.

Considering the current device limitations, a critical question for the future is whether the development of TAVI devices specifically designed for pure aortic insufficiency could overcome the challenges identified thus far. Results from the ALIGN-AR trial (JenaValve® Pericardial TAVR Aortic Regurgitation Study), which investigates the transfemoral JenaValve® Trilogy® system for high-risk patients with aortic insufficiency, may shed light on this issue when published at the end of 2023. Until then, the existing data suggest that off-label TAVI use should be reserved for patients with aortic insufficiency, calcification, and no surgical alternative. Another aspect worth considering is comparing outcomes in this patient group with minimally invasive surgical approaches, where more competitive results may favor surgery.

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Elio Martín Gutiérrez

Minimally Invasive Approach in Aortic Valve Replacement vs. TAVI: From Classic to Derby

Patient-level meta-analysis comparing survival outcomes of TAVI vs. aortic valve replacement across different approaches: sternotomy and, innovatively, minimally invasive approach.

Reviewing a new meta-analysis comparing survival outcomes in patients treated with TAVI versus aortic valve replacement (AVR), with a focus on the studies and the follow-up of currently available evidence, may lead to the tedium of a nearly predictable outcome: benefit for TAVI in the first two years, a technical draw in the short period that follows, and surgical benefit thereafter. However, the authors of this work introduce a twist by providing data that had previously been unavailable, allowing for an unexpected reconsideration of the evidence.

The minimally invasive approach to the aortic valve (mini-AVR) has been revisited over the past decade, given that it was a previously known technique that had likely been abandoned due to a lack of motivation within the surgical community. In a competitive environment such as the present, those who believed in preserving chest stability for better early perioperative results and in surgical bioprosthesis implantation for favorable long-term outcomes endured the disappointment of a technical alternative that had yet to gain traction over the sternotomy approach, mistakenly labeled “conventional,” since a highly technical, complex procedure is anything but conventional. Against TAVI, the almost non-existent inclusion rate of mini-AVR in clinical trial protocols condemned it to exclusion from decision algorithms, with its field of application reduced alongside its partner, the “conventional” approach.

This study offers a fresh perspective with previously unavailable data for three reasons: it performs the most extensive meta-analysis of mini-AVR vs. TAVI to date; it presents an analysis at the patient level rather than at the study level, almost resembling a multicenter propensity-adjusted study with substantial statistical power; and it leverages data from studies that could not previously be analyzed, using an advanced computational methodology to examine Kaplan-Meier curve cancellations, extracting raw individual data that the authors of the original studies had not intended to publish. This methodology, now increasingly popular in creating meta-evidence, is a transparency exercise that should be demanded from original studies. Tools like WebPlotDigitalizer enable this type of high-value analysis.

All analyses were designed using an all-comers approach, covering patients with multiple risk profiles, provided they were properly adjusted. All available evidence from propensity-adjusted observational studies and clinical trials among the three treatment options—TAVI, AVR, and mini-AVR—was included. For the TAVI vs. AVR comparison, trials such as Evolut Low Risk, US CoreValve, NOTION, SURTAVI, UKTAVI, and the PARTNER series (1, 2, and 3) were analyzed alongside a few observational studies. The analysis yielded unsurprising results in a 4-5-year follow-up of individual patients: improved survival with AVR beyond two years and a technical draw when the analysis was restricted to clinical trial data and the TAVI cohort with transfemoral access.

However, before giving in to discouragement, it is worth highlighting the results from 11 propensity-adjusted studies of TAVI vs. mini-AVR, with 1,497 and 1,318 patients in each arm, respectively, all well-designed with low bias risk. Regarding surgical risk, one study included low-risk patients, two moderate-risk, four high-risk, and four had mixed risk profiles. Mortality with mini-AVR was nearly half that with TAVI (HR = 0.56, 95% CI 0.46

– 0.69; $p < 0.01$), with separation of the curves in early post-procedure phases and extended benefit over a maximum follow-up of 6 years. Sensitivity analysis confirmed that no individual study accounted for the observed outcome.

The authors conclude that despite the long-term survival benefit of AVR over TAVI, mini-AVR further enhances the advantage of the surgical option. This finding should be considered in the design of future clinical trials.

COMMENTARY:

As acknowledged by the authors, this is the first study to robustly analyze the treatment alternatives AVR, mini-AVR, and TAVI through a patient-level meta-regression with extended follow-up.

While it may be viewed as just another study, evidence of this kind is necessary to gauge the reality. In fact, its publication in the *American Journal of Cardiology* speaks to its significance. Firstly, it allows for real-world data (multicentricity, multiple risk profiles) with less controlled populations, since many of the patients we encounter in decision-making sessions may not meet the inclusion criteria of renowned clinical trials. Secondly, procedures are performed at multiple centers, with real-world outcomes and technical variations in both interventional and surgical approaches. With the early clinical trials, transcatheter therapy was still in its technological infancy, and from a current perspective, it is no longer viable to isolate outcomes based on the chosen access route. Today, all units have access to multiple approaches with different devices, allowing the selection of the best option according to the assigned treatment. Consequently, if TAVI is chosen, the results are equally analyzable "regardless of the route." In the case of surgery, most mini-AVR cases analyzed were via mini-sternotomy, though mini-thoracotomy approaches were also included. The prostheses implanted were primarily sutureless (Livanova® Perceval®) or rapid deployment (Edwards® Intuity®). This surgical population is vastly different from those included in clinical trials, where TAVI—a high-tech alternative—is compared to a surgical approach that, rather than "conventional," might be better described as classical to antiquated. Worse yet, our decision-making guidelines are based on a supposedly equal comparison that is in reality highly unequal.

Therefore, the analyzed study brings hope for a resurgence of the surgical option, a sign that the seemingly categorical indications are not as well-defined as presumed, and a call to continue offering an updated surgical therapeutic alternative. The comeback for surgeons should not only involve adopting transcatheter therapies but also continuing to offer surgical options adapted to today's times, resources, and patient needs. What began over 10 years ago as a hopeful outlook with J-sternotomies, superior vena cava venous cannulation, and changes in cardioplegic strategy now appears to bear fruit. We hope these or other authors will provide new subgroup analyses by risk groups between TAVI and mini-AVR and that new clinical trials will be planned to balance the competition. Based on the discussion, the final whistle has yet to sound—there is still game time left.

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Elio Martín Gutiérrez

Evolut Low-Risk Study at Three Years: Clinical Benefit or Statistical Fallacy

A review of the three-year outcomes of the Evolut Low-Risk study and comparison with the published follow-up at one and two years.

Recently, the three-year follow-up results of the Evolut Low-Risk study, a wholly American endeavor and one of the studies supporting the indication of TAVI for patients with low surgical risk, have been published. This study utilized the Medtronic® platform prosthesis and paved the way for FDA approval to cover the full indication spectrum for patients with symptomatic aortic stenosis. The study's results have been presented in three follow-up series: perioperative and at one year, two years, and, most recently, three years. Previous versions showed no superiority of TAVI over surgical aortic valve replacement (SAVR). However, the study was initially designed as a non-inferiority trial, and for the first two years, both therapeutic options were considered equivalent across all analyzed clinical events, whether individual or composite.

The authors' primary conclusion from the three-year outcomes indicated that, for the first time, TAVI demonstrated an almost statistically significant benefit ($p = 0.05$) in the composite event of mortality and disabling stroke, with a trend towards diverging curves that suggest an increasing benefit for TAVI compared to SAVR.

The conclusions and results obtained warrant a detailed analysis, which we provide below. This will help to understand the reasons behind this finding within the published material and foresee the successive results that will likely be published as the study continues to be of interest.

COMMENTARY:

There is a well-known saying, "from those dusts come these muds," and the Evolut Low-Risk study is a clear example. To begin our analysis, we must go back to 2019 when the study's first version was published. It was a randomized, multicenter design that included 1,468 patients with severe aortic stenosis, randomized 1:1 (734 per group) to TAVI (98% transfemoral) or SAVR.

The first notable observation is that only 86 U.S. centers participated, contributing between one and 130 patients each. Such variability likely includes centers with very low volumes of activity, which may have impacted the results we will discuss. Selection criteria were balanced for both techniques from a clinical standpoint. However, from a technical standpoint, TAVI results were safeguarded by specific anatomical requirements for the ascending aorta (absence of aneurysm), the aortic root and sinuses of Valsalva (appropriate for TAVI deployment), the left ventricular outflow tract (free of calcification or other distortions), septal hypertrophy, maximum and minimum sizes (30 mm and 18 mm, respectively), and absence of bicuspid aortic valve.

Regarding patient numbers, 11 patients in the TAVI group and 56 in the surgical group were excluded from the initial recruitment, with analysis performed by treatment rather than by intention-to-treat. This resulted in the inclusion of 725 patients in the TAVI group and 678 in the SAVR group. No crossover introduced additional selection bias, but the decision to reject patients was influenced by study coordinators, who removed 20 patients from the surgical group; 33 patients also refused to sign informed consent. The study does not elaborate on the content of the information provided or the reasoning behind these arbitrary decisions. Interestingly, candidates for SAVR who were not treated showed no significant differences from treated patients, although they had a

lower incidence of variables such as COPD. It is essential to note that these were low-risk surgical patients who could have largely undergone SAVR with favorable outcomes.

In the surgical group, results were “within mortal reach,” with cardiopulmonary bypass and aortic clamp times of 93.3 and 68.7 minutes, respectively. Most prosthetic implants were between 23 and 29 mm, indicating a “comfortable” aortic root size. Although concomitant valvular disease was an exclusion criterion, 178 patients required additional procedures, including 13.6% of all SAVR patients who underwent surgical revascularization. Over 10% also required procedures on the aortic root, including augmentations or replacements (BioBentall-De Bono). The study does not specify the types of prostheses used, approaches, or surgical protocols followed. Only bioprostheses, stented or non-stented, available in various U.S. centers, were permitted.

These data contrast and limit comparability with the TAVI group, where only 6.9% of patients required coronary intervention (not necessarily concurrent with TAVI). Embolic protection devices were used in 1.2% of cases (off protocol), and two TAVI prostheses were necessary in 1.2% of cases, with an extremely low surgical rescue rate of 0.6%. The implanted prostheses included various evolutionary generations, such as Evolut R® (74.1%) and Evolut PRO® (22.3%), which offer reduced paravalvular leakage, smaller profiles, suitability for larger aortic rings, and improved navigability compared to the first-generation CoreValve® (3.6%). These differences reflect the varying care in selecting centers and procedures between the two study arms.

The initial follow-up version showed an early penalty in 30-day all-cause mortality, which, though not statistically significant, was a difference carried throughout the follow-up. It was a typical initial handicap for the surgical alternative over the interventional one, as often seen in this type of study design. Mortality was 0.5% for TAVI and 0.8% for SAVR, totaling eight cases. Misfortunes seemed to cluster in this group initially, with causes of death including a rupture at the aortic cannulation site, two coronary ostia obstructions (one requiring mechanical circulatory support while the other died in surgery), one severe stroke, two cardiac arrests (etiology unspecified), one cardiac tamponade after pacemaker lead removal, one mesenteric ischemia, and one multiorgan failure of unspecified origin.

Postoperative events were as follows for TAVI vs. SAVR: cardiovascular mortality 0.5% vs. 0.6%; stroke 2.1% vs. 1.9%, with disabling stroke 0.4% vs. 0.9%; rehospitalization 0.9% vs. 1.1%; prosthetic thrombosis 0.1% in both groups; new aortic valve procedure 0.2% vs. 0.4%; mild paravalvular leakage 36% vs. 3%; moderate-severe 3.4% vs. 0.4%.

The one-year follow-up data were not fully available until the two-year publication, covering only 432 TAVI and 352 SAVR patients. One-year results officially reported data for 706 TAVI (out of 725 initially enrolled, -19 patients) and only 628 SAVR (out of 678 initially enrolled, -50 patients). Comparable results for TAVI vs. SAVR included cardiovascular mortality of 1.7% vs. 2.6%, stroke of 4% vs. 4.2% (disabling: 0.8% vs. 2.1%), rehospitalization of 3.6% vs. 6.7%, prosthetic thrombosis of 0.3% for both groups, and new valve procedure of 0.7% vs. 0.6%. Paravalvular leakage artifacts began to appear, with an apparent reduction in mild degree 33.9% vs. 2.5% but not in moderate-severe degree 3.6% vs. 0.6%.

Although full follow-up was unavailable, the study performed a Bayesian statistical analysis to predict two-year results, a largely theoretical exercise showing a rush for partial results. The actual two-year follow-up data included 685 TAVI (-40 patients) and 594 SAVR (-84 patients). The data, expressed as percentages without absolute values,

included all-cause mortality of 4.5% in both groups, cardiovascular mortality of 2.8% vs. 3.5%, stroke of 4.9% vs. 5.3% (disabling: 1.1% vs. 3.5%), rehospitalization of 5.4% vs. 7.9%, and prosthetic thrombosis of 0.6% vs. 0.5%.

Finally, in the current three-year study, the authors struggled to cover up the same criticisms of prior work, reporting 624 TAVI patients (-101 patients) compared to the 537 remaining SAVR patients (-141 patients). The authors now present both percentages and absolute values, with TAVI vs. SAVR showing all-cause mortality of 6.3% vs. 8.3%, cardiovascular mortality of 4.1% vs. 5.6%, stroke of 7.4% vs. 6.6% (disabling: 2.3% vs. 3.4%), rehospitalization of 7.4% vs. 9.2%, and prosthetic thrombosis of 0.7% vs. 0.6%.

Many follow-up losses could be attributed to paravalvular leakage or pacemaker rates during the first year (19.4% vs. 6.7%), impacting the results and needing distinction in responsibility between groups. This almost significant difference the authors found in the three-year composite event likely results from pressure by the sponsor (Medtronic®) and their affiliates, aiming to extend the indication for TAVI in low-risk patients.

For all the reasons mentioned, it will be difficult to justify any present or, especially, future conclusions drawn from this study. The issue is that it will influence future meta-evidence results as well as clinical recommendations, as seen in the recent 2020 joint guidelines by the AHA/ACC. Although it may not be possible to contain the pressure exerted, a call for responsibility, transparency, and avoiding confusion in published data is, at the very least, necessary. As the saying goes, “noise does no good, as good does no noise.”

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José Manuel Martínez Comendador

Aortic valve reintervention in patients with previous TAVI: Comparable outcomes to reoperations with conventional prostheses?

An American study analyzed the incidence and outcomes of reinterventions in patients with dysfunctional transcatheter prostheses, drawing from the Michigan Transcatheter Valve Therapy Registry and the STS registry data. Although transcatheter aortic valve implantation (TAVI) has gained widespread adoption, surpassing surgical prostheses in the United States, there is still limited understanding of the frequency and outcomes of reinterventions in patients with such prostheses.

This study reviewed reinterventions in patients who underwent TAVI from 2012 to 2019, utilizing data from the Society of Thoracic Surgeons (STS) database and Michigan's Transcatheter Valve Therapy Registry. The analysis included the reintervention frequency and clinical outcomes, particularly examining the observed-to-expected mortality ratio based on the STS Predicted Risk of Mortality index. Among the 9,694 patients who received TAVI, 87 (0.90%) required reintervention, either through surgical transcatheter valve explantation with surgical aortic valve replacement (SAVR) or a second TAVI procedure (TAVI-in-TAVI). The SAVR group showed a higher STS-predicted mortality risk. The number of reintervention cases rose from zero in 2012-2013 to 26 by 2019, with the proportion of transcatheter prosthesis explants with SAVR increasing from 13% in 2013 to 65% in 2019. Self-expanding devices exhibited a higher reintervention rate due to a greater need for SAVR (0.58% versus 0.19%; $p = 0.001$). However, TAVI-in-TAVI rates were similar. For patients requiring SAVR, contraindications for TAVI-in-TAVI included unfavorable anatomy (75%), need for another cardiac surgery (29%), structural issues with the transcatheter prosthesis (18%), and endocarditis (12%). Thirty-day mortality was 15% for SAVR and 2% for TAVI-in-TAVI ($p = 0.032$), with an observed-to-expected mortality ratio of 1.8 and 0.3, respectively ($p = 0.018$).

The authors conclude that reintervention on transcatheter prostheses in the aortic position remains rare but is on the rise. The significant clinical impact of surgical explantation is emphasized, particularly in patients with self-expanding devices.

COMMENTARY:

One primary finding from Fukuhara et al.'s study is that, to date, the reintervention rate after TAVI remains low—under 1%—similar to other studies (1.4% in PARTNER II and 2.8% in SURTAVI). Additionally, reintervention occurs relatively soon after TAVI (median of 9.6 months). However, this low rate does not fully reflect the true incidence of structural deterioration or dysfunction of bioprostheses, nor their durability, as reintervention patients in this series were carefully selected. Therefore, age, frailty, and other considerations for reintervention candidates were not adequately captured in the study. Furthermore, there are limited studies on TAVI's long-term outcomes (beyond 5 years), as short survival following TAVI initially limited assessments of long-term prosthesis durability. As TAVI indications expand to all surgical risk categories, we anticipate a rise in reintervention rates for these prostheses, and, consequently, more data on durability and true reintervention criteria.

Another key takeaway is that nearly half of patients needing reintervention required surgical explantation and replacement of the aortic prosthesis rather than a second TAVI. Notably, surgical mortality was high, around 15%, similar to other series. This elevated

mortality, contrasting with lower surgical reintervention mortality for surgically implanted bioprostheses (<3%), underscores the technical challenge of this procedure. Possible explanations may include the high percentage of concomitant procedures (two-thirds of patients) and aortic root structure damage during explantation (one-third required aortic repair). Given these figures and knowing most patients needing concomitant procedures likely had other valvulopathies or ischemic heart disease prior to their first TAVI, it raises the question of the most appropriate initial procedure for these patients. Additionally, surgical reintervention is technically challenging due to firm adhesions, not only at the aortic annulus (similar to conventional surgical prostheses) but also at the aortic root wall and sinotubular junction, especially with self-expanding prostheses, as evidenced by the high aortic repair rate in these cases.

These concerning reintervention outcomes highlight particular relevance in low-surgical-risk patients requiring definitive aortic stenosis treatment, whose life expectancy may exceed bioprosthesis durability. Both SAVR and TAVI offer excellent short-term prognoses in these patients, but in cases where a percutaneous prosthesis is chosen, future high-risk surgical reintervention may be necessary. While Fukuhara et al.'s study shows favorable short-term TAVI-in-TAVI outcomes, data beyond one year on this approach's durability is lacking, and emerging evidence links it to accelerated structural deterioration and leaflet thrombosis. Thus, it is crucial for the Heart Team to consider these long-term challenges and risks when evaluating TAVI as an option in low-risk aortic stenosis patients, as it may offer initially favorable outcomes with potential future complications yet to be clarified.

The relationship found between self-expanding devices and higher reintervention rates lacks sufficient detail to draw significant conclusions. Although self-expanding prostheses continue to show favorable short-term outcomes, with low pacemaker implantation rates and paravalvular leakage, other questions remain unresolved. For instance, is there a higher risk of coronary obstruction during TAVI-in-TAVI procedures? Should we consider SAVR and concomitant coronary surgery for cases with difficult coronary artery access?

Indications for choosing SAVR over TAVI-in-TAVI typically include severe paravalvular leak, small prosthesis size with structural deterioration, unfavorable coronary anatomy, the need for concomitant procedures, and prosthetic endocarditis. Notably, the latter condition, with its exponential growth, is a rising concern, further elevating reintervention risk. Therefore, increased prosthetic endocarditis prevalence necessitates a multidisciplinary and personalized approach for patient management.

This study provides a comprehensive view of post-TAVI reinterventions, prompting a reevaluation of patient discussions regarding aortic stenosis interventions. Often overlooked, it is vital to address both short- and long-term risks and benefits of intervention options, whether TAVI or SAVR, especially in younger, low-risk patients, as the need for reintervention after a first transcatheter prosthesis may negatively impact their long-term prognosis.

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Elio Martín Gutiérrez

Impact on Survival of Paravalvular Leak Following TAVI: A Call for Accountability

A patient-level meta-analysis involving 38 studies and over 25,000 patients, assessing the impact on survival and readmission needs among patients with residual paravalvular leak classified as none, mild, or moderate-severe after TAVI.

The rapid evolution of TAVI has encountered certain challenges, spurred by independent and responsible publications that, in my view, are beginning to define the role of this excellent therapeutic alternative within increasingly specific indications. To date, TAVI's proliferation has largely depended on an accelerated expansion of indications, recently bolstered by: (1) the shift from surgical risk criteria to age as a determinant, once non-inferiority at low and moderate risk was demonstrated; (2) research extensions toward asymptomatic aortic stenosis profiles; and (3) treatment strategies targeting increasingly younger patients, where the simple recommendation for bioprosthetic valve implantation opens the door for TAVI, despite the probable need for future re-interventions that may still require surgery. This scenario unfolds as TAVI durability remains uncertain, and findings reveal that this transcatheter approach is not free from complications impacting patient survival and quality of life, rendering it more invasive than initially perceived. Examples include conduction disturbances requiring pacemaker implantation, thromboembolic events from the neosinuses, and restricted coronary bed access.

Successive generations of TAVI devices have aimed to address paravalvular leak, a complication resulting from implantation within the pathological valve with inherent irregularities. This reflects the significance of paravalvular leak as a complication and highlights a main difference with surgical procedures, where pathological tissue is excised to allow replacement with differently designed prostheses. Moderate-severe paravalvular leak was recognized early on as a critical factor in initial surgical versus TAVI comparisons, with the argument that new device generations would correct this. However, the impact of mild paravalvular leak has been controversial, with varying evidence across studies and follow-up durations. Added to the complexity of echocardiographic grading of some leaks, this led to the classification of mild or lesser leaks as a technical success, excluding moderate-severe degrees.

The following work comprehensively examines the impact of paravalvular leak after TAVI, consolidating the scientific evidence available. Authored by cardiologists, it serves as a reference for professionals involved in TAVI device implantation programs. With notable social media traction, it will likely influence future consensus documents. Its significance lies in its meta-analysis using patient-level data and extended follow-ups of up to 12 years. The study encompasses international experience with this procedure, highlighting registries such as Japan's OCEAN-TAVI, SAPIEN-3, UK-TAVI, Brazilian, German GARY, French FRANCE 2, Italy's CoreValve registry, and major clinical trials like PARTNER, PARTNER 2, US Pivotal CoreValve high-risk, NOTION, SURTAVI, CHOICE, PRAGMATIC, and REVIVAL. In total, 38 studies, encompassing 25,164 individual patients; 61% with no residual paravalvular leak. Among the 39% with paravalvular leak, approximately 25.6% presented moderate-severe leak, while 74.4% had mild leak. Patients with any degree of paravalvular leak faced a 50% higher risk of all-cause or cardiovascular mortality and an 81% increased readmission rate ($p < 0.001$). For moderate-severe leaks, these three outcomes were more than double compared to patients without residual leak ($p < 0.001$). Mild leaks were associated with 35% higher

all-cause mortality, 27% higher cardiovascular mortality, and a 64% increase in readmission likelihood ($p < 0.001$).

The authors conclude that any degree of residual paravalvular leak after TAVI is linked to an increased risk of adverse events, including higher all-cause and cardiovascular mortality, as well as the need for rehospitalization. Although the impact of moderate-severe leaks is greater than mild leaks, the latter exhibits persistent adverse effects that seem to intensify over time.

COMMENTARY:

The work by Pompeu Sá et al. is the largest meta-analysis on the impact of paravalvular leak after TAVI. Prior blog entries have discussed potential etiopathogenetic mechanisms contributing to the poor outcomes in these patients, which can be summarized as follows:

– Impact of regurgitant volume on ventricular function, particularly in patients with established diastolic dysfunction, especially in cases initially graded as mild but actually more severe or progressing over time.

– Development or persistence of blood disorders, such as acquired von Willebrand factor deficiency and Heyde syndrome.

– Complications associated with paravalvular leak, including hemolysis and endocarditis, and the progression of the leak itself, which further exacerbates the initial conditions.

These findings underscore the need to maximize efforts to avoid any degree of paravalvular leak, even mild, from the treatment planning phase, extending into selection. This approach is especially crucial in patients with longer life expectancy, challenging the recommendation to lower implantation age for patients under 75 with suitable life expectancy. The added complexity of further interventions or reoperations is examined in other blog entries and will also serve as a counterargument against this approach.

The reduction in life expectancy to a half or third in patients with moderate-severe paravalvular leak is well-documented in the literature, and this study's findings are consistent with this. However, excluding certain high-risk subgroups (e.g., bicuspid aortic valve and/or left ventricular outflow tract calcification, especially with self-expandable devices) is insufficient, as moderate-severe leaks occur in only 10% of procedures, leaving 30% with paravalvular leaks (three-quarters of the 40% presenting any leak grade), where patients also face adverse clinical trajectories. Moreover, high degrees of calcification, particularly asymmetrical, are predictors of complications like rhythm disorders, further compromising these patients' survival and quality of life. While the authors recommend considering reintervention (balloon post-dilation or closure device) only in patients with TAVI and moderate-severe or mild leak with recurrent hospitalizations for heart failure, perhaps a more proactive approach would be beneficial. In patients with acceptable surgical risk, opting for aortic valve replacement with a bioprosthesis—offering <2% mortality, <1% paravalvular leak rate, and <5% pacemaker implantation requirement—might be the best solution.

In conclusion, while surgical invasiveness is undeniable, its gradual yet steady refinement over decades has yielded reliable outcomes, meeting the complex needs of modern patients. Pompeu Sá et al.'s article serves as a call for accountability, as optimal outcomes stem not only from well-executed procedures but also from sound indications.

Although TAVI's technological evolution is indisputable, let us proceed with caution as we push its boundaries, guided by common sense.

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Bunty Ramchandani

Delirium and quality of life in surgical and percutaneous treatment of aortic valve disease

This prospective, observational, single-center study compares the incidence of postoperative delirium and quality of life in patients treated for aortic valve disease via surgery versus transcatheter procedure.

The incidence of delirium following cardiac surgery is highly variable, ranging between 3-32% depending on the study. Among patients over 60, this incidence can rise to 50-70%. These figures require cautious interpretation due to heterogeneity in delirium diagnosis and assessment across studies. Risk factors such as a history of cerebrovascular disease, stroke, dementia, advanced age, alcohol use, renal disease, liver failure, and thyroid abnormalities increase the brain's vulnerability to this complication. Anesthesia policies, sedative agents, and opioid use also play a role in delirium onset, making it challenging to attribute this complication solely to surgical procedures.

The article analyzed today is a prospective, observational, single-center study comparing patients over 70 years old treated surgically for aortic valve disease versus percutaneous treatment. The study aimed to assess postoperative delirium incidence and subsequent impact on quality of life. Patients were recruited from September 2018 to January 2020. The primary event was daily delirium assessment over the first five postoperative days, conducted by specially trained personnel through various questionnaires. Secondary events included perioperative inflammation (measured by C-reactive protein), postoperative complications, quality of life (EuroQol-5 questionnaire), and six-month mortality. Given the heterogeneity of the two population groups, a weighted inverse probability adjustment was applied, considering EuroSCORE II, age, and frailty.

A total of 250 patients were included, with 166 patients treated surgically and 84 percutaneously. The mean age was 80 years, with an average EuroSCORE II of 5 points. Following the weighted inverse probability adjustment, it was observed that the surgical group exhibited a higher incidence of postoperative delirium: 51% versus 15% ($p < 0.0001$). The surgical group also experienced greater perioperative inflammation, deeper anesthetic sedation, and more intraoperative hypotension events. Nevertheless, despite the higher incidence of postoperative delirium, at six months, 41% of surgically treated patients reported improved quality of life compared to 12% in the percutaneous group ($p < 0.0001$). Within the surgical group, those operated via median sternotomy were compared to those undergoing minimally invasive techniques, with no statistically significant differences observed.

The authors concluded that transcatheter techniques are associated with a lower incidence of postoperative delirium, but surgical valve replacement provided greater long-term quality-of-life benefits. Hoogma et al. advocate for incorporating these variables into Heart Team decision-making to determine the optimal treatment for patients.

COMMENTARY:

The etiology of delirium following surgical procedures is multifactorial, influenced by inherent patient risk factors, surgical specifics, and anesthesia protocols. Regarding surgery-specific factors, particularly in cardiac surgery, several hypotheses attempt to explain the high delirium incidence. Cardiopulmonary bypass use and surgical stress trigger systemic inflammation, with studies linking elevated C-reactive protein (CRP)

levels, an unspecific biomarker, as an independent risk factor for postoperative delirium. In line with inflammation and surgical stress, prolonged operative times are also associated with higher delirium incidence. Similarly, significant perioperative hypotensive events induce cerebral injury and may trigger postoperative delirium. Such hypotensive events must be substantial enough for cerebral autoregulation mechanisms to fail in compensating for blood pressure drops. However, literature offers mixed findings on the association between perioperative hypotension and delirium incidence. Lastly, anesthetic depth appears to play a critical role in this neurological complication. Indeed, in the percutaneous group, patients requiring deep sedation had the highest postoperative delirium incidence. Surgical valve replacement generally necessitates deeper anesthetic sedation than the percutaneous technique, as evidenced by the high proportion of surgical patients with a BIS below 40 during the procedure.

The study's limitations complicate the interpretation of its results for clinical practice. Starting with design limitations that affect its internal validity—single-center, non-randomized, and two non-comparable population groups despite weighted inverse probability adjustment. The percutaneous group had a higher EuroSCORE II, indicating more comorbid and frail patients. Frailty limits perceived quality of life and could explain the low improvement rate in six-month questionnaires. The surgical group included patients with concomitant revascularization and ablation procedures, prolonging cardiopulmonary bypass times and surgical aggression, directly related to delirium incidence. Furthermore, a significant percentage of percutaneously treated patients were discharged before the five-day period established for postoperative delirium detection, likely overestimating the difference noted by researchers.

In conclusion, this study, while having the strengths of a prospective design and comprehensive delirium assessment, has significant weaknesses that affect its internal validity and limit the extrapolation of results to clinical practice. We do agree, however, on valuing the perceived quality of life of our patients post-procedure. Quality-of-life measurement through various parameters should be a mandatory item for discussion in Heart Teams before any decision-making.

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Hoogma DF, Venmans E, Al Tmimi L, Tournoy J, Verbrugghe P, Jacobs S, et al. Postoperative delirium and quality of life after transcatheter and surgical aortic valve replacement: A prospective observational study. J Thorac Cardiovasc Surg. 2023 Jul;166(1):156-166.e6. doi: 10.1016/j.jtcvs.2021.11.023.

Elio Martín Gutiérrez

Pacemaker after TAVI: From a Minor Setback to Reduced Survival

A multicenter study based on NEOPRO and NEOPRO-2 registries analyzes the prognostic impact and predictors of pacemaker implantation following Medtronic Evolut® and Acurate NEO® self-expanding TAVI.

The findings of this study should come as no surprise, as some of the main TAVI vs. surgery clinical trials have established three well-supported conclusions:

- Patients requiring a pacemaker post-TAVI have reduced survival rates.
- Patients who develop left bundle branch block post-TAVI often exhibit higher pacemaker implantation rates during follow-up.
- Patients with post-TAVI left bundle branch block experience reduced survival.

While the rate of paravalvular leakage has notably improved due to newer prosthesis adaptations, the pacemaker implantation rate remains unresolved, likely due to procedural constraints. Implantation onto a calcified valve compresses the conductive tissue in the membranous septum, which could be modulated by specific implantation techniques but remains difficult to prevent.

Despite this potentially redundant work, its significance lies in three aspects: methodological quality, a patient population closer to real clinical practice than those in trials, and the inclusion of influential authors, mostly from the interventional cardiology field, published in a prestigious cardiology journal (JACC).

This study included 3,211 patients from the NEOPRO and NEOPRO-2 registries, comprising multinational experiences with two self-expanding prosthesis types—Medtronic Evolut® PRO® and PRO+® and Acurate® NEO® and NEO2®. Procedures occurred from 2012 to 2021 exclusively through transfemoral access, comprising 1,090 Acurate NEO® implants, 665 Acurate NEO2®, 1,312 Evolut PRO®, and 144 Evolut PRO+®. The pacemaker implantation rate was 11.3% within 30 days. However, rates varied markedly between Evolut® (15.2% for PRO® and 10.4% for PRO+®) and Acurate® (8.8% for NEO® and 7.7% for NEO2®); $p < 0.001$.

Pacemaker implantation post-TAVI led to observable consequences:

- Left ventricular ejection fraction was reduced in patients needing a pacemaker prior to hospital discharge.
- Pacemaker necessity was linked to higher mortality within one year of follow-up (HR = 1.66, $p < 0.01$).
- Higher rehospitalization rates were noted, impacting patients' quality of life.
- This was particularly notable in patients with left ventricular ejection fraction depression, both mild (LVEF <50%; HR = 2.48, $p = 0.021$) and moderate (LVEF <40%; HR = 1.5, $p = 0.07$).

- In patients with normal left ventricular function, post-TAVI pacemaker implantation did not affect survival within the first year, though it may have longer-term implications.

The included population reflects typical registry characteristics, with an average age of 81.6 years and moderate surgical risk based on average STS scores of 4.5 points and EuroSCORE II of 5%. The authors conducted a univariate analysis revealing that patients needing a pacemaker were often male, diabetic, with previous surgical revascularization, poorer NYHA III-IV functional class, lower glomerular filtration rates, and higher surgical risk scores, as well as a higher preprocedural right bundle branch block rate (26% vs. 7%, $p < 0.001$). These factors should have been considered in the analysis, as they might serve as confounders impacting survival. Surprisingly, the authors did not mention this in the limitations section.

Multivariate analysis identified STS score and preoperative right bundle branch block (HR > 5) as the sole independent clinical predictors for pacemaker implantation necessity.

The authors conclude that post-TAVI pacemaker implantation with self-expanding devices is frequent and associated with increased mortality at one year in patients with some degree of left ventricular dysfunction. They highlight the importance of planning the procedure with these prostheses, emphasizing patient selection and identification of predictors influencing implantation technique variations that may help reduce this complication rate.

COMMENTARY:

As the saying goes, "prevention is better than cure." When atrioventricular block occurs post-TAVI, pacemaker implantation may be too high a price, especially if not anticipated during procedural planning. The authors' suggestion of using resynchronization therapy devices in patients with ventricular dysfunction reveals a partial view of the issue and a potentially costly solution in terms of efficiency and added patient morbidity.

The reported pacemaker implantation rates, though high, align with literature standards, ranging from 8.3% to 11% for Acurate® and 11.8% to 20.7% for Medtronic Evolut®. Literature consistently shows that clinical trials provide the lower rate limits, while observational studies and registries provide the upper limits.

Beyond the preprocedural right bundle branch block, which quintupled the pacemaker need risk, understanding how prostheses interact with left ventricular outflow tract anatomy remains crucial for self-expanding devices. The specific characteristics of these TAVI devices should ideally make them less vulnerable to this complication, given their recapturability, adaptability to an irregular annulus, and lower radial force. However, the potential for post-implant expansion due to the nitinol material may be a factor justifying these outcomes.

The authors found that neither annular nor outflow tract calcification significantly affected post-TAVI pacemaker need. This places responsibility on the technique and device itself, where implantation depth emerged as an independent predictor, with thresholds of 5.9 mm for Acurate® (ROC AUC 0.58) and 4.3 mm (ROC AUC 0.58) for Evolut®. However, in my opinion, such precise measurements are impractical in real imaging. The authors emphasize Acurate®'s lower pacemaker need rate compared to Medtronic Evolut®, likely due to lower radial force, as well as technical aspects like alignment with native

valve structure and a radiopaque marker on the Acurate NEO2® for more precise implantation depth control.

In summary, while TAVI has revolutionized aortic stenosis treatment, significant issues remain after 20 years. Atrioventricular block incidence is one of them. And amid competition with surgical techniques, a stronger internal comparison between devices is needed. This study, by interventional cardiologists, sets the stage by comparing two widely-used self-expanding devices, as previously done with studies like SCOPE2. This approach is necessary as not all devices will perform equally, and as in evolution, the best designs will endure.

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Elio Martín Gutiérrez

PARTNER 3, Evolut-low risk and NOTION: trick or treat?, in low-risk patients

An update on outcomes and impressions from the recent TCT Congress in San Francisco on studies examining TAVI vs. surgical aortic valve replacement in low-risk patients: PARTNER 3, Evolut-Low Risk, and NOTION.

Concern spread through the October 24 session at the TCT Congress in San Francisco when Martin B. Leon presented the 5-year results of the PARTNER 3 study. Survival curves, which showed a crossover trend favoring surgery at 4 years in the previous year, now indicate superior outcomes for surgery (10% vs. 8.2%, HR 1.23). Although not reaching statistical significance, the trend indicates a likely advantage for surgery, which would be statistically significant if we consider the survival curve from two years onward when initial surgical mortality (2.5% vs. 1%) was balanced.

The same day, the NEJM published the complete study results, forming the basis of this blog entry. With 91.6% follow-up of the initial sample (496 patients in the TAVI arm and 453 in the surgical arm), updated 5-year results are shown. First, it is essential to highlight a greater follow-up loss in the surgical arm (454 patients; 88.3% of the initial sample) compared to the TAVI arm (469 patients; 94.6%). The primary reason for patient loss in the surgical group was voluntary withdrawal (45 participants), compared to only 21 patients in the TAVI arm. Regarding stroke outcomes, there remains a technical tie, with a less steep slope for surgery, which the TAVI arm has now overlapped: 6.4% for surgery vs. 5.8% for TAVI. This trend also reflects a balancing of the initial penalty suffered by the surgical option (3.1% vs. 1.2% at one-year results). Finally, the readmission rate, primarily responsible for significant differences in the composite event at one year, continues the initial 4% disadvantage of surgery, marked early postoperatively. However, for the first time, the composite event combining all three outcomes loses statistical significance between the two options.

This, combined with the technical tie in clinical events (endocarditis <2%, new coronary events, or need for revascularization, and even the need for pacemaker implantation at 5-6% when not considering the postprocedural period), hemodynamic performance (for gradients and structural degeneration, 3.3% vs. 3.8%), and quality of life measured by the KCCQ-OS score, makes it possible, in Martin B. Leon's words, "to inform our low-risk aortic stenosis patients eligible for either treatment that, after five years, they have more than an 85% chance of being alive, doing well, and with a prosthesis free from structural degeneration."

Such comments call for a review of past literature, as the same forum predicted TAVI's superiority in low-risk profiles with one- and two-year results. While explanations currently focus on most of the developed mortality being non-cardiac (the cardiac origin difference being only 0.4% between procedures), it has been repeatedly discussed on this blog that mortality classification methods may not be entirely accurate. Notably, more deaths occurred in the TAVI group due to cancer (9 vs. 5), COVID-19 (3 vs. 1), or sepsis (4 vs. 1), alongside the mentioned imbalance in follow-up losses.

The study's conclusion is that, in patients with severe symptomatic aortic stenosis undergoing TAVI vs. surgery, no significant differences exist between groups for primary outcomes at five-year follow-up.

COMMENTARY 1:

Reactions to the assumed result followed swiftly. Comments like, “Surgery has set a high standard for TAVI in low-risk patients” (Kendra Grubb, Emory University, Atlanta), “the age threshold reduction should be postponed... reducing to 65 years in the US may have been too bold a step” (B. Pendergast, Cleveland Clinic, London) echoed throughout the session. As expected, Michael Reardon’s analysis (Methodist DeBakey, Houston), lead investigator for the PARTNER 3 equivalent Evolut study, noted that “TAVI has an early advantage over surgery in mortality, stroke, and recovery... but the real question is whether this is sustainable.”

At this same session, an update from the Evolut-Low Risk study results was presented, showing an opposite trend to that of PARTNER 3. Briefly, with 94.7% of the initial sample, four-year outcomes showed no significant mortality differences between surgery and TAVI (12.1% vs. 9%) and none for stroke (3.8% vs. 2.9%) or valve-related reintervention (1.7% vs. 1.3%). These results were accompanied by a JACC publication promising five-year outcomes in the next issue.

With this analysis, the focus remains on clarifying why there is a discrepancy between studies and ensuring transparency on underemphasized aspects.

Regarding the first point, the initial reaction was to avoid extrapolating results and, above all, refrain from asserting that one TAVI prosthesis is superior to another. Survival results correlate closely with patient selection, and such trials typically involve highly selected populations. In fact, PARTNER 3’s selection criteria were stricter concerning TAVI implantation technique, using the Sapien 3 prosthesis versus self-expanding devices and the technology gap of the Evolut Low-Risk. Moreover, teams involved, surgical prosthesis types, etc., are not comparable, thus neither are the results. Hopefully, as this represents the first setback in the TAVI field, these points will be considered in meta-analyses. However, when preprocedural variables are evaluated, both studies involve similar low-risk surgical patients (mean STS score 1.9%) and comparable ages, ensuring minimal comorbidity. Only COPD showed a higher proportion (15-17% vs. 5-6%) in PARTNER 3. While minor, one-year mortality differences of 2.5% vs. 1% for SAVR vs. TAVI in PARTNER 3 and 3% vs. 2.4% in Evolut Low-Risk, and stroke (4.3% vs. 4.1% in Evolut Low-Risk and 3.1% vs. 1.2% in PARTNER 3) are crucial in understanding presented results. We must remember significant differences in associated procedures in the surgical group (up to a quarter of SAVR patients in both studies) compared to the interventional arm, which has affected outcomes from the start. These differences persist over Evolut Low-Risk study follow-up, while trends in PARTNER 3 have crossed. This reflects the prognosis of the surgery group cohort, appearing either early (PARTNER 3, now balanced) or later in follow-up (Evolut Low-Risk, not yet balanced), biasing studies and resulting in disparate findings.

The second point involves the absence of paravalvular leakage results in the 5-year PARTNER 3 report. Evolut-Low Risk’s four-year JACC update indicates 98.4% freedom from leakage in the surgical group vs. 84.7% for TAVI ($p < 0.05$), with a worrisome leakage rate of mild or higher: 38% in the first year, 27.5% in the second, 22.5% in the third, and 16.6% in the fourth, with complete disappearance of severe leakage by the second year (shown only at TCT). Minimal attention was given to prosthetic thrombosis in PARTNER 3, which was over 10 times higher for TAVI (2.5% vs. 0.2%). In Evolut Low-Risk, pacemaker need remains at 24.6% vs. 9.9% ($p < 0.001$) at four years; a prognostic factor previously analyzed on this blog.

Finally, the durability of TAVI’s superior early results depends on adequate prosthetic durability. Four- and five-year studies have shown excellent durability for both prosthesis

types under VARC-3 criteria. However, durability's importance in low-risk patients was underscored by NOTION's 10-year findings. This all-comers intermediate-risk study demonstrated the bias consequences in its design: >30% Abbott Trifecta and Livanova Mitroflow bioprostheses, both now withdrawn, and a biased structural deterioration definition using VARC criteria based on fixed gradients >20 mmHg when >40% of implants were size 21 mm or less.

The PARTNER 3 five-year publication has served as a "fright" for the TAVI world, emphasizing that extending low-risk indications, especially in younger patients, requires patience. The current study's conclusion is that the "treat" is to celebrate the "draw" that real aortic valve replacement now enjoys, contrary to predictions of doom based on one- and two-year results.

REFERENCE:

Mack MJ, Leon MB, Thourani VH, Pibarot P, Hahn RT, Genereux P, et al.; PARTNER 3 Investigators. Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years. N Engl J Med. 2023 Oct 24. doi: 10.1056/NEJMoa2307447.

COMMENTARY 2:

Given these findings, the STS and EACTS issued a joint statement on October 30 reiterating the results and arguments in this blog. They remind us that real-world SAVR survival rates, such as those from the STS, covering over 42000 patients, are excellent: 92.9% at five years and 90% at eight years; with 95% at eight years for patients under 75 with an STS score <1%. Therefore, both societies urge caution and consensus on expanding TAVI indications, particularly for younger, low-risk patients.

Partial results in this and other interventional areas cannot be taken as definitive conclusions. As stated in the past by EACTS President Patrick Perier, such results should be seen as hypothesis-generating rather than as set dogma, pending confirmation by further studies with adequate follow-up and comparisons against real-world registry outcomes. Surgery has evolved technically over decades, progressing slowly and steadily to reach the level of excellence it holds today. It has responded to setbacks, removing poorly performing prostheses, reinventing itself through the resurgence of minimally invasive techniques initially proposed decades ago, and innovating with new devices like sutureless prostheses.

We are grateful for the publication of these recent study results, something that has not been consistently available for intermediate-risk studies such as PARTNER 2, SURTAVI, and others, apart from NOTION, which offers nearly a decade of follow-up data. It seems the "nightmare before the next guidelines" is upon us, and we hope that clinical and scientific responsibility will prevail.

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Mack MJ, Leon MB, Thourani VH, Pibarot P, Hahn RT, Genereux P, et al.; PARTNER 3 Investigators. Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years. N Engl J Med. 2023 Oct 24. doi: 10.1056/NEJMoa2307447.

José Manuel Martínez Comendador

Results of Valve-in-Valve on Percutaneous Bioprosthesis (Redo-TAVI) Using Balloon-Expandable Percutaneous Prostheses

The STS/ACC TVT registry analysis compares outcomes for patients undergoing TAVI based on whether they receive treatment on a native valve or a previous percutaneous prosthesis (valve-in-valve).

The growing number of patients undergoing transcatheter aortic valve implantation (TAVI) underscores the need for more data on managing dysfunctional percutaneous prostheses, including repeat "valve-in-valve" procedures. This study aimed to evaluate the safety and effectiveness of percutaneous valve-in-valve implants in the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) national registry. The study included all consecutive patients recorded from November 9, 2011, to December 30, 2022, who underwent TAVI with balloon-expandable valves, either for dysfunctional transcatheter prostheses (redo-TAVI) or native aortic valves (native-TAVI). Procedural, echocardiographic, and clinical outcomes were compared between redo-TAVI and native-TAVI cohorts using propensity score matching.

Among 350,591 patients (1,320 redo-TAVI; 349,271 native-TAVI), 1,320 propensity-matched pairs undergoing redo-TAVI and native-TAVI were analyzed (redo-TAVI cohort: mean age 78 years, 57.7% male, average predicted 30-day mortality risk 8.1%). Procedural complication rates for redo-TAVI were low (coronary compression or obstruction: four [0.3%]; intraprocedural death: eight [0.6%]; conversion to open-heart surgery: six [0.5%]) and similar to those of native-TAVI. There was no significant difference between redo-TAVI and native-TAVI populations in 30-day mortality (4.7% vs. 4.0%, $p = 0.36$) or one-year mortality (17.5% vs. 19.0%, $p = 0.57$), nor in stroke at 30 days (2.0% vs. 1.9%, $p = 0.84$) or one year (3.2% vs. 3.5%, $p = 0.80$). Redo-TAVI effectively reduced aortic valve gradients at one year, although they remained higher in the redo-TAVI group compared to the native-TAVI group (15 mmHg vs. 12 mmHg; $p < 0.0001$). Rates of moderate or severe aortic insufficiency were similar between redo-TAVI and native-TAVI groups at one year (1.8% vs. 3.3%, $p = 0.18$). Mortality or stroke after redo-TAVI were not significantly affected by the timing of redo-TAVI (before or after one year from TAVI) nor by the type of transcatheter valve (balloon-expandable or non-balloon-expandable). Redo-TAVI with balloon-expandable valves effectively addressed previous dysfunctional percutaneous prostheses, with low rates of procedural complications and mortality and stroke rates comparable to patients with a similar clinical profile undergoing TAVI for native aortic valve stenosis.

COMMENTARY:

Before delving into the analysis of this article, it is essential to provide historical context for the world of TAVI. Over the years, clinical trials involving Edwards® Sapien® and Medtronic® CoreValve®/Evolut® prostheses with patients of progressively lower surgical risk have evolved. Today, age has become the key factor in the decision between TAVI and SAVR according to current clinical guidelines. This decision is based on five-year follow-up in high- and intermediate-risk patients, as observed in trials such as PARTNER IA, CoreValve US, PARTNER 2A, and SURTAVI. These studies have shown no significant differences in mortality, although consistently yielding slightly better results in the surgical cohort.

For low-risk surgical patients, the five-year follow-up of the PARTNER 3 study and the four-year follow-up of Evolut-Low Risk, recently published and discussed in this blog, show no significant differences in mortality or stroke (which is, incidentally, worse than data for conventional SAVR in the low-risk cohort of the STS registry). Initially, poorer performance was observed in the surgical arm in both studies, but it balanced out in PARTNER 3 starting from the fourth year. Additionally, the similarity in the incidence of endocarditis, gradients, and quality of life suggests that both procedures have comparable outcomes at 4-5 years. Although the studies do not explore deficiencies in data and poorer outcomes in the TAVI group, such as paravalvular leakage, prosthetic thrombosis, or pacemaker implantation, the key question remains: will these results persist in the long term? The durability of percutaneous prostheses in trials has been demonstrated with only five years of follow-up, an insufficient time to justify reducing age as a criterion for TAVI. The increased use of TAVI in younger patients suggests that the lifespan of the bioprosthesis may be exceeded by the patient's life expectancy, increasing the likelihood of percutaneous valve dysfunction and, therefore, the need for reintervention.

The STS/ACC TVT registry analysis, published in *The Lancet* by Makkar et al., is notable for three main reasons: (1) it is the largest study to date on patients undergoing redo-TAVI with balloon-expandable valves for dysfunctional bioprostheses, (2) it confirms the safety and efficacy of TAVI reimplantation in this clinical context, and (3) it shows a mortality rate up to three times lower than surgical reintervention studies for TAVI.

Comparing redo-TAVI and native-TAVI groups yielded notably similar outcomes in critical clinical endpoints, including 30-day and one-year mortality and stroke rates. These findings are of great significance, as 30-day mortality in redo-TAVI (4.7% in this study) is consistently lower compared to mortality following surgical reintervention after TAVI, which some studies place close to 15%, as we have previously analyzed in blog articles.

Redo-TAVI accounted for only 0.4% of all TAVI cases (1,320 of the 350,591 TAVI patients in the study). This low number is unsurprising, as TAVI was initially indicated only for elderly patients with high or prohibitive surgical risk, in whom it was expected that the transcatheter valve would "outlive" the recipient.

The STS/ACC TVT registry still leaves important questions unanswered. For instance, data were not collected on the timing or mechanism of transcatheter bioprosthetic dysfunction. The etiology of bioprosthetic dysfunction can include endocarditis, thrombosis, or structural versus non-structural valve degeneration. Non-structural valve degeneration is mainly caused by paravalvular leakage (more common in TAVI) or patient-prosthesis mismatch (more common in surgically implanted bioprostheses). It could be argued that non-structural valve degeneration manifests early, requiring reintervention in the first years after the initial procedure. Structural deterioration, however, involves intrinsic degeneration of the bioprosthetic leaflets due to chronic inflammatory processes (e.g., pannus formation and degenerative calcification) or wear, thus taking more time to develop and typically occurring later, usually after five years from the initial procedure. Numerous historical publications demonstrate the long-term durability of conventional bioprostheses, often based on reoperation or mortality rates over long periods. However, the historical lack of rigorous durability studies and the recent emergence of consensus documents that define structural deterioration and bioprosthetic dysfunction with a unified terminology partly invalidate past evidence based on studies that did not employ these definitions. From this perspective, many

cardiologists argue that there are no contemporary studies with mean echocardiographic follow-ups of 5-8 years that show less structural degeneration in conventional bioprostheses compared to percutaneous ones.

The study by Makkar et al. suggests that redo-TAVI may be the preferred therapeutic option in cases of transcatheter prosthesis dysfunction, provided it is technically feasible. However, it is essential to note that this analysis contains significant selection bias. Moreover, redo-TAVI was exclusively performed with balloon-expandable stents and low-profile stents, a relevant choice to ensure coronary access and avoid obstruction of coronary arteries. On the other hand, certain specific anatomical conditions, such as a high proportion of bioprostheses with paravalvular leaks, low coronary implantation, or prosthetic endocarditis, can only be adequately addressed through surgical extraction rather than redo-TAVR. This critical aspect was not considered in the STS/ACC TVT registry.

Younger and lower-risk patients often choose an aortic bioprosthesis over a mechanical valve. These patients are likely to need multiple procedures on their valve throughout their lives. At the time of the initial procedure, it is essential to design a personalized management plan that considers both initial and future strategies (whether transcatheter or surgical), adapting them to the patient's risk and specific anatomy.

As a surgeon, and by conviction, I advocate for the SAVR-TAVI-TAVI strategy as the preferred choice to maximize the durability of the bioprosthesis in young, low-risk patients. Here are my reasons:

Starting with the implantation of a surgical bioprosthesis offers clear advantages:

- It facilitates better support for subsequent percutaneous procedures, with specially designed supports such as the Edwards® Inspiris® or the possibility of performing aortic root/ring enlargement techniques to prevent mismatch with the surgical prosthesis or future valve-in-valve implants.

- The long-term durability of surgical bioprostheses is known and reliable, while that of percutaneous ones remains uncertain.

- It has a significantly lower incidence of paravalvular leaks compared to TAVI, which has prognostic implications.

- It is associated with a lower incidence of pacemaker requirements.

- It also has a lower incidence of prosthetic thrombosis.

It makes sense for the second procedure to be a TAVI, provided that certain technical criteria are met, as suggested by the results of this study. Opting for surgical reintervention in TAVI seems to imply a greater risk of complications and mortality. In fact, if reintervention is required due to endocarditis or patient-prosthesis mismatch after repeated valve-in-valve procedures, the technical aspects and risks of explanting the surgical prosthesis (with or without a TAVI bioprosthesis inside) are more predictable than those needed for explanting a first TAVI implanted over the native aortic valve. In this "biological pathway," reintervention at the third stage (SAVR-TAVI-SAVR) opens the possibility for an eventual fourth implant (TAVI), minimizing the risk of patient-prosthesis mismatch.

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Section V B:

Mitral valve disease

José Manuel Martínez Comendador

"Resect" vs "respect" in posterior leaflet prolapse: impact on left ventricular function

This retrospective study investigates which mitral repair technique for treating posterior leaflet prolapse best preserves left ventricular (LV) function, evaluated through global longitudinal strain (GLS).

Mitral valve repair surgery is the standard treatment for posterior mitral leaflet prolapse in severe mitral regurgitation (MR). For many years, resection was the only surgical solution for this pathology. Later, the teams of Tirone David and Perier described the functional replacement of native chordae with polytetrafluoroethylene sutures as an equally effective alternative, potentially preserving mitral-ventricular continuity more effectively. Since then, there has been a growing preference for chordal replacement techniques, though this approach may not be suitable for all cases.

The purpose of this study was to compare the effect of these two surgical techniques on the postoperative morphology and function of the LV, using, in addition to standard echocardiographic parameters, GLS as a more sensitive and volume-independent echocardiographic parameter for representing LV function.

This study included 125 patients divided into two groups: segmental posterior leaflet resection techniques (resect group, n = 82) and isolated artificial chordal implantation (respect group, n = 43). In all cases, the procedure included annuloplasty. Advanced and standard echocardiographic assessments were performed preoperatively, immediately postoperatively, and during follow-up. Additionally, GLS was measured and adjusted for LV end-diastolic volume to account for significant volume changes.

At baseline, there were no significant differences between groups in LV function as measured by corrected GLS (resect: 1.76% ± 0.58%/10 mL vs respect: 1.70% ± 0.57%/10 mL, $p = 0.560$). Postoperatively, corrected GLS worsened in both groups but improved significantly during late follow-up, returning to preoperative values (resect: from 1.39% ± 0.49% to 1.71% ± 0.56%/10 mL, $p < 0.001$, and respect: from 1.30% ± 0.45% to 1.70% ± 0.54%/10 mL, $p < 0.001$). Mixed model analysis showed no significant effect on corrected LV GLS when comparing the two surgical repair techniques over time ($p = 0.943$).

COMMENTARY:

Both segmental posterior leaflet resection and artificial chord implantation are surgical techniques that may be chosen based on the size, height, and thickness of the prolapsing posterior leaflet. Patients with fibroelastic deficiency may benefit more from neochords since the leaflet is often smaller, making it advisable to preserve all segments. Conversely, patients with advanced myxomatous degeneration can be treated with some form of resection reliably, as they tend to have larger, bulkier, and thicker posterior leaflets. Currently, many surgeons prefer neochord implantation, reasoning that in the event of future repair failure, re-repair (including the new transapical percutaneous neochord implantation devices) is more feasible if the posterior leaflet remains intact from the initial surgery.

There are various ways to assess a successful mitral repair. The most apparent is through the evaluation of mitral echocardiographic parameters, such as the absence of residual MR, sufficient coaptation length, or confirmation of low transmitral gradients. Another indirect method is the echocardiographic assessment of LV function parameters, such as LVEF, LV GLS, or volume diameter. From the patient's perspective, the most

important way to assess mitral repair is through the analysis of clinical outcomes (symptoms, morbidity, and mortality). One limitation of this study by Wijngaarden et al. is the lack of data on clinical outcomes.

The debate regarding whether one surgical technique is superior to another in terms of durability and mitral-ventricular continuity preservation remains ongoing. Existing evidence for assessing 20-year durability among different repair techniques, mostly from retrospective studies, shows equivalence among them. Other studies, like that of Falk et al., favor the neochord technique when aiming for greater coaptation length, lower gradients, and larger ring sizes.

Assessing LV function after repair is relatively straightforward. The main novelty of this study lies in the evaluation of LV function using corrected GLS rather than merely LV ejection fraction. Although its measurement requires a significant learning curve, GLS corrected provides valuable information on LV function, particularly in asymptomatic patients and synergistically with other parameters. Other useful indicators that could be included in future studies are various biomarkers, LV volume measurements, and other imaging modalities like MRI.

This is a retrospective study with all its inherent limitations. We must wait for additional randomized studies that include more clinical outcomes and better markers to settle the “resect versus respect” debate definitively. Meanwhile, it is time to move forward and accept the obvious: some things are equivalent yet different. We should do what works best in our hands.

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César Augusto Rodríguez Canedo

Elevated Mitral Gradients Following Mitral Repair: Contributing Factors

This commentary presents a sub-analysis of the CAMRA CardioLink-2 clinical trial, which investigates risk factors associated with elevated mean mitral gradients following mitral repair.

Currently, valve repair is the surgical treatment of choice for patients with severe mitral regurgitation due to degenerative disease. In practice, two primary repair techniques exist: leaflet preservation, involving artificial neochordae, and leaflet resection, including common procedures such as triangular or quadrangular resections, with or without sliding plasty. After repair, some patients may experience higher mean transvalvular gradients compared to those without mitral valve disease, independent of the chosen repair technique. These elevated gradients may adversely affect long-term hemodynamics, potentially leading to left atrial dilation, which predisposes to atrial fibrillation, or incomplete resolution of pulmonary hypertension, ultimately impacting exercise capacity and quality of life post-surgery.

The CAMRA CardioLink-2 study is a multicenter, double-blind, randomized study that included 104 patients with primary degenerative mitral regurgitation and posterior leaflet prolapse. Patients were randomized to undergo either a leaflet preservation or resection repair. Patients with anterior leaflet prolapse, rheumatic mitral disease, endocarditis, or extensive calcification were excluded. The Carpentier-Edwards Physio II® ring was used for annuloplasty in all repairs, with edge-to-edge repair techniques (central or commissuroplasty) also applied. Logistic regression was used to analyze risk factors associated with residual elevated transvalvular gradients post-repair. At 12-month follow-up, functional outcomes were compared between patients with elevated mitral gradients (≥5 mmHg) and those with gradients <5 mmHg. Elevated mitral gradients were identified in 15 patients (14.4%) without significant differences between repair strategies. Risk factors identified included female gender ($p = 0.02$), lower preoperative hemoglobin levels ($p = 0.01$), smaller intercommissural diameters ($p = 0.02$), and smaller annuloplasty ring sizes ($p = 0.001$). The ratio between intercommissural diameter and annuloplasty ring size was similar among patients with and without elevated gradients, indicating no deliberate undersizing of the implanted rings, as seen in repairs for ischemic mitral regurgitation. At 12-month follow-up, patients with elevated gradients demonstrated worse NYHA functional classification ($p = 0.001$), lower peak oxygen saturation during exercise ($p = 0.01$), lower body weight-walking distance ratio ($p = 0.02$), and higher fatigue scores on the Borg scale during the six-minute walk test ($p = 0.01$).

The authors conclude that female gender, smaller mitral anatomy, and lower preoperative hemoglobin levels are associated with higher residual transvalvular gradients following mitral valve repair, correlating with reduced postoperative functional capacity.

COMMENTARY:

Mitral repair techniques should aim to restore the valve's normal physiology alongside correcting regurgitation. Avoiding elevated transvalvular gradients is essential, and considering identified risk factors in the surgical technique could improve long-term outcomes. Tirone David's additional commentary in this publication raises points not addressed in the study. While the study compared patients with similar pathology (severe primary mitral regurgitation from posterior leaflet prolapse) randomized to different repair strategies, David notes the study's lack of differentiation by underlying valvular degeneration etiology. He observes that fibroelastic deficiency patients tend to have

thinner, smaller, and more mobile leaflets, while myxomatous degeneration patients often have larger, thicker, and more rigid leaflets. Consequently, small, rigid annuloplasty rings may be better suited for fibroelastic deficiency cases than myxomatous degeneration cases, which might result in higher residual gradients. David suggests using preservation techniques for fibroelastic deficiency and resection techniques for myxomatous degeneration. Additionally, utilizing a single ring type ensures study consistency, reducing residual gradient variability. However, surgical variability in annuloplasty ring types limits the generalizability of these findings to settings employing rings with different dimensions and mechanical properties. Despite statistically significant findings, a larger sample is needed to confirm these results in clinical practice and perform robust subgroup analyses.

In summary, considering fibroelastic or myxomatous deficiency profiles in repair strategy is essential, as smaller annuloplasty rings and/or reduced ring size may lead to higher postoperative gradients. Preoperative optimization and technique adaptation to individual anatomical characteristics are crucial for repair success. Failing to address these factors could exchange mitral insufficiency for residual stenosis, with potentially negative long-term impacts on functional outcomes and patient quality of life.

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Hibino M, Pandey AK, Chan V, Mazer CD, Rumman R, Dhingra NK, et al. Risk Factors for Postrepair Elevated Mitral Gradient: A Post-hoc Analysis of a Randomized Trial. Ann Thorac Surg. 2023 Feb;115(2):437-443. doi: 10.1016/j.athoracsur.2022.05.053. Epub 2022 Jun 29. PMID: 35779599.

Bunty Ramchandani

The diverse facets of primary mitral regurgitation

This retrospective, multicenter study utilizes latent class analysis on 2321 patients undergoing surgery for primary mitral valve disease, aiming to identify phenotypes with distinct long-term prognoses.

The mitral valve apparatus is a highly sophisticated cardiac structure with complex functions. It comprises six components: atrial wall, annulus, two leaflets, chordae tendineae, papillary muscles, and the left ventricular wall. It functions dynamically, with the mitral annulus—having a three-dimensional morphology—shifting from a rounder, flatter shape during diastole to an enhanced saddle shape during systole, reducing its anteroposterior diameter. This adaptation minimizes hemodynamic stress and optimizes leaflet coaptation. Any failure in the interaction among the mitral annulus, leaflets, chordae, ventricular function, and geometry can lead to coaptation failure, resulting in mitral regurgitation (MR).

Primary mitral regurgitation (MR) is a prevalent valvular disease, with mitral valve prolapse being the most common form, affecting approximately 2-3% of the global population. In populations over 75 years in developed countries, moderate-to-severe mitral prolapse has a prevalence of about 8-10%. Primary MR has several causes, including myxomatous degeneration (Barlow's syndrome and fibroelastic deficiency), rheumatic valve disease, infective endocarditis, annular calcification, hypertrophic cardiomyopathy, carcinoid syndrome, radiation effects, and medication-related conditions. Secondary forms of MR include dilated cardiomyopathy, either ischemic or non-ischemic, where the valve-ventricle interaction is emphasized. Additionally, secondary MR may arise from annular dilation due to atrial remodeling associated with atrial fibrillation, where annulus-atrial interaction becomes relevant. Other forms of annular disruption are common in Barlow’s disease, primarily affecting the posterior annulus, suggesting that mechanisms leading to MR may combine both primary and secondary causes.

The current study attempts to address the high heterogeneity of primary MR to identify distinct risk profiles. The study aims to classify severe primary MR patients into differentiated phenotypes and relate these to long-term post-surgical prognosis. Researchers reviewed patients who underwent mitral valve surgery between 2006 and 2020 in three South Korean tertiary hospitals. Part of the cohort (n = 1629) was used for model development. Latent class analysis identified subgroups based on 15 prognostic variables described in the literature. The remaining cohort (n = 692) served to validate the model. The primary outcome measured was all-cause mortality following mitral valve surgery. Patients under 18 years, those with any cardiac reintervention, double mitral lesions, concomitant other valvular lesions, infective endocarditis, and secondary MR were excluded.

With a median follow-up of 6 years, 149 patients (9.1%) died in the model-development cohort. Univariate Cox analysis identified age, female sex, atrial fibrillation, left ventricular end-diastolic volume, left ventricular ejection fraction, left atrial size, and tricuspid regurgitation peak velocity as mortality predictors after mitral surgery. Latent class analysis identified five phenotypes; three younger patient groups (groups 1-3) and two older groups (groups 4-5): group 1, low-comorbidity subgroup; group 2, men with left ventricular enlargement; group 3, women with rheumatic disease; group 4, elderly patients with few comorbidities; and group 5, high-risk elderly patients. The 5-year survival rates for groups 1 to 5 were 98.5%, 96%, 91.7%, 95.6%, and 83.5%, respectively ($p < 0.001$). Group 5 (high-risk elderly) showed the lowest survival, followed by group 3

(women with rheumatic disease). The phenotypes' predictive value was confirmed using the validation cohort (n = 692) and showed similar predictive performance to the International Mitral Regurgitation Database risk score.

The authors concluded that five distinct phenotypes of patients with severe primary MR were identified. They advocate that grouping patients by phenotypes may improve risk stratification for planning mitral valve surgery.

COMMENTARY:

The study by Kwak et al. uses an innovative statistical approach in cardiac surgery: latent class analysis. More commonly used in social sciences, this analysis identifies groups or clusters by applying a probabilistic model to the data. Unlike traditional clustering, where groups are defined arbitrarily by setting a range or predefined value, latent class analysis first describes the data distribution and then evaluates the probability that cases belong to one latent subgroup or another. Conversely, traditional clustering first identifies groups and then defines the model.

As with any study, this one has limitations. One primary issue is the model's development using a cohort undergoing surgery. This limits the external validity of these subgroups for patients evaluated in outpatient settings who are not yet surgical candidates, as their subgroup assignment could change due to clinical evolution while awaiting surgery. Additionally, the 14-year time span is long enough for significant changes in clinical practice, surgical techniques, and postoperative care to have occurred. Finally, the latent class analysis model was based on data from a single center (n = 1629), which might not produce identical subgroups if another region's cohort were analyzed.

In conclusion, primary MR is a heterogeneous entity. Statistical models, such as that described in this article, can help determine risk groups. However, they might be more useful in patients with mitral pathology who are not yet surgical candidates to better define the timing and priority for surgery and study the clinical impact based on the type of MR they present. This approach would enable more personalized care compared to the generic recommendations published in clinical guidelines.

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José Manuel Martínez Comendador

Effect on Left Ventricular Reverse Remodeling After Mitral Valve Repair: A Clinical Trial Response

Sub-analysis of the CardioLink-2 clinical trial, evaluating the effect of mitral repair (resect vs. respect) on left ventricular (LV) reverse remodeling.

Mitral valve surgery, including mitral valve repair, can alleviate the state of volume overload in the left ventricle (LV) caused by mitral regurgitation (MR) and initiate the process of reverse remodeling. Various studies have demonstrated that mitral valve surgery significantly reduces LV volumes and dimensions, effects which persist over time. The left ventricular end-diastolic volume (LVEDV), primarily influenced by preload, tends to decrease more than the end-systolic volume (LVESV), which is more affected by afterload. Generally, these changes result in an initial decrease in ejection fraction (EF) post-surgery. However, as time progresses following MR surgical correction, LV reverse remodeling may occur, manifesting as an increase in EF after the initial decrease. Nonetheless, several questions remain regarding reverse remodeling after mitral valve repair. Most available data are derived from observational studies, which are prone to various biases, such as analyzing only patients with successful mitral repairs or those with good long-term survival rates.

The CardioLink-2 trial of the Canadian Mitral Research Alliance (CAMRA) examined resection-based mitral repair techniques (primarily quadrangular resection) versus posterior leaflet preservation (neochord implantation) as mitral repair options for patients with posterior leaflet prolapse. At 12 months postoperatively, no significant differences were found in the effect on mean mitral gradient at peak exercise. The objective of this sub-analysis of the same trial was to evaluate the impact of both mitral repair techniques on LV reverse remodeling after one year of follow-up.

A total of 104 patients were randomly assigned to either a leaflet resection or preservation strategy. Blinded echocardiograms were analyzed preoperatively, prior to discharge, and at 12 months postoperatively in an independent central imaging lab. All patients underwent successful mitral repair. At discharge, 3 patients presented with moderate MR, while the remainder had mild or lesser degrees of MR. Compared to baseline, indexed LVEDV was significantly reduced at the discharge echocardiogram ($p < 0.0001$) and further decreased at the 12-month echocardiogram ($p = 0.01$). In contrast, indexed LVESV did not change significantly from baseline in the predischarge echocardiogram ($p = 0.32$) but improved significantly at 12 months postoperatively ($p < 0.0001$), resulting in a corresponding improvement in EF at 12 months ($p < 0.0001$).

The authors concluded that the type of mitral repair technique used did not affect LV reverse remodeling after surgery, which occurred in distinct phases. Although LVEDV improvement was noted pre-discharge, significant improvement in LVESV was observed one year postoperatively.

COMMENTARY:

Recently, in a retrospective study reviewed on this blog, Wijngaarden et al. demonstrated the equivalency of both mitral repair techniques in preserving postoperative LV function in cases of degenerative MR. Today's featured article by Hibino et al. is a post-hoc analysis of the CAMRA CardioLink–2 trial, which again shows LV function preservation following different mitral repair techniques. In this study, early LV reverse remodeling was documented in predischarge echocardiograms and was especially notable at 12 months, with progressive improvement in indexed LVEDV reduction. However, indexed

LVESV showed no significant change in predischarge measurements but decreased at the 12-month follow-up. Consequently, EF dropped sharply by 10 points (preoperative 61.1% vs. predischarge 51.7%; $p < 0.0001$). Although there was significant improvement in indexed LVESV and EF at 12 months (56.4%; $p < 0.0001$), EF never returned to preoperative levels. This early decrease in EF, with only partial recovery over a year, has been previously observed in other studies and likely reflects the prolonged delay in surgical intervention in these patients. Asymptomatic or minimally symptomatic patients are often managed with a "watchful waiting" strategy until symptoms become more evident, significant pulmonary hypertension develops, atrial fibrillation occurs, or LV dimensions and/or EF worsen before surgery is considered. However, irreversible LV function changes may occur in a significant proportion of these patients before the criteria indicating surgery are detected. In such cases, although mitral repair is performed, these irreversible changes may influence long-term prognosis and survival.

This study also revealed other relevant findings, including an early and sustained reduction in pulmonary pressures and indexed left atrial volume. In contrast, no changes were observed in tricuspid regurgitation over time (only 4 patients in the study underwent tricuspid annuloplasty). As shown in the retrospective study by Wijngaarden et al., both leaflet resection and chord replacement are effective mitral repair techniques in preserving LV function post-surgery. Additionally, this latest study incorporated the novel measurement of global longitudinal strain (GLS) as a more sensitive and less volume-dependent echocardiographic parameter for assessing LV function.

Hibino et al.'s study, although with some limitations worth noting, does not appear heavily biased. The reported results are based on an intention-to-treat analysis, whereas most previous studies focus exclusively on actual treatment received, which may be more useful for predicting retrospective outcomes. Furthermore, the series analyzed comprises a homogeneous and well-compensated population, as all patients presented posterior leaflet prolapse and EF over 40%, which is usually the case for patients undergoing mitral repair in clinical practice. However, it is unclear whether these results can be applied to patients with more impaired EF or other MR etiologies. We should also consider that echocardiographic follow-up was limited to a maximum of 1 year, which may be considered a relatively short period. Indeed, retrospective studies have demonstrated full EF recovery at 2 years in patients with baseline EF below 50%. A future sub-analysis of this study may confirm these findings. In contrast, it is important to highlight the study's significant strengths, as it is prospective, randomized, and features high-quality echocardiographic follow-up, independent and far more rigorous than most published retrospective series to date.

Current guidelines establish that an EF of 60% or an LVESD of 4 cm are the thresholds indicating the need for repair. These criteria were designed based on studies that defined mitral repair success as achieving an EF of at least 50% in 75% of patients at 1 and 12 months post-repair. Hibino et al.'s study also supports the idea that a 1-year EF assessment is the appropriate measure for evaluating mitral repair outcomes. Therefore, these findings align with current recommended surgical criteria. The question that remains unanswered is whether we should be less permissive with current repair thresholds to avoid irreversible changes and improve prognosis in these patients.

The true value of this study lies in its high quality as a randomized clinical trial and its prospective echocardiographic findings, which demonstrate that a full year, rather than just 30 days, is required to assess the real and complete effectiveness of mitral repair. In any case, the practical takeaway from this article is that both surgical repair techniques perform well regarding LV recovery. Therefore, it is crucial to select the mitral repair technique that provides confidence and comfort, but more importantly, to ensure no

residual MR greater than mild remains at the end of surgery. This is the only guarantee of sustained reverse remodeling over time.

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José Manuel Martínez Comendador

Combined Aortic and Mitral Valve Replacement with Mitral-Aortic Curtain Reconstruction (Commando Procedure): Indications, Outcomes, and Surgical Advice

This article describes the short- and long-term outcomes from the largest published series of patients who underwent combined aortic and mitral valve replacement with mitral-aortic curtain reconstruction (Commando procedure).

The combined aortic and mitral valve replacement with cardiac fibrous skeleton reconstruction (mitral-aortic continuity or curtain), commonly referred to as the "Commando procedure," is a surgical technique designed to treat complex diseases of the heart's fibrous skeleton, such as infective endocarditis with paravalvular extension to the mitral-aortic curtain or extensive calcification of the mitral-aortic continuity and adjacent valve annulus.

Although there are series describing the short-term morbidity and mortality of this procedure, data on long-term outcomes remain sparse.

The objective of this study was to evaluate the surgical and long-term outcomes of the Commando procedure. A total of 182 consecutive patients, operated on by a single surgeon between 1985 and 2020, underwent mitral-aortic curtain reconstruction, with posterior mitral annulus reconstruction in 63 cases. The median follow-up was 7.5 years (interquartile range 2.1-12.6 years), with 98% of the sample achieving complete follow-up. The mean age of patients was 62 years, with 69% having one or more previous valve surgeries, and 92% in NYHA functional class III or IV due to dyspnea. The indications for reconstruction were extensive calcification of the fibrous skeleton (34%), abscess (13%), tissue damage secondary to previous operations (39%), and mitral valve prosthesis-patient mismatch (13%). Bovine pericardium was used in two-thirds of cases, while a tailored Dacron conduit was employed in the remaining third. The operative mortality rate was 13.2%, with a high incidence of postoperative complications. Survival rates at 1, 10, and 20 years were 81.8%, 51.1%, and 23.7%, respectively. Fourteen patients required reoperation, and three underwent percutaneous intervention. The cumulative probability of reoperation at 1, 10, and 20 years was 3.3%, 5.8%, and 9.1%, respectively. Most patients experienced symptom improvement postoperatively.

Based on these results, the authors conclude that reconstruction of the heart's fibrous skeleton is associated with high operative mortality, but the long-term outcomes are satisfactory, considering that most patients would not have survived without surgical intervention.

COMMENTARY:

David et al. from Toronto present the largest published series of patients undergoing combined aortic and mitral valve replacement with mitral-aortic continuity reconstruction, performed by a single surgeon. This series is not only notable for the large number of patients included but also provides, for the first time, long-term follow-up information for patients undergoing such an aggressive procedure. Initially, Tirone David described this technique in 1997, publishing a series of 43 patients; the subsequent series in 2005 included 73 patients, and this most recent series with 182 patients spans a 35-year period.

One notable point is the favorable short-term or in-hospital mortality rate of just 13.2%, a remarkable outcome considering that 69% of the procedures were reoperations, with 16% being third-time operations and even 7% fourth-time surgeries.

Tirone David's team underscores that this series involved a complex learning curve and imparts technical lessons that cardiac surgeons should not overlook. Among the standout recommendations, they describe techniques for performing tension-free patch reconstruction between the medial and lateral fibrous trigones using individual sutures, measuring and positioning the mitral prosthesis to avoid left ventricular outflow tract obstruction, preoperative imaging guidelines, reconstructing the posterior mitral annulus, and when and what type of patch material to use. Regarding patch material, the authors report late calcification and fracture of bovine pericardium, which has sometimes led to late paravalvular leakage. Consequently, their team has recently preferred Dacron patches, especially for younger patients, although Dacron may be less versatile in the surgical field than bovine pericardium.

Several questions without clear answers remain, such as whether any preoperative imaging characteristics (computed tomography or echocardiography) or clinical factors contraindicated this procedure. Occasionally, particularly in cases of native valve endocarditis, the intraoperative findings of tissue destruction may exceed preoperative expectations, necessitating more radical debridement and, at times, a spontaneous shift to a Commando procedure. What percentage of these cases were unplanned, and did these unexpected scenarios impact outcomes?

This pioneering publication provides an exhaustive and exceptional technical surgical description, accompanied by excellent short- and long-term outcomes, setting the reference standard for Commando surgery.

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Elio Martín Gutiérrez

In pursuit of improved outcomes in reoperative mitral valve surgery: resternotomy, minimally invasive approach, and transcatheter procedures

Data from the Dutch registry comparing perioperative outcomes of patients undergoing reoperative surgery for isolated mitral valve disease using either resternotomy or minimally invasive approaches.

Reoperative mitral valve surgery is conventionally performed via resternotomy, which is associated with higher morbidity and mortality compared to primary surgery. Indications for mitral valve reintervention are typically linked to degeneration or complications of previous prostheses (e.g., endocarditis, thrombosis), failure of previous repairs, or progression of native mitral valve disease that did not warrant surgery during the initial treatment of cardiac disease. New mitral interventions can be challenging due to interference with previous surgical techniques (e.g., aortic prostheses, coronary grafts). To avoid an analogous route to the original intervention and reduce the risk of injury to the right heart chambers, the right thoracotomy approach was traditionally described as an alternative to resternotomy. This technique limits the interaction of pericardial adhesions with the procedure, as these adhesions are often more robust anteriorly. The miniaturization of this approach through peripheral cannulation, videothoracoscopy, and specialized surgical tools via ports has allowed the development of the minimally invasive approach as an alternative to the conventional technique. While this approach can be used for initial mitral valve surgery, it is technically advantageous in reoperative settings by combining the benefits of thoracotomy and minimized tissue trauma.

The Dutch school includes pioneering centers with extensive experience in minimally invasive mitral valve surgery. This study presents findings from their national registry, focusing on patients who underwent isolated reoperative mitral valve surgery between 2013 and 2018. A total of 290 patients, initially treated through median sternotomy, were classified based on whether they underwent resternotomy (205 patients) or minimally invasive surgery (85 patients). Of these, 158 patients (54%) had previously undergone mitral surgery. Valve intervention consisted of repair in 59 cases (28.8%) and prosthetic replacement in 144 (70.2%), with no differences between groups. Perioperative variables were adjusted using propensity score analysis to achieve comparability between groups. However, patients who underwent resternotomy were significantly younger (66 vs. 70 years), had lower rates of previous coronary revascularization (36.1% vs. 49%) or mitral surgery (22.9% vs. 42%), and underwent tricuspid valve repair at a higher rate (33.2% vs. 12%).

No significant differences in 30-day mortality were observed between groups (3.4% for minimally invasive vs. 2% for resternotomy). Perioperative morbidity was also comparable, with similar postoperative stays (7 days), rates of cerebrovascular accident (1%), renal failure (4-6%), and surgical reintervention due to bleeding (5% for resternotomy and 10% for minimally invasive approach). Only the incidence of postoperative atrial fibrillation differed, favoring the minimally invasive approach (21% vs. 41%), which may be attributed to reduced manipulation and lower inflammatory response within the pericardial cavity. Five-year survival was 86.3% in the resternotomy group and 89.4% in the minimally invasive group, with no statistically significant differences. Multivariable analysis showed no association between surgical approach and mid-term mortality.

COMMENTARY:

Mitral valve reoperative surgery outcomes in Dutch centers align closely with results in our own context, with similar repair rates and perioperative morbidity and mortality. The authors suggest that outcomes, particularly in terms of survival, might have been better if smaller centers with less repair experience had been excluded, as repair procedures can enhance survival outcomes in mitral valve surgery.

The study concludes that there were no significant differences in outcomes related to the chosen surgical approach, a finding consistent across numerous comparative studies of minimally invasive and conventional approaches. Differences in secondary outcomes did not translate to clinically relevant outcomes like survival or major complications. Despite reduced tissue trauma, once the learning curve for both techniques is surpassed, they become equivalent in expert hands, as extracorporeal circulation remains the primary factor affecting patient physiology. Various transcatheter procedures are currently under development to find their therapeutic niche within the spectrum of mitral valve disease. In the future, these new tools will likely play a central role, enabling truly minimally invasive correction of mitral valve disease, especially in high-risk surgical patients who have undergone prior cardiac surgery.

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Elio Martín Gutiérrez

Mitral Reoperation Due to Bioprosthesis Degeneration: An Issue of the Past?

This meta-analysis evaluates outcomes from comparative studies on transcatheter mitral valve-in-valve (ViV) implantation versus reoperation for valve replacement in patients with degenerative mitral bioprostheses.

Mitral bioprosthesis degeneration is a challenge we wish we never had to communicate to any patient. Many cardiac surgeries were traditionally considered "once-in-a-lifetime" interventions, effectively addressing the heart condition and extending the patient's survival without further procedures. The currently available mitral bioprostheses demonstrate excellent durability, with some series showing over 85% of patients with functional preservation exceeding 20 years. Criteria for defining structural degeneration of bioprostheses have evolved in recent years, especially with the introduction of TAVI as a therapeutic option. However, beyond these technical criteria, symptomatic bioprosthesis degeneration (causing heart failure and/or hemolysis) presents a reoperation challenge due to the inherent complexities of repeat surgical interventions.

As the preference for bioprosthetic implantation continues to grow, the need for reinterventions will increase, compounded by earlier surgical indications and a progressively reduced tolerance for suboptimal bioprosthesis performance—conditions previously managed medically due to the complexity of reoperations. Minimally invasive approaches that avoid the median sternotomy could emerge as a promising alternative. In the quest to minimize invasiveness, TAVI, initially used on a compassionate basis, has gained popularity as a valve-in-valve (ViV) mitral solution.

ViV is primarily performed using a transapical (retrograde) access, although it can also be accessed through the transeptal approach via peripheral femoral vein access (antegrade). To assess the benefits of this alternative compared to conventional surgical reoperation, the authors conducted a systematic review of PubMed, EMBASE, Cochrane, and Google Scholar, with their registration in PROSPERO, the international database for health-related systematic reviews. Using rigorous methodologies (bias and quality analysis with the Newcastle-Ottawa scale), six comparative studies were identified. These studies analyzed preoperative characteristics of patients allocated to each treatment option, with primary outcomes focusing on mortality during perioperative periods, at one month, and at one- and two-year follow-ups. Secondary outcomes examined post-procedure complications (stroke, myocardial infarction, bleeding, acute kidney injury, permanent pacemaker requirement, and hospital stay) and residual transprosthetic mean gradient after correcting prosthetic dysfunction.

All studies were retrospective observational, with two of them employing propensity score matching. A total of 707 patients were included in the analysis. Reoperations were performed via median sternotomy, while ViV procedures were conducted using transseptal and transapical access routes nearly equally. In most reoperations, a new bioprosthesis was implanted, while ViV predominantly used the balloon-expandable Edwards SAPIEN prosthesis across its various iterations. Despite the older age and higher comorbidity burden in ViV patients, mortality rates for hospital stays (OR = 0.52; p = .14), 30-day mortality (OR = 0.65; p = .15), one-year mortality (OR = 0.97; p = .89), and two-year mortality (OR = 1.17; p = .60) were comparable with the conventional surgery group. ViV was associated with a lower incidence of adverse perioperative events such as stroke (OR = 0.31; p = .03), bleeding (OR = 0.21; p < .00001), acute kidney injury (OR = 0.43; p = .01), permanent pacemaker requirement (OR = 0.18; p = .005), and shorter hospital stay (mean difference = -0.64 days; p < .00001). Only the transprosthetic gradient marginally but significantly favored the new surgical prostheses

(mean difference = 0.25 mmHg; *p* = .04), considering both bioprosthetic and mechanical prostheses implanted after removal of the degenerated biological prosthesis.

The authors concluded that ViV was associated with better outcomes compared to prosthetic mitral valve reoperation in patients with degenerated mitral bioprostheses, with lower perioperative complication rates and shorter hospital stays, and without significant differences in mortality rates.

COMMENTARY:

This quantitative review updates the role of percutaneous approaches for degenerated mitral prostheses. Current evidence is based on recent retrospective studies, given the novelty of the procedure. However, research in percutaneous treatment for mitral valve pathology is gaining traction and is expected to disrupt patient management similarly to TAVI's impact on aortic stenosis treatment in the coming years.

The ViV procedure has unique aspects that make it somewhat more "surgical." First, the larger size of the mitral valve limits device maneuverability, making the transeptal approach more aggressive than for other procedures like balloon valvuloplasty or edge-to-edge therapy. This has renewed interest in the transapical approach, which had been unfairly sidelined due to TAVI's success. Secondly, implantation within the existing bioprosthetic frame renders it more predictable and safer than implantation in rings (valve-in-ring) or native valves (transcatheter mitral valve implantation or TMVI, valve-in-MAC, etc.) where the anterior leaflet remains intact. The risk of left ventricular outflow tract obstruction, the main concern of the procedure, is mitigated by the existing prosthesis that occupies a similar position to where the TAVI device will be deployed. Nevertheless, this should not be misconstrued; the obstruction risk remains but is more predictable in pre-procedure models than with native mitral valve implants. Although leaflet laceration, as seen in aortic procedures to prevent coronary ostia occlusion, is theoretically possible in ViV, it remains anecdotal. If, after adequate planning, the procedure is deemed feasible, avoiding the complexities and risks of surgical reoperation and cardiopulmonary bypass with an implant that demonstrates almost comparable hemodynamics to surgical prostheses in terms of gradients and residual leaks makes it a viable therapeutic alternative to be integrated into our therapeutic arsenal.

The results support this treatment option, particularly in high surgical risk patients, as well as in cases where the known durability of TAVI device biological tissue is not a concern. The use of balloon-expandable devices is almost mandatory, and in the future, we may see some adapted for ViV, as is done for the aortic valve. However, its use remains compassionate and restricted. Large-scale randomized trials are required to mitigate biases and validate these findings. This meta-analysis highlights the need to act proactively rather than wait and observe. We must incorporate these techniques into daily practice to stay competitive when the next "PARTNER I" trial for transcatheter mitral therapy arrives.

Does this mean mitral reoperations are a thing of the past? Absolutely not. Patients at low risk will continue to undergo reoperations where residual gradients matter, such as those with 25 mm mitral bioprostheses or mechanical prostheses with pannus/thrombosis, where TAVI device durability, left ventricular outflow tract obstruction risk, or prosthetic endocarditis are concerns. This broadens the spectrum of therapeutic options tailored to patient needs, with insufficient knowledge or reluctance no longer justifying the exclusion of these options. Offering them requires collaboration with our cardiologist colleagues. The mitral bastion is starting to become less of a stronghold. Only training, continuous updates, critical evidence review, and open discussion will lead

us to success. We boarded the TAVI train late for aortic treatments... let's be on time for mitral.

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Bunty Ramchandani

What is the Prosthetic of Choice in Rheumatic Mitral Valve Disease?

This nationwide retrospective study from Taiwan evaluates outcomes of biological versus mechanical mitral valve replacement in 1,576 patients.

Rheumatic heart disease is a global problem affecting over 40 million individuals worldwide, causing over 300,000 deaths each year—outnumbering infectious diseases like HIV. This devastating disease primarily impacts young people, leading to 10.7 million years of life lost due to disability. Group A streptococcal infection ranks fifth in mortality among contagious diseases, with half of these deaths resulting from cardiac involvement. The REMEDY study indicates that 20% of cases were previously undiagnosed for rheumatic fever, up to 40% presented with advanced heart failure at diagnosis, and one in five patients died within two years of diagnosis. Rheumatic heart disease has a latency period of 10–15 years from pharyngeal infection to cardiac impact, so data likely reflect only severe cases, potentially underestimating the full scope due to undiagnosed subclinical cases.

Today's study demonstrates that rheumatic valvulopathy remains significant, even in developed regions. Here, the authors aim to compare the long-term outcomes of mechanical and biological mitral prostheses in patients who underwent surgery for rheumatic mitral valve disease. Data from Taiwan's national health system database (2000–2013) were analyzed, focusing on all-cause mortality and the need for reintervention as primary outcomes. Propensity score matching was employed to achieve homogeneous cohorts. Patients under 20 (15 cases), those with incomplete demographic data (4 cases), and those with mitral valvulopathy of other etiologies were excluded. The hypothesis was that mechanical prostheses would be used in younger patients, while biological ones would be chosen for older, comorbid patients. The authors were interested in determining the age threshold favoring one prosthesis over the other.

The study identified 3,638 patients with mitral valve replacement due to rheumatic disease. About 30% (1,075 patients) received a biological prosthesis, and 70% (2,563 patients) a mechanical one. Propensity matching yielded 788 homogeneous pairs. In-hospital mortality showed no significant differences. However, long-term outcomes favored mechanical mitral prostheses: 10-year actuarial mortality estimates were 50.6% for biological prostheses versus 45.5% for mechanical prostheses (HR 1.19, $p < .05$); reintervention rates were 8.9% for biological prostheses versus 0.93% for mechanical prostheses (HR 4.56, $p < .01$). Notably, mechanical prostheses showed a slightly higher stroke rate, though not statistically significant (28% vs. 29.4%). The survival advantage of mechanical prostheses was most pronounced in younger patients and remained evident in those up to 65 years old.

The authors conclude that, for patients with rheumatic mitral valve disease, mechanical prostheses are associated with favorable long-term outcomes in patients younger than 65 years.

COMMENTARY:

Choosing between biological and mechanical prostheses for either aortic or mitral positions is never a trivial decision. At the extremes of adulthood, the choice is straightforward: mechanical prostheses are advised for patients under 50, while biological prostheses are preferred for those over 70. The decision becomes more complex for the large patient cohort between 50 and 70 years of age. Here, life expectancy is a determining factor, heavily influenced by age and comorbidities. However, lifestyle considerations, adherence factors, and potential anticoagulation

complications are also crucial. In fact, patient preference is key in prosthesis choice at any age.

In an era promoting patient empowerment, surgeons are responsible for providing the most current information to help patients clarify their preferences. A shared decision-making approach is recommended, discussing not only durability, anticoagulation regimens, reintervention rates (surgical or percutaneous), thromboembolism, bleeding, endocarditis, pannus formation, etc., but also lifestyle changes, pregnancy concerns for women of childbearing age, follow-up visits, and even the sound of the mechanical prosthesis. Innovations such as new-generation anticoagulants, On-X mechanical valves, and results from the PROACT and PROACT Xa studies must be mentioned. Physicians are responsible for guiding patients through an overwhelming information landscape to make a decision aligned with their needs.

Just as with different prostheses, this study has limitations as it relies on administrative data, lacking access to detailed clinical or surgical data, which prevents adjusting for rheumatic severity. Potential coding errors and the absence of echocardiographic follow-up data limit our understanding of bioprosthesis structural deterioration in reintervention contexts.

In conclusion, Chen et al.'s study supports the latest European and American guidelines regarding mitral prosthesis choice. Yet, the final decision must be individualized, as José Ortega y Gasset said: “I am myself and my circumstances, and if I do not save them, I cannot save myself.”

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Bunty Ramchandani

On-X mitral: Is Reduced Oral Anticoagulation Feasible?

This study is a randomized, multicenter, prospective, open clinical trial comparing clinical outcomes 3 months after implanting an On-X mechanical mitral prosthesis in patients with standard anticoagulation ranges versus a lower target.

Each year, it is estimated that over 300,000 cardiac valve prostheses are implanted worldwide. When mitral valve repair is not feasible, replacement with a prosthesis becomes the offered solution. Mitral prostheses provide excellent long-term outcomes, conferring a survival advantage, albeit not reaching the effectiveness and durability seen in successful mitral valve repair. For patients under 70 years old, mechanical prostheses are often preferred; however, bioprostheses also yield favorable outcomes for selected cases. The key drawback of mechanical prostheses is the requirement for lifelong oral anticoagulation (OAC), which can add morbidity that bioprosthetic alternatives might mitigate. Furthermore, even in patients needing anticoagulation for other indications, the presence of a mechanical prosthesis mandates the use of coumarin-based agents with a target INR of 3 (previous range 2.5-3.5, now less commonly used).

The potential role of direct-acting anticoagulants as substitutes for coumarins in valve prosthesis patients has been evaluated in the RE-ALIGN (Dabigatran vs. Warfarin in Patients with Mechanical Heart Valves) and RIWA (Rivaroxaban vs. Warfarin in Patients with Metallic Prostheses) trials. In RE-ALIGN, a higher bleeding risk was identified, contrasting with RIWA's findings. However, other published cohorts reported serious valve thrombosis complications with Rivaroxaban. This evidence has led to the formal contraindication of direct-acting anticoagulants in patients with mechanical valve prostheses, with coumarins remaining the first-line therapy.

This study aims to provide new evidence by examining a less aggressive anticoagulation regimen in mitral prostheses, akin to the PROACT (Prospective Randomized On-X Anticoagulation Trial) study on the On-X prosthesis in the aortic position. From 2006 to 2020, a total of 401 patients undergoing mitral valve replacement with an On-X mechanical prosthesis were prospectively randomized across 44 centers and with the participation of 100 implanting surgeons. After three months post-surgery, patients were divided into two anticoagulation groups: 200 patients adhered to a standard anticoagulation regimen (target INR of 3, range 2.5-3.5) following clinical guidelines, while 201 patients followed a lower anticoagulation target (INR 1.5-2). All patients also received concurrent aspirin therapy. Patients younger than 18 years, those with double-valve prostheses, active endocarditis, a history of thromboembolic events within the past year, terminal illness, or urgent intervention were excluded. Candidates could be randomized between 3-12 months post-valve replacement, and INR monitoring was conducted by the patients themselves. The primary outcome included thromboembolism, valve thrombosis, and major and minor bleeding events. Secondary outcomes were all-cause mortality and adverse prosthesis-related events such as endocarditis, hemolysis, hemolytic anemia, paravalvular leakage, and structural or non-structural dysfunction. A non-inferiority analysis was conducted following FDA performance criteria for cardiac valve prostheses, with primary combined event rates set at 6% patient-years in the low-range group and 7.3% patient-years in the standard group, with a 1.5% non-inferiority margin.

The study succeeded in randomizing 401 patients over 14 years, with an average follow-up of over 4 years and 1,600 patient-years analyzed. The primary combined event occurred in 11.94% of the low-dose group and 12.01% of the standard-dose group. The absolute difference was -0.07% (95% confidence interval, -3.40% to 3.26%), with the

upper limit exceeding the preset 1.5% non-inferiority margin. No differences were found in secondary outcomes, including mortality, thromboembolism, valve thrombosis, major bleeding, or event-free survival at 5 and 8 years. In a post-hoc analysis of patients with preoperative atrial fibrillation, there were also no differences in these variables.

The authors concluded that a low OAC regimen for managing On-X mitral prostheses cannot be recommended, as non-inferiority in the primary combined event was not achieved.

COMMENTARY:

Establishing OAC ranges for mechanical valve prostheses has always been a trial-and-error process. In the early 1990s, an INR range of 3-4.5 was recommended for any mechanical cardiac prosthesis. However, various teams reduced the INR range due to frequent bleeding episodes. The study by Gohlke-Barwolf et al. first established distinctions in OAC ranges between aortic and mitral prostheses. The multicenter AREVA (Anticoagulation in Patients with Mechanical Prosthetic Heart Valves) study demonstrated that an INR range of 2-3 was comparable to 3-4.5, with fewer bleeding events. The LOWERING-IT (Lowering the Intensity of Oral Anticoagulation Therapy in Patients with Bileaflet Mechanical Aortic Valve Replacement) study further reduced the range, showing the non-inferiority of an INR range of 1.5-2.5 for low-risk patients. Finally, the German Experience with Low Intensity Anticoagulation trial established an INR range for mechanical mitral prostheses of 2-3.5, and for combined multiple mechanical prostheses of 2.5-4 (provided a St. Jude prosthesis was used).

The limitations of this study include significant overlap in the OAC ranges within each group, with the low OAC group frequently surpassing the established upper limit, likely due to OAC regimen adjustments. This affects the study's internal validity, complicating the interpretation of comparisons. The majority of patients managed their OAC at home, a scenario uncommon in our setting, which also impacts external validity. Additionally, only On-X mechanical mitral valves were studied, meaning these findings cannot be applied to other mechanical mitral prostheses. Finally, all patients received antiplatelet therapy; thus, these results do not apply to patients managed exclusively with OAC.

In conclusion, the negative findings of Chu et al. add to the evidence that for mechanical mitral prostheses, we cannot justify lower INR ranges than 3 (range 2.5-3.5), not even for the new-generation On-X mechanical prostheses. These results do not align with the PROACT study findings and, therefore, do not support the alternative anticoagulation management approach for these prostheses in the aortic position.

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José Manuel Martínez Comendador

Surgical Implantation of Balloon-Expandable Valve Prosthesis in Cases of Severe Mitral Annular Calcification: Another Tool in the Armamentarium

An analysis of the technique and outcomes of the largest published series on the surgical implantation of balloon-expandable valves (Sapien) in patients with severe mitral annular calcification (MAC).

Surgical treatment of mitral valve disease in the presence of MAC presents a significantly increased risk of cardiovascular and all-cause mortality. Until recent years, surgical options were rarely offered to these patients due to their prohibitively high-risk profile. However, over the past decade, various surgical and transcatheter techniques involving balloon-expandable valves (BEV) have been described to treat mitral disease complicated by severe MAC. Nevertheless, reported case series remain limited, and outcomes still correlate with high operative morbidity and mortality.

This article presents the experience of two hospitals in Virginia, USA, with the open surgical implantation of a BEV in the mitral annular position through a transatrial approach (BEV-in-MAC transatrial) as an alternative strategy for patients with severe MAC. The BEV implantation was performed with direct visualization via the left atrium, using either a median sternotomy or a minimally invasive approach. The midportion of the anterior leaflet was excised, and, in cases with a high risk for left ventricular outflow tract (LVOT) obstruction, a septal myectomy was performed via a transatrial approach. The primary endpoint was technical success as defined by the Mitral Valve Academic Research Consortium, with secondary outcomes including 30-day and 1-year mortality. Between October 2015 and October 2020, a total of 51 patients from these institutions underwent BEV-in-MAC implantation (mean age: 73.9 years; 60.8% female; predicted mortality risk by STS score: 6.8%). Technical success was achieved in 94.1% (48/51) of cases. Thirty-day and 1-year mortality were 13.7% (7/51) and 33.3% (15/45), respectively. Stroke rates were 3.9% (2/51) at 30 days and 4.4% (2/45) at one year.

Surgical implantation of a BEV in the mitral position offers a treatment option for patients with mitral valve disease complicated by severe MAC who face elevated risks with conventional open surgery and/or a high risk of LVOT obstruction with percutaneous treatment.

COMMENTARY:

The primary results of this study can be summarized as follows: (1) BEV-in-MAC transatrial can be performed with a high rate of technical success (94%) and low incidence of LVOT obstruction and paravalvular leakage; (2) thirty-day mortality was 13.7%, and one-year mortality was 33.3%. This study represents the most extensive published series on BEV-in-MAC to date and positions this technique as a valuable alternative to conventional surgical and purely percutaneous treatment, particularly in cases with a high risk of LVOT obstruction and embolization.

With the traditional surgical approach, options were limited to modifications of valve implantation, such as heterotopic and orthotopic implantation. In the heterotopic approach, the mitral prosthesis was anchored to non-calcified tissue, often the left atrium, with ventricularization of part of the structure, which commonly involved the left atrial appendage, requiring ligation. Orthotopic implantation within the native annulus demanded limited resection of calcified tissue when feasible or complete decalcification of the mitral annulus with or without sealing through pericardial patch addition. Ensuring a watertight suture line was imperative in both approaches. These techniques have been

associated with a high percentage of atrioventricular groove disruption, circumflex artery injury, and extended ischemic times, ultimately contributing to a mortality rate between 9% and 24%. Conventional surgery in these patients is also associated with smaller prosthetic sizes, frequently mechanical, and a higher risk of paravalvular leakage.

From the pioneering work of Guerrero et al. on the first percutaneous prostheses implanted in MAC (valve-in-MAC via transeptal or transapical approaches), it became clear that one of the major limitations was the difficulty in achieving a stable seal without paravalvular leakage, alongside limitations related to the annular sizes that could be treated. Other notable drawbacks included the high likelihood of LVOT obstruction without the possibility of anterior mitral leaflet resection, and the risk of prosthesis migration. One-year mortality with this approach hovers around 50%, with LVOT obstruction emerging as the most potent independent predictor of poor prognosis.

The transatrial BEV-in-MAC approach described in this article offers several potential advantages compared to conventional surgery or transeptal or transapical valve-in-MAC approaches:

- It avoids the need for annular debridement, reducing the risk of groove rupture and circumflex artery damage.

- Direct visualization of the prosthesis deployment and manual stabilization verification, along with additional sutures in atrial tissue or calcified leaflets, anchor the struts, reducing the risk of prosthesis migration and paravalvular leaks. Some authors suggest adding Teflon bands around the prosthesis's intended location to fill irregular spaces and secure the prosthesis upon expansion, thereby improving anchoring and peri-prosthetic sealing.

- LVOT obstruction is prevented in two ways: by excising the anterior leaflet in all cases and performing a prophylactic septal myectomy in patients with a predicted small LVOT area.

- The transatrial approach permits concomitant surgeries, such as aortic or tricuspid valve procedures, coronary surgery, or other interventions.

Regarding the results of this procedure, the mean cross-clamp time exceeded two hours (128 minutes), likely because more than half of the patients underwent concomitant surgery, which could have contributed to the relatively high 30-day (13.7%) and one-year (33.3%) mortality rates. These outcomes are consistent with those reported by other groups performing the same intervention. Furthermore, these results are slightly better than those reported with transapical or transeptal valve-in-MAC techniques, which yield a 30-day mortality of 20% and a one-year mortality of 40%. Consequently, no technique currently offers low morbidity, and none appears to be clearly superior; therefore, the choice should be individualized based on patient characteristics and surgeon preference.

The main limitations of this study arise from its retrospective nature. Additionally, the absence of a control group limits our ability to make comparisons, and the sample size is small. Caution is needed in interpreting one-year outcomes due to the high rate of missing echocardiographic data during follow-up. Awaiting the results of the ongoing SITRAL (Surgical Implantation of Transcatheter Valve in Native Mitral Annular Calcification) study is essential to gain further insights into cases where a hybrid approach, as described here, could be most beneficial.

Lastly, the importance of preoperative imaging studies and meticulous surgical technique for the success of this procedure cannot be overstated. Both aspects are detailed within this study's methodology. Preoperative assessment requires at least a transthoracic and transesophageal echocardiogram and, crucially, a 4D computed tomography for mitral valve reconstruction, LVOT size estimation, and optimal surgical planning. Consequently, transcatheter valve-in-MAC generally necessitates near-circumferential annular calcification (at least three-quarters of its circumference), while the transatrial approach can address less extensive calcification (often confined to the posterior leaflet, two-thirds of the circumference). This factor, along with others such as LVOT obstruction risk, makes imaging the cornerstone of approach allocation.

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Bunty Ramchandani

Which Is the Mitral Prosthesis of Choice in Dialysis Patients? The Debate Continues

This single-center, retrospective American study evaluates outcomes of prosthesis choice in patients with advanced renal disease on dialysis.

Valve treatment for patients with advanced renal disease poses a significant challenge for any cardiac surgeon. These patients are complex, fragile, and consequently high-risk, and the literature regarding the optimal type of prosthesis remains controversial. The choice of prosthesis type must consider several specific factors in this patient group, such as their limited life expectancy, hemorrhagic and thrombotic risks, accelerated valve degeneration due to electrolyte imbalance, and increased risk of endocarditis due to frequent arteriovenous fistula manipulations. Some studies show certain advantages of mechanical prostheses over biological ones in the aortic position, though this does not settle the debate (as previously discussed in a blog entry). The decision for the mitral position is even more challenging, as there are no conclusive studies favoring one type of prosthesis. This uncertainty led the American College of Cardiology (ACC) and the American Heart Association (AHA) in 2006 to retract their 1998 recommendation on mechanical mitral prostheses for these patients, as it was based on two studies from the 1970s with a total of only 4 patients.

The current study analyzes the outcomes of mitral valve replacement in dialysis-dependent patients with advanced renal disease at a high-volume tertiary center. All patients who underwent mitral valve surgery from 2002 to 2019 were retrospectively reviewed, excluding those with mitral valve repair. Only patients with advanced renal disease on dialysis were selected. The decision on prosthesis type was based on patient preferences and the discretion of the physicians. The primary goal of the study was to assess, at 5 years, mortality, the mitral prosthesis reintervention rate, and the incidence of moderate or greater prosthetic stenosis.

During this period, approximately 8,168 mitral valves were operated on, with about 480 surgeries on the mitral valve each year. Among these, 177 patients were on dialysis, representing roughly 10 cases per year. Of these, 118 (67%) were biological prostheses and 59 were mechanical. Patients who received a biological prosthesis were older and had more comorbidities such as diabetes mellitus, dyslipidemia, previous myocardial infarction, and a history of cerebrovascular accidents. In contrast, patients with mechanical prostheses, besides being younger (48 years vs. 61 years; $p < .001$), had a higher prevalence of previous mitral valve repair. No significant differences were found in the length of hospital stay between the two groups. With a median follow-up of 234 days, adjusted 5-year survival was similar for both groups. Both groups showed a high early mortality rate of over 20%, with actuarial survival of less than 50% at 2 years. No statistically significant differences were observed in reintervention rates or structural valve degeneration. Stroke events were more frequent in patients with mechanical prostheses (15% vs. 6%; $p = .041$). Endocarditis was the most common reason for reintervention, with 9 cases, 5 of which occurred in the mechanical prosthesis cohort. Four patients with bioprostheses underwent reintervention due to structural degeneration.

The authors conclude that mitral valve replacement in dialysis-dependent patients carries high midterm morbidity and mortality. When choosing a prosthesis, the decreased life expectancy of these patients should be considered.

COMMENTARY:

Having references on outcomes in high-risk procedures is essential for making informed decisions and for comparing outcomes with other centers. Nowadays, this is even more relevant due to the option of transcatheter access. In fact, this approach today would be purely compassionate, as patients with advanced renal disease on hemodialysis are currently excluded from clinical trials on transcatheter mitral prostheses. If equivalence between biological and mechanical prostheses were eventually demonstrated, the transcatheter mitral bioprosthesis would not be the option of choice for this group of patients unless they were formally rejected for surgical treatment.

Various published studies on this topic show that it is difficult to generalize for this patient group. One of the main concerns when implanting a bioprosthesis is the potential for early degeneration. Patients with advanced renal disease have tertiary hyperparathyroidism, which leads to hypercalcemia and hyperphosphatemia, both of which contribute to valve calcification and, therefore, accelerated degeneration of bioprostheses. This led to 4 reinterventions (3%) among 118 bioprosthesis patients in a cohort with a median survival of less than 2 years. However, what should catch our attention most is the high rate of endocarditis in these patients. Dialysis patients have an 18-fold increased risk of endocarditis compared to the general population. This explains why 70% of reoperations in this study were due to endocarditis. Therefore, our primary concern should be endocarditis rather than prosthetic degeneration. Although this study lacked sufficient power to determine in which type of prosthesis this was more common, a prior meta-analysis suggested higher rates of endocarditis in bioprosthesis recipients. This could be explained by the greater susceptibility of bioprostheses to transient bacteremia due to germ adhesion to tissue material, as well as the larger volume and surface area of artificial structures in bioprostheses compared to mechanical prostheses. Future studies should explore this hypothesis.

It is essential to mention the limitations of this study to interpret the results in context. The retrospective nature of the study prevents randomization of the groups, making comparisons, although adjusted, not entirely comparable. There may be confounding effects from variables such as age and the duration until cardiac surgery, with associated risk factors such as diabetes mellitus or renal disease, which add to the consideration of whether these are present or absent. Lastly, despite the availability of data from a high-volume center, the sample size of these patients was very limited, which hinders solid conclusions.

In conclusion, when determining a prosthesis type for dialysis-dependent patients with advanced renal disease, we should not only consider age, patient preference in terms of anticoagulation, and the risk of prosthetic degeneration but also the bleeding risk, thromboembolic events, increased risk of endocarditis, and life expectancy, among other aspects. The decision will never be easy, so the debate continues.

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Elio Martín Gutiérrez

Durability of Bioprostheses in the Mitral Position: Surgery Sets the Standard

This review article consolidates 21 studies and nearly 16,000 patients to establish outcomes regarding the durability of bioprostheses in the mitral position.

"Surgical bioprostheses are no longer the reference for long-term durability." This statement has been repeated by some interventional cardiologists at meetings over the past year. One of these instances occurred at the annual EACTS Congress in Vienna, sparking murmurs of disapproval with no significant repercussions. Although this argument has been applied primarily to bioprostheses in the aortic position, it is likely to extend to bioprostheses in any position with the evolution of transcatheter mitral valve implants.

Beyond competition with the transcatheter field, understanding the real outcomes of surgical bioprostheses is essential, considering the progressively growing trend favoring bioprostheses over mechanical ones. We have moved from an era where a commitment to implant a prosthesis "that would outlast the patient" was expected (with structural degeneration viewed as a true failure) to one where only early failure is considered adverse. This shift allows patients to avoid long-term oral anticoagulation with dicoumarin if a mechanical prosthesis were implanted. Additionally, simply reinstating oral anticoagulation with direct oral anticoagulants (DOACs) in patients with atrial fibrillation has become a strong enough reason to promote the implantation of mitral bioprostheses. When combined with the positive outcomes of TAVI-in-mitral-bioprosthesis implants that avoid reoperation, the potential disadvantage of structural degeneration is more tolerable.

Surgical bioprostheses have undergone multiple designs and evolutionary generations, with porcine valves being more prevalent than in the aortic position. The lack of data on some aortic bioprostheses (e.g., St. Jude Trifecta® and Sorin Mitroflow®/Livanova Crown®) led to the well-known poor outcomes that affected many surgical cohorts in studies, both intentionally and retrospectively, focusing on durability, while also providing cases for TAVI-in-aortic-bioprosthesis procedures worldwide.

For this reason, the authors conducted a comprehensive review of all published literature from the past 20 years to determine the true durability of mitral bioprostheses. While much has been written about their durability in the aortic position, there are hardly any studies for the mitral position. This study is aligned with the PROSPERO registry. The authors included studies with at least 50 patients who underwent isolated or concomitant mitral valve replacement with bioprosthesis, published between 2003 and 2023, and with at least 5 years of follow-up, reporting on survival and freedom from reintervention and/or structural degeneration.

A total of 21 studies encompassing 15,833 patients from 11 countries, with surgeries performed between 1984 and 2018, were identified. Therefore, this is considered the largest study published to date on this topic.

The etiologies of the mitral pathology treated included rheumatic (32%), degenerative (25%), functional (13%), and endocarditis (8%). The most commonly implanted bioprostheses were bovine pericardium (Balmedic® and Carpentier-Edwards®) and porcine (Biocor®/St. Jude Epic®, Hancock II®, and Medtronic Mosaic®). The most frequently implanted prosthesis was the Medtronic Mosaic® (n = 1825), followed by the Carpentier-Edwards® (n = 1397), with St. Jude Epic® in third place. The most common size implanted was 29 mm. Up to two-thirds of the patients underwent concomitant

procedures, especially coronary revascularization (28.8%) and tricuspid valve repair (24.4%). Comorbidities were appropriately documented, with atrial fibrillation (AF) in 35% of patients and diabetes mellitus in 15.4%. Regarding hemodynamic performance, mean gradients were favorable, ranging from 4 to 6.3 mmHg.

Structural degeneration was defined by the criteria proposed by Atkins et al. in most studies. In others, severe dysfunction was indicated by transprosthetic gradients >8 mmHg and/or a regurgitant orifice >40 mm^2. In less frequent cases, pathological criteria based on findings from surgical explants or autopsies were applied without hemodynamic data. The freedom from structural degeneration at 15 years was 58.3% to 93% for porcine bioprostheses and 61.6% to 86.7% for pericardial prostheses. The outcomes for porcine prostheses were primarily attributed to the Medtronic Mosaic®, with structural degeneration rates of 5.8% and reoperation rates of 4.8% at 10 years. For other porcine bioprostheses, like St. Jude Epic®, structural degeneration occurred in 7 cases, with a reoperation rate of 4.3% at 10 years. The best-performing pericardial bioprosthesis was the Carpentier-Edwards, with 20-year structural degeneration rates of 23.7% and a reoperation rate of 40.5% as reported in Bourghignon et al., estimating a "lifespan" of the bioprosthesis at 16.6 years. Similar results were reported by Beute et al., with a reoperation rate of 13.2% at 15 years.

A subgroup analysis based on age groups revealed that the freedom from structural degeneration at 10 years improved as patient age increased, ranging from 58% in patients <55 years to >90% in those >65 years. Particularly in this age group, all bioprostheses demonstrated excellent survival outcomes, with >95% freedom from structural degeneration at 5 years and 78% at 10 years.

The authors concluded that despite considerable variability in study reporting, follow-up duration, structural degeneration criteria, and disease phenotypes, this study provides the most significant reference for the durability of bioprostheses in the mitral position.

COMMENTARY:

This is undoubtedly a landmark article that establishes long-term durability benchmarks for currently available mitral bioprostheses. The primary findings from the data presented are as follows:

The performance of porcine and pericardial bioprostheses is nearly comparable, with porcine valves possibly showing slightly better durability, keeping them relevant in clinical practice. This may be because mitral bioprostheses experience greater hemodynamic stress than their aortic counterparts due to higher closure pressures. However, given the larger size of mitral bioprostheses, prosthesis-patient mismatch is rare (moderate mismatch <1.2 cm^2/m^2 and severe <0.9 cm^2/m^2), thus not allowing pericardial bioprostheses to demonstrate a true design advantage. Conversely, the fact that porcine prostheses are actual cardiac valves grants them a definitive performance advantage. The performance of newer platforms such as Edwards Mitris® with Resilia® pericardial tissue remains to be seen, as they are currently in the early stages of the COMMENCE durability registry follow-up.

The disadvantage of implanting mitral bioprostheses at a younger age is greater than for aortic bioprostheses. Although clinical guidelines recommend bioprosthesis implantation starting at age 70, this study shows positive outcomes from age 65, which seems reasonable to extend this strategy. Beyond this, it is unadvisable, especially for patients without significant life expectancy limitations or contraindications to oral anticoagulation with dicoumarin.

Altogether, structural degeneration rates ranging from zero to 41% at 10 years, and from 7% to 41.3% at 15 years, with freedom from reoperation rates of 65% to 98.7% at 10 years and 78.5% to 91% at 15 years, represent the benchmarks to beat. However, it should be noted that this information may reflect publication biases. The authors identified only 2 studies (of 21) with severe biases, while the others showed lesser biases. Data come from independent studies, such as national registries or single-center experiences, with minimal conflicts of interest. This aspect does not eliminate the bias of positive result selection, but since these studies come from periods without as much industry pressure, they may even appear more reliable and closer to real-world performance. None of the studies were randomized, and thus the inherent heterogeneity in design, associated procedures, and patient characteristics is extensive. Lastly, structural degeneration criteria have also varied, with many studies not following the standardized criteria proposed by Atkins et al. in EACTS guidelines for reporting mortality and morbidity in valvular surgery, introduced in 2008. Consequently, even if considered inappropriate, reoperation rates take on added value in assessing the "clinical" durability of bioprostheses. Notably, this field lacks VARC-defined criteria, which were only developed for mitral valve repair procedures, especially for percutaneous edge-to-edge repair.

Until percutaneous mitral valve implants become widespread and compete with surgical prostheses, patients who are not candidates for mitral valve repair (surgical or percutaneous) will continue to rely on these devices to address their cardiac condition. Long-term outcomes are generally favorable, though predictably inferior to aortic bioprostheses. Therefore, more than ever, it is crucial to engage in shared decision-making with the patient, considering potential longevity, comorbidities, anticoagulation needs, and individual preferences in choosing between a “mechanical or bioprosthetic” path, as a fully biocompatible permanent solution does not yet exist.

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Mercedes L. Castro Pinto

Complete Annular Decalcification in Mitral Valve Replacement: From the Impossible to the Possible

This retrospective study reports on the experience with 15 patients presenting extensive mitral annular calcification (MAC), where a technique utilizing the Cavitron® ultrasonic surgical aspirator (CUSA) was applied during mitral valve replacement procedures.

The condition, termed massive mitral annular calcification (MAC), involves significant calcium deposition on the mitral annulus. This degenerative process is generally associated with aging but may also relate to chronic kidney disease, diabetes, and hypertension. Its incidence stands at 2.8%, occurring more frequently in women. Mitral valve surgery mortality in these patients remains high, ranging from 6% to 14% in selected series and outcomes.

This retrospective study covered a mean follow-up of 21 months and examined 15 patients who underwent mitral valve replacement due to severe valvular dysfunction associated with MAC. Patients were treated between January 2016 and May 2022. During the intervention, the Cavitron® ultrasonic surgical aspirator was employed for annular decalcification, and the posterior annulus was reconstructed using a bovine pericardial patch.

The mean age of the patients was 73 ± 8 years, with an 86.7% female predominance. Indications for mitral valve surgery included degenerative mitral regurgitation in 8 patients (53.3%), mitral stenosis in 4 patients (26.7%), infective endocarditis in 2 patients (13.3%), and left ventricular rupture salvage after an attempted implant without decalcification in 1 patient (6.7%). Concomitant procedures included aortic valve replacement in 11 patients (73.3%), tricuspid annuloplasty in 9 patients (60.0%), coronary revascularization in 1 patient (6.7%), and arrhythmia surgery in 7 patients (46.7%). During surgery and the hospital stay, there were no recorded deaths or complications specifically associated with mitral annular calcification. Postoperative complications included stroke in 1 patient (6.7%), initiation of hemodialysis in 1 patient (6.7%), temporary tracheostomy in 2 patients (13.3%), and re-exploration for bleeding in 2 patients (13.3%). Medium-term follow-up showed four deaths, with two attributed to respiratory sepsis at 6 and 19 months, one due to an unknown cause at 7 months, and one due to cerebral hemorrhage at 31 months.

The authors concluded in this article that the treatment strategy employed yielded satisfactory clinical outcomes, demonstrating safety and reproducibility even in high-risk patients requiring multiple surgical procedures.

COMMENTARY:

Mitral valve surgery in patients with severe MAC is a complex procedure, not only because of the surgical technique but also due to comorbidities associated with advanced patient age. Currently, no ideal therapeutic strategy exists for managing MAC. Techniques range from calcium “mold” resections with subsequent reconstruction to conservative approaches with non-orthotopic implantation, such as intra-atrial mitral prosthesis placement. However, the latter carries risks, including aneurysmal atrial dilation and valve dehiscence.

Transcatheter techniques have been developed as options for high-surgical-risk patients, but despite a 72% periprocedural success rate, the 30-day mortality remains high at 29.7%, suggesting it may not be the optimal strategy. In prior blog entries, the role of

open TAVI prosthesis implantation has also been examined as a hybrid technique for treating this condition.

The partial resection technique aims for minimal debridement to allow mitral prosthesis implantation without disrupting the annulus, with studies reporting a 78.8% survival rate at 5 years. However, this strategy is not free of complications, including risks of atrioventricular groove rupture due to suture placement through or behind residual calcification, and paravalvular leakage. Additional risks include circumflex coronary vessel injury and/or permanent complete atrioventricular block.

Although complete resection is the most aggressive approach, the authors propose a comprehensive approach to managing MAC, from preoperative planning to postoperative intensive care. Key steps include adequate mitral valve exposure through a superior transseptal incision, selective decalcification using CUSA, annular reconstruction with bovine pericardium, and implementing measures to reduce left ventricular afterload in the acute postoperative phase, including pharmacotherapy, deep sedation, and intra-aortic balloon pumping.

The main drawback of this strategy is the need for prolonged intubation, which may lead to complications such as respiratory infections, critical illness polyneuropathy, and respiratory distress syndrome. However, these complications are considered manageable given the high complexity of the procedure. The small patient cohort and short follow-up period limit the generalizability of the findings. Furthermore, only 33% of patients had complete posterior annular calcification, and 13.3% had circumferential calcification, with the remainder exhibiting calcification over less than two-thirds of the posterior annulus. In cases of mortality, the degree of MAC was not specified but did not appear related.

The technique appears safe, but its reproducibility requires availability and expert handling of the Cavitron® ultrasonic surgical aspirator (CUSA). It is advised to perform this procedure in specialized centers with dedicated mitral valve teams and intensive care units experienced in managing postoperative care for high-complexity cardiovascular surgeries.

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Bunty Ramchandani

How to Orient Mechanical Prosthesis Leaflets in the Mitral Position?

This retrospective single-center study evaluates the relationship between anatomical or non-anatomical disc orientation in mechanical mitral prostheses and the development of pannus.

Mechanical mitral prostheses are frequently employed due to their long-term durability. Despite advancements in design, a dysfunction rate of 10–30% is still observed after ten years. One primary complication is the growth of fibrous tissue known as pannus, which is a consequence of chronic inflammation and, in some cases, can cause prosthesis dysfunction by restricting disc mobility. The exact pathophysiology of pannus is not fully understood, although it is more common in younger patients, regions with turbulent or high-shear flow, patients with double valve replacements, and smaller prosthetic rings. Diagnosing pannus-related prosthetic dysfunction in mechanical mitral valves is challenging. Clinical presentation is insidious, and it can take up to two decades post-surgery for overt dysfunction to emerge.

The aim of this study was to investigate pannus formation in bileaflet mechanical mitral prostheses. It is a single-center study where all transesophageal echocardiograms from patients with mechanical mitral prostheses performed between May 2017 and April 2021 were retrospectively reviewed. Patients with less than one year since prosthesis implantation and those with inadequate anticoagulation were excluded. The 141 patients with bileaflet mechanical mitral prostheses were divided into two groups: those with anatomical disc orientation (parallel to the native leaflet axis) and those with non-anatomical orientation (perpendicular or oblique to the native leaflet axis). Forty-six patients had anatomical orientation, and 95 had non-anatomical orientation. Since there are no guidelines for diagnosing pannus via echocardiography, Barbetseas et al.'s recommendations, which assess a combination of echogenicity and the echotexture of fibrous tissue on ultrasound, were utilized.

Out of 141 patients, pannus was identified in 26 patients with anatomically oriented prostheses (56.5%) and in 71 patients with non-anatomical orientation (74.7%) ($p = .03$). Patients with pannus generally had a longer postoperative duration (13.4 years vs. 6.8 years; $p < .01$). Of the 97 patients diagnosed with pannus, 11 required reoperation due to symptomatic obstruction. Among these, 3 had anatomical orientation, and 8 had non-anatomical orientation. The most common cause of dysfunction in these patients was pannus growth in the disc hinges. Multivariable analysis showed that anatomical orientation acted as a protective factor against pannus development (OR = 0.39; $p = .04$), while mitral-aortic prosthesis increased the risk (OR = 2.73; $p = .04$).

The authors concluded that anatomical orientation of mechanical mitral prosthesis discs reduces the incidence of pannus overgrowth.

COMMENTARY:

Traditionally, selecting a non-anatomical orientation for mechanical mitral prostheses has been preferred to avoid interference with the preserved subvalvular apparatus, either partially or completely. However, this study conveys a significant message: non-anatomical orientation of discs may increase the long-term incidence of pannus. Two mechanisms could explain why patients in the non-anatomical orientation group might be more prone to pannus formation. First, turbulent flow and shear stress across the discs may activate platelet function and promote pannus formation. In fact, several studies show that flow across anatomically oriented bileaflet mitral prostheses is less turbulent than in non-anatomical settings, as anatomical orientation generally allows for greater and more stable disc opening angles. Second, all patients in this study were diagnosed with rheumatic valve disease, which is itself a risk factor for pannus development. Preserving the posterior leaflet to prevent atrioventricular groove rupture places the prosthesis, especially the disc pivots, in contact with rheumatic tissue when oriented non-anatomically.

Therefore, does this justify implanting mechanical mitral prostheses in anatomical orientation? The data must be considered with perspective: out of 141 patients, two-thirds were diagnosed with pannus growth, but only 11 required surgery. It should also be noted that all patients in this study had rheumatic valve disease, which may not be representative of our clinical environment.

Moreover, the study has significant limitations that prevent extrapolation to our clinical practice. Information on the brand and size of the prosthesis was not available for over half of the patients. Additionally, there were no other imaging studies to corroborate pannus diagnosis beyond echography, which is operator-dependent. Lastly, surgical reports were unavailable for most patients, leaving uncertainties regarding implantation techniques (intra- or supra-annular) and the degree of subvalvular apparatus preservation.

In conclusion, today's article does not provide enough evidence to change our approach to implanting mechanical mitral prostheses. However, it prompts reflection while we await larger studies with more diverse patient diagnoses and more specific imaging studies. Until then, the best orientation is the one that ensures optimal disc opening and closure.

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José Manuel Martínez Comendador

Transapical neochord implantation: a promising future

This study evaluates the five-year clinical and echocardiographic outcomes of patients with severe degenerative mitral regurgitation (MR) treated with transapical neochord implantation using the NeoChord DS 1000® device.

The standard treatment for degenerative MR is mitral valve repair surgery, which can be performed through a median sternotomy or minimally invasive access. Recently, the concept of microinvasive cardiac surgery has emerged, aiming to replicate conventional surgical techniques through smaller incisions on a beating heart without the need for extracorporeal circulation. In this context, transapical neochord (NC) implantation represents an example of microinvasive cardiac surgery, proposed as an option for degenerative MR using the NeoChord DS 1000® device (NeoChord Inc.), CE marked since 2012 and awaiting FDA approval. Currently, two devices are commercially available for this approach: the NeoChord DS 1000® and the Harpoon® (Edwards Lifesciences®), both showing promising results, though mid-term data are scarce. This study aims to evaluate the clinical and echocardiographic outcomes in patients treated with NC over five years.

All patients undergoing NC at the University of Padua's cardiac surgery department from November 2013 to March 2016 were included in this study. Indications for the procedure were symptomatic severe degenerative MR due to leaflet prolapse or flail. Patients were categorized based on favorable anatomy (FA: isolated P2 prolapse without annular dilation) or unfavorable anatomy (UA: other MR mechanisms) based on the extent and severity of the mitral valve disease in terms of NC transapical repair feasibility. Clinical and echocardiographic evaluations were conducted at 1-, 3-, 6-, and 12-months post-procedure, followed by annual follow-ups. Data were prospectively collected and retrospectively analyzed, with outcomes based on Mitral Valve Academic Research Consortium (MVARC) guidelines. The analysis included 100 consecutive patients (FA: 81%; UA: 19%) with a median age of 66 years and a mean EuroSCORE II of 1.4%. Technical and procedural success rates were 98% and 94%, respectively. Thirty-day mortality was 2%. Repair success rates were 94%, 92%, and 78% at 30 days, 1 year, and 5 years, respectively. The median follow-up duration was 5.1 years. At 5 years, overall survival was 83%, with no significant differences between FA and UA patients. The cumulative incidence of severe MR recurrence at 5 years was 14% in FA patients and 63% in UA patients ($p < .001$). FA patients showed a lower reintervention rate compared to UA patients (14.7% vs. 43.4%; $p < .001$).

The authors concluded that transapical NC implantation may be an acceptable option for patients with degenerative mitral valve disease with FA.

COMMENTARY:

Mitral repair surgery for degenerative MR is regarded as one of the most successful interventions in adult acquired heart disease surgery. According to the latest STS data, the average 30-day mortality is only 0.4%, with 75% of patients having a predictive mortality risk below 1.2%. It is one of the few "curatives" cardiac surgeries, with survival comparable to the general population when successful repair is achieved. Additionally, the percentage of practitioners performing this surgery continues to increase, with over 80% of cases opting for mitral repair as the first approach to MR, achieving a 10-year reoperation-free rate of 99.7% at centers of excellence. However, outcomes at referral centers differ from real-world results; data from the STS indicate that 27% of all mitral valve replacements follow an unsuccessful repair attempt, with mitral repair success

rates of 80% (compared to 98% in reference centers) and relatively high long-term recurrence rates. In other words, the impressive results from these centers of excellence are a minority and do not reflect real-world practice.

Any successful new surgical technique should aim to improve current outcomes or at least match them without compromising patient recovery. In this study by D'Onofrio et al., 30-day mortality was 2%, while at five years, 16.7% of patients required reoperation and 23.7% experienced severe MR recurrence. While these results are acceptable, they do not yet match the levels reported by centers of excellence for conventional mitral valve repair. However, compared to other large registries, the results are becoming comparable. It is also noteworthy that patients with FA (e.g., P2 prolapse without annular dilation) achieved excellent outcomes, with no differences in MR recurrence or reintervention rates compared to conventional surgery outcomes reported in other major registries.

It is easy to critique new therapies, as was the case in the early days of TAVI. Microinvasive and transcatheter approaches for degenerative MR represent a complex concept with multiple facets. It is well known that most patients with this condition present annular dilation, which is not addressed by neochord or edge-to-edge therapies. Although the Alfieri repair technique without annuloplasty has generally shown limited success and is reserved for exceptional cases, its percutaneous version has been increasingly adopted in structural interventions. Even in randomized trials like REPAIR MR and PRIMARY, it has proven effective in selected patients, with favorable comparisons to surgical mitral repair.

The main challenge is identifying the ideal candidate for this procedure. Data so far suggest two key criteria: first, an absence of annular dilation, optimizing coaptation area; and second, an absence of ventricular dilation, as some patients exhibit reverse remodeling leading to relative NC shortening, potentially causing MR recurrence. Therefore, ideal candidates would be those at an early stage of mitral valve disease, without the aforementioned features. Another relevant question is determining the options available if the initial procedure fails, including the feasibility of repeat surgical repair (and via which approach) or a direct transition to valve replacement. With this innovative surgical technique, significant damage to the mitral leaflets is avoided, as only Gore-Tex neochords are implanted, without the need for devices (as in the case of the mitral clip). Therefore, it remains compatible with alternative approaches, allowing for repeat repair or replacement, including transcatheter mitral valve replacement, if needed in the future.

Transapical percutaneous neochord techniques continue to evolve, with several new devices under development. It is our responsibility to engage with this technology to improve our skills, critically evaluate outcomes demanding repair quality and durability comparable to conventional surgical techniques, and optimize patient selection for each type of approach. TAVI experience has shown that technological evolution is associated with improved clinical outcomes, making microinvasive NC a potential alternative for a select subgroup of carefully chosen patients. Let us remember that the primary advantage of the cardiac surgeon over other specialists is the ability to offer the most appropriate strategy to each patient according to their specific characteristics, whether through conventional, minimally invasive, microinvasive, or even structural intervention approaches.

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Emilio Amigo Otero

Results of the COAPT Study at 5 Years: Sustained Benefit of the MitraClip When Surgery Is Not Feasible?

The COAPT study's 5-year outcomes assess clinical parameters and mortality in patients with severe secondary mitral regurgitation (MR) after MitraClip implantation.

Secondary or functional moderate-to-severe MR occurs in about a third of patients with heart failure (HF) and is an independent marker of poor prognosis, typically resulting from left ventricular remodeling. This condition arises from myocardial disease—both ischemic and non-ischemic—that leads to myocardial distortion and reduced mitral leaflet coaptation.

Although surgical management is regarded as the best treatment for severe MR, high-risk patients are often unsuitable for surgery due to fragility, advanced age, left ventricular dysfunction, and comorbidities. Surgery is particularly recommended when combined with coronary revascularization or other valve surgery (recommendation level I B, per the 2021 ESC guidelines on valvular heart disease). On the other hand, isolated mitral valve surgery—whether repair or replacement—yields better outcomes in select populations with early-stage HF (IIb C).

The COAPT study, published in *NEJM* in 2018, assessed the efficacy and safety of MitraClip® in patients with moderate-to-severe secondary MR. This was a multicenter, open-label, 1:1 randomized study involving 614 patients who received either MitraClip® implantation or optimal medical therapy. The MitraClip® group saw a significant reduction in the primary outcome, which evaluated cumulative HF hospitalizations, and in several pre-specified secondary outcomes, including all-cause mortality at two years.

This article presents the five-year follow-up results of the COAPT study, involving 270 patients (89.4%) in the device group and 264 (84.6%) in the control group. The primary outcome revealed a 47% reduction in cumulative hospitalizations (HR = 0.53) and a 51% reduction in first HF hospitalization (HR = 0.49), with consistency across all pre-specified subgroups. However, this difference disappeared in the post-hoc analysis examining first HF hospitalization beyond the third year of follow-up (HR = 0.85). All-cause mortality also significantly decreased at five years (HR = 0.72), driven by a reduction in cardiovascular mortality (HR = 0.71). Similar to the primary outcome, the post-hoc analysis of total mortality beyond the second follow-up year showed no significant differences.

In terms of device safety, 89.2% of patients remained free of device-related complications. Only four device-related safety events (1.2%) were reported, all within the first 30 days post-implantation. Additionally, although 23 patients (7.6%) in the device group developed severe mitral stenosis, none required mitral surgery. Unplanned mitral valve procedures were more frequent in the control group than in the device group.

The authors conclude that in patients with HF and moderate-to-severe secondary MR who remain symptomatic despite optimal medical therapy, transcatheter edge-to-edge repair is safe and reduces all-cause mortality and HF hospitalizations over a five-year follow-up.

COMMENTARY:

Secondary MR has historically been managed surgically via mitral valve repair. However, transcatheter edge-to-edge repair has emerged as a viable alternative for high-risk patients. Reviewing the literature, only one clinical trial (EVEREST II) directly compares both strategies. At five years, the composite outcome of absence of death, surgery, or residual grade III-IV MR was 44.2% versus 64.3% (p = .01) favoring surgery. This finding

was explained by a higher incidence of grade III-IV MR (12.3% vs. 1.8%; p = .02) and increased surgical need (27.9% vs. 8.9%; p = .003). However, five-year mortality rates, functional class improvements, and ventricular function parameters were similar to those in the surgical group.

The latest evidence comes from a 2021 meta-analysis including 12 studies with 4,219 patients (MitraClip®: 1,210; surgery: 3,009). Patients in the MitraClip® group were significantly older, had worse left ventricular function, and a higher proportion were in NYHA class III-IV. In-hospital, medium- and long-term mortality (4-5 years) were similar between groups. Mean hospital stay was shorter in the MitraClip® group, though moderate MR recurrence and reinterventions were significantly lower in the surgery group.

In contrast, the French MITRA-FR registry, published the same week in *NEJM*, also evaluated MitraClip® versus optimal medical therapy in secondary MR. However, unlike COAPT, it did not find benefits in terms of hospitalizations, cardiovascular mortality, or total mortality. This discrepancy may be due to MITRA-FR's smaller sample size (307 vs. 614 patients), more severe MR, larger left ventricular dimensions, poorer treatment optimization, and higher procedural complication rates (14.6% vs. 8.5%), indicating greater interventionist experience in COAPT.

Stone et al.'s study has certain limitations and has faced criticism. Firstly, patient loss was higher in the control group (15.4%) than in the device group (10.6%) at five years. Moreover, the MitraClip® device used in the study was first-generation, whereas third- and fourth-generation devices are now more commonly used, potentially affecting generalizability. Another notable limitation was the highly selective recruitment, as only 614 patients from 78 U.S. centers were included over five years (1.5 patients per center annually). Additionally, the study permitted patient crossover from the control to the device group after two years, with edge-to-edge repair performed on 67 control patients, representing 44.9% of the group's 138 survivors, with similar net benefits to those treated from the outset. This may explain the attenuation in mortality and HF readmission benefits observed beyond two and three years, respectively, under an intention-to-treat analysis.

Ultimately, the COAPT study's five-year results confirm the trend toward clinical improvement and mortality reduction initially observed in the two-year follow-up, compared with optimal medical therapy alone.

In conclusion, mitral valve repair has proven effective and durable in secondary MR in clinical trials and should remain the first choice when surgical risk is acceptable. Edge-to-edge percutaneous repair is a good alternative for high-risk surgical patients who meet specific anatomical criteria. However, clinical trials are needed to establish long-term efficacy and durability, as well as to understand the impact of moderate-to-severe MR recurrence and high reintervention rates.

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Elio Martín Gutiérrez

Percutaneous versus Surgical Treatment of Functional Mitral Regurgitation: Lessons Learned

A bicentric retrospective study adjusted by propensity score analysis examining 2-year outcomes of percutaneous edge-to-edge therapy compared to surgical intervention for functional mitral regurgitation.

Surgical intervention for secondary or functional mitral regurgitation has generated both interest and challenges over the decades. This stems from its complexity as a therapeutic endeavor, aiming to restore coaptation to an anatomically normal valve affected by underlying ventricular myocardial pathology. Numerous approaches have been proposed to address this condition, systematically categorized as annular correction, leaflet correction, and subvalvular apparatus modification.

The surgical approach, primarily restrictive annuloplasty techniques, was initially suggested by Bolling's studies, utilizing various suture methods or devices like the Carpentier-Adams-McCarthy asymmetrical ring and the now-discontinued Edwards® GeoForm®. However, these strategies proved insufficient in counteracting the subvalvular traction forces that limit coaptation (tenting). Consequently, additional approaches were proposed, such as papillary muscle approximation or anchoring to the posterior or, more recently, the anterior ring (mitral-aortic continuity) as advocated by Schäfers. In cases where annular interventions alone were ineffective, leaflet extension techniques using patches were implemented to maintain the structural integrity of the chordal-papillary apparatus and mitigate further distortion of already compromised ventricular geometry.

When all other repair strategies failed, prosthetic replacement was considered as a last resort, with an emphasis on preserving as much of the subvalvular apparatus as possible, ideally both anterior and posterior structures. Although replacement was perceived as a compromise given the removal of an anatomically intact valve, it has since become the primary approach recommended in current clinical guidelines due to its favorable outcomes over reparative attempts, which often carry a high recurrence risk.

Throughout the years, numerous reports documenting reparative experiences have been published, though no randomized comparative study against medical therapy has been conducted. Observational studies have shown no survival benefit associated with isolated surgical interventions targeting the mitral valve. As a result, surgery holds a Class IIb indication in current guidelines for isolated mitral repair, except in cases of concomitant revascularization (Class I if LVEF >30%, Class IIa if LVEF <30%).

This scientific gap paved the way for structural interventional techniques, leading to the development of several devices targeting the mitral leaflet free edge and annulus. Abbott® MitraClip® and Edwards® Pascal® mimic the Alfieri technique, originally described for organic or primary mitral pathology and certain functional cases, such as those related to hypertrophic cardiomyopathy (SAM). Although these devices do not affect the annulus or chordal-papillary apparatus, clinical trials like COAPT (LVEF 20-50%, LVEDD <70 mm) have shown favorable outcomes against medical therapy, with COAPT now reporting 5-year results, previously discussed on this blog. In contrast, similar success was not observed in MITRA-FR (LVEF 15-40%), which allowed greater ventricular dilation without selection criteria, potentially explaining the absence of therapeutic efficacy.

Other devices, which target the annulus either directly (Edwards® Cardioband®, Mitraling®, Boston® Millipede®, and ANCORA® AccuCinch®) or indirectly via the

coronary sinus (Carillon®, among others), remain in early clinical stages and lack robust evidence. Multimodal procedures combining these techniques are still rare, though likely to increase. Following the COAPT findings, edge-to-edge therapy has achieved a Class IIa recommendation in recent European guidelines.

Okuno et al. present a pioneering study comparing outcomes between surgical (isolated restrictive annuloplasty) and percutaneous edge-to-edge intervention for functional mitral regurgitation. This retrospective analysis involved consecutive patients from two Swiss centers, with propensity score matching. After matching, each group consisted of 101 patients from the 199 and 222 patients who underwent percutaneous and surgical intervention, respectively. This high adjustment rate underscores significant preprocedural differences, with intervention patients generally presenting more comorbidities (age, EuroSCORE II, diabetes mellitus) and advanced cardiac disease (AF, severe pulmonary hypertension, previous MI, or revascularization). Although there were no significant pre- and post-adjustment differences, this highlights the study's limited statistical power to detect group differences.

Mortality rates showed no significant difference either perioperatively or at 2-year follow-up (23-24%). However, recurrence of significant mitral regurgitation (grade 2+ or higher) was notably lower in the surgical group at 2 years (13.5% vs. 40.4%). Furthermore, LVEF improvement was more pronounced with surgery (+10.1% for surgery vs. -1.3% for intervention), as was functional class improvement (NYHA III or IV, 13.3% vs. 29.5%).

The authors conclude that despite the absence of a 2-year mortality difference, surgical intervention demonstrated superior outcomes in terms of mitral regurgitation recurrence and reverse remodeling, which may translate into enhanced functional class and survival in longer follow-ups.

COMMENTARY:

Okuno et al. present one of the few comparative experiences between mitral valve repair surgery and percutaneous edge-to-edge therapy for functional mitral regurgitation. The first comparable data emerged from a subgroup analysis in the EVEREST trial, which showed no significant differences at 3 years, though the edge-to-edge therapy was in early development, and the surgical alternative included a heterogeneous mix of repair and prosthetic replacement cases. Although Okuno's study is retrospective, it opens the door for future randomized trials that could redefine clinical guideline indications. Additionally, it allows for the highlighting of specific findings, discussed below.

Firstly, this study uniquely correlates improved mitral regurgitation recurrence with LVEF improvement, a correlation not clearly demonstrated in the COAPT study. However, many patients in these groups underwent revascularization, leaving open the question of the relative contributions of mitral coaptation restoration versus revascularization (surgical or percutaneous) to LVEF improvement and consequent valvular function preservation.

Secondly, the study's technical success rates reflect real-world practice, with a mild or no postprocedural residual regurgitation rate of 72% for the percutaneous approach, significantly lower than the 96-98% success rates reported in COAPT and MITRA-FR studies. Though success rates vary by criteria, the study achieved at least a one-grade reduction in mitral regurgitation for 92% of patients in both approaches, likely the criterion used in clinical trials. Furthermore, COAPT findings suggested a lack of prognostic benefit for achieving residual regurgitation levels of 0/1+ compared to 2+ or higher, while multiple surgical studies have emphasized the prognostic importance of achieving optimal repair results in terms of both recurrence and survival.

The repair technique in this study was highly standardized, although other authors suggest the superiority of "double repair," which combines annular approaches with chordal-papillary apparatus interventions to reduce traction forces. Prosthetic replacement with complete subvalvular apparatus preservation may be preferable in cases where suboptimal repairs yield 2+ postprocedural regurgitation.

It is desirable that studies like Okuno's continue to shed light on this debate, paving the way for larger-scale studies (from registries and clinical trials) and future meta-analyses. In the race to position devices for functional mitral regurgitation intervention, pseudoevidence and biased standards should not overshadow the honesty, prudence, and independence that surgical practice has long respected. Adequate power and follow-up will be essential to detect differences and draw conclusions that, until then, remain speculative. If guidelines drive indications prematurely, it may result in ethical violations where patient interests serve commercial ends. Through diligent work, case-by-case discussion, research, and critical analysis, the future remains in our hands.

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Carlos Esteban Martín López

Current Status of Transcatheter Mitral Prostheses: Expert Commentary

Expert commentary from Dr. Carlos E. Martín provides an update on the percutaneous treatment of the mitral valve using transcatheter prostheses, reviewing the main technical aspects and results in studies published to date.

Advances in transcatheter technology have revolutionized the treatment of aortic valve disease, with its implantation now approved for patients of any risk category. However, the most frequent valve disease in the developed world is mitral regurgitation (MR). Clinically significant MR prevalence is approximately 2% in the general population, increasing with age, affecting more than 10% of individuals older than 75 years. This, along with rising life expectancy, results in a growing group of elderly patients and/or those with high comorbidity who may not be candidates for open surgical treatment. In fact, various publications have estimated that approximately 50% of patients with severe MR are declined for surgery due to age, comorbidities, and high surgical risk. This has led to the development of less invasive transcatheter therapeutic options to improve symptoms and quality of life for these patients.

Despite the growing evidence of feasibility and favorable outcomes with transcatheter mitral repair options (especially with edge-to-edge devices), almost 25% of treated patients exhibit moderate residual regurgitation in the short to medium term, which is associated with increased mortality. Moreover, certain valvular anatomies are not suitable for repair, such as calcified or retracted leaflets, clefts, and multiple regurgitant jets. Consequently, there has been a growing interest in developing transcatheter mitral valve prostheses (TMVR) to achieve more durable and versatile outcomes across different types of MR mechanisms. However, TMVR currently presents various technical challenges for implantation:

1. Access: The transfemoral approach, through transeptal puncture, requires large navigation systems (≥24 Fr), presenting a risk of residual interatrial shunt; these systems must also possess a high degree of flexibility to cross the interatrial septum and orient coaxially within the native mitral valve. The transapical access has shown favorable early results, but in an effort to extrapolate TAVI results, it has been suggested that it may be associated with worse outcomes than transfemoral access.

2. Device Anchoring: Unlike TAVI, where the aortic valve is often calcified and rigid, facilitating relatively easy and stable prosthetic implantation, mitral anchoring is more complex as it is performed on a generally non-calcified annulus with a three-dimensional D-shaped morphology and dynamic behavior throughout the cardiac cycle.

3. Risk of Left Ventricular Outflow Tract (LVOT) Obstruction: The degree of left ventricular dilation, septal hypertrophy, and the angle formed between the aortic and mitral annuli are important factors to consider in the planning of TMVR implantation.

4. Uncertainty Regarding Durability and Thrombogenicity.

Currently, several transcatheter mitral valve prosthesis models are designed for implantation via both transfemoral/transeptal (Evoque™ (Edwards), Sapien M3™

(Edwards), Highlife™ (Highlife), etc.) and transapical (Tendyne™ (Abbott), Intrepid™ (Medtronic), Tiara™ (NeoVasc), etc.) access. All except for the Tendyne™ prosthesis have been implanted in a limited number of patients, within clinical trials or under compassionate use, with short-term results available.

The Tendyne™ prosthesis is currently the only transcatheter mitral valve prosthesis with CE marking, with over 1,000 implants performed worldwide. It has shown favorable short- and medium-term results across various mechanisms of mitral regurgitation, even in cases of double mitral lesion and severe mitral annular calcification (MAC). This prosthesis is implanted via a transapical approach and consists of three porcine pericardial leaflets attached to two self-expanding nitinol stents, one internal, leaving a minimum effective orifice area of 3.2 cm^2, and an external asymmetric stent designed in the D-shape of the native mitral annulus. The device is completed with a polyethylene tether, ensuring adequate sealing and enabling prosthetic repositioning/retrieval, connected to a pad anchored at the ventricular apex, providing prosthetic stability and hemostasis. Six sizes of prostheses are available (29, 33, 35, 37, 39, and 41 mm) with standard or reduced profile. A key aspect in determining the anatomical suitability for this prosthesis implantation is preoperative assessment via TTE/TEE and cardiac CT angiography. The annular and left ventricular diameters must fall within specific ranges (especially LV end-systolic diameter >40 mm) to avoid the risk of LVOT obstruction. Using these measurements and a virtual recreation of the prosthesis implant, the neo-LVOT should be >250 mm^2.

Sorajja et al. published the initial outcomes in 100 patients, showing a technical success rate of 96% with no intraoperative mortality. Mortality and stroke at 30 days were 6% and 2%, respectively, with no MR in 98% of cases. The mean follow-up was 13.7 months, with a one-year survival rate of 72.4%, and 88.5% of survivors were in NYHA functional class I-II/IV.

Recent publications reported two-year outcomes, confirming the good performance of the prosthesis with more than 93% of patients without MR or evidence of prosthetic dysfunction. The survival rate was 61%, with a high functional class maintained (81.6% in class I-II/IV of NYHA).

In the subgroup of patients with severe mitral annular calcification, Gössl et al. reported outcomes in 20 patients who underwent Tendyne™ prosthesis implantation. All patients had severe MR, with 31% also presenting significant stenosis. Procedural success was 95%, with MR elimination in all cases, adequate safety (5% in-hospital mortality), and symptomatic improvement in most patients during one-year follow-up. These data represent a substantial improvement in outcomes for this high-risk surgical population compared to other published transcatheter treatments.

To provide a realistic perspective on the current status of transcatheter mitral prostheses, recent results from the CHOICE-MI (CHoice of Optimal Transcatheter Treatment for Mitral Insufficiency) multicenter registry have been published. This study involved 746 patients with severe MR, high surgical risk (mean EuroSCORE II of 6.3%), and deemed suboptimal candidates for percutaneous mitral repair, who were evaluated for transcatheter prosthesis implantation. After preoperative assessment, 229 patients met the anatomical criteria, and 10 different devices were implanted. The access route was transapical in 89.5% of cases, with a 95.2% implantation success rate. During the procedure, mortality, malposition, LVOT obstruction, and migration rates were 1.8%, 3.7%, 3.2%, and 2.3%, respectively. At one-year follow-up, residual MR >1+ occurred in 4.8% of patients, and the combined endpoint of mortality/hospitalization due to heart failure occurred in 39.2% of patients.

The role of transcatheter aortic prostheses implanted in the mitral position has also gained attention in cases of valve-in-valve (ViV) and valve-in-ring (ViR) procedures for patients with high surgical risk. The VIVID international registry, with 1,079 patients (857 ViV and 222 ViR), represents the most extensive experience to date. In most cases, the Sapien 3™ prosthesis (Edwards) was implanted, with more than 60% of cases using transapical access. Peri-procedural and 30-day mortality were 1.8% and 7%, respectively, with significant residual MR occurring more frequently in ViR than in ViV cases (16.6% vs. 3.1%, p=.001). Four-year survival was 62.5% for ViV and 49.5% for ViR (p<.001).

In patients with severe annular calcification, the MAC Global Registry reported data from 64 patients (mean STS score of 14±9.5) who underwent implantation of balloon-expandable aortic prostheses. Access routes included transapical (43.8%), transeptal (40.6%), and surgical transatrial (15.6%). Implant success was 72%, with four cases of prosthesis embolization to the left atrium and severe LVOT obstruction in 9.3% of patients. In-hospital mortality was 29.7%, and at one-month follow-up, more than 80% of patients had no residual MR and maintained a good functional class.

In summary, for patients with severe MR who are inoperable, at high surgical risk, or not candidates for percutaneous repair, transcatheter mitral prostheses have shown favorable initial clinical and hemodynamic outcomes.

The procedure's success depends on appropriate patient selection, meticulous preoperative planning, and teamwork between cardiac surgeons, imaging specialists, and interventional cardiologists. There remain various anatomical limitations that restrict implantation indications, preventing its universalization for all potential candidates and all mitral pathologies. Although short- and medium-term outcomes are promising, further studies are required to assess the long-term safety and efficacy of these devices.

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Section V C:

Tricuspid valve disease

Adrián Muinelo Paúl

Isolated Tricuspid Surgery: Analysis of The Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database

The American Society of Thoracic Surgeons (STS) registry analyzed 6,507 patients who underwent isolated tricuspid valve surgery.

This study evaluated contemporary practices and outcomes of isolated tricuspid valve surgeries at the population level, using the STS Adult Cardiac Surgery Database.

After excluding patients with certain conditions (endocarditis, tricuspid stenosis, emergency surgeries, prior heart transplant), 6,507 patients were analyzed. Endpoints included intraoperative mortality and major postoperative complications.

The results indicated an increase in isolated tricuspid valve operations, from 983 cases in 2012 to 2,155 cases in 2019. The median annual volume per center was 2 cases, and 40% of patients had New York Heart Association (NYHA) class III/IV heart failure (HF). Intraoperative mortality was 7.3%, and the rate of new permanent pacemaker implantation was 10.8%. Factors associated with perioperative mortality included NYHA class III/IV HF, non-elective surgeries, tricuspid replacement, annual volume of 5 or fewer cases per center, and higher scores on the Model for End-Stage Liver Disease (MELD). Beating heart surgery was associated with a lower adjusted risk of pacemaker implantation, renal failure, and blood transfusions compared to arrested heart surgery with cardioplegia.

In conclusion, this study found that isolated tricuspid valve repair was associated with lower adjusted mortality and complication rates compared to tricuspid valve replacement. Beating heart surgery was associated with fewer major complications.

COMMENTARY:

The tricuspid valve has often been referred to as the "forgotten valve." However, its prevalence is increasing with the aging population, and its study is gaining attention in the medical community. Surgical treatment is more commonly performed in conjunction with left-sided valve operations, while isolated tricuspid valve replacement is performed in only 14% to 20% of cases.

Current European clinical practice guidelines for isolated tricuspid valve surgery recommend surgery at a level I, with level C evidence, for symptomatic patients with severe tricuspid stenosis. Regarding tricuspid regurgitation, surgery is recommended at a level I and level C evidence for cases of severe symptomatic tricuspid regurgitation without right ventricular dysfunction. Surgery is also recommended at a level IIa and level C evidence for asymptomatic or mildly symptomatic patients with primary tricuspid regurgitation and right ventricular dilation. For secondary tricuspid regurgitation, a level IIa recommendation with level B evidence suggests considering surgery for symptomatic patients or those with right ventricular dilation in the absence of severe left or right ventricular dysfunction and severe pulmonary hypertension.

These recommendations are primarily based on level C evidence, that is, expert consensus or retrospective studies or studies with small sample sizes. Therefore, this STS registry provides valuable insights into the outcomes of tricuspid surgery that may assist decision-making for a relatively uncommon procedure (in the United States, an average of 2 cases per center per year).

It was observed that markers indicating worsening valvular disease severity, such as NYHA class III/IV functional class, non-elective surgeries, advanced age, and a high

MELD score for liver disease, were associated with higher mortality. Identifying these risk factors may assist the medical team in decision-making for cases where an interventional alternative may be considered. In symptomatic cases with some of these characteristics and specific anatomical particularities, percutaneous tricuspid valve intervention is a viable option, as discussed in a recent publication on this blog.

Regarding differences between repair and replacement, prosthesis implantation was preferred for patients with more comorbidities. After statistical adjustment, replacement was associated with higher mortality and complications, including an increased rate of permanent pacemaker implantations and renal failure. However, these results should be interpreted cautiously. In cases where valve replacement was performed, a biological prosthesis was chosen in over 90% of cases, following the trend of avoiding mechanical prostheses in the right chambers, which could be associated with a higher risk of thrombosis.

Finally, another technical aspect considered in the registry was performing the surgery with a beating heart or cardiac arrest using cardioplegia. Better outcomes were observed for surgeries performed with a beating heart, with no differences in mortality and a lower rate of major complications. However, the authors acknowledge that this should be a decision based on surgeon preference.

The STS registry provides extensive knowledge about a rare surgery, as it is a prospective study that includes a large sample size. However, it lacks variables analyzing right ventricular function in operated patients. Additionally, there is a need for variables and elements that could provide evidence-based guidance on decisions for patients with pacemakers who receive prostheses in the tricuspid position, as well as long-term follow-up outcomes for isolated tricuspid surgery.

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José Manuel Martínez Comendador

Early surgery in isolated tricuspid regurgitation: better long-term outcomes?

This retrospective study from the Cleveland Clinic group assesses short- and long-term outcomes of tricuspid valve surgery for severe tricuspid regurgitation (TR) based on surgical indication (class I vs. non-class I).

Tricuspid valve disease is a common condition, affecting approximately 16% of the general population with at least moderate tricuspid regurgitation (TR). Isolated moderate or severe TR has been linked to increased morbidity and mortality, particularly when associated with factors like advanced age, pulmonary hypertension (PH), or right ventricular (RV) dysfunction. Despite these complications, isolated tricuspid surgery remains rare, comprising less than 1.5% of total valve surgeries in our practice. This is partly because only a small fraction of patients with isolated TR are referred for surgical treatment, likely due to the historical perception of higher morbidity and mortality with isolated tricuspid surgery compared to other single-valve procedures. This has created uncertainty about the prognosis for patients undergoing this intervention. Numerous studies have reported perioperative mortality near 10% for isolated tricuspid surgery. For instance, analysis of the American STS registry, published months ago and commented on in a prior blog post, places it at 7.3%. Some series even describe a one-year mortality of 24%.

Current clinical guidelines are clear on this issue. American guidelines do not provide a class I indication for isolated TR, while European guidelines grant a class I indication for severe, symptomatic TR. Consequently, most patients presenting for surgery already display severe right heart failure (HF) symptoms, such as ascites, edema, or dyspnea, with obvious prognostic implications. In cases without symptoms, a class II indication is considered if there is RV dysfunction or dilation. Therefore, controversy persists around the optimal timing and appropriate surgical indications for isolated tricuspid surgery. This study we now analyze raises the critical question of whether earlier intervention, before class I surgical indications develop, could improve outcomes.

The study's objective was to compare the characteristics and outcomes of surgery for isolated severe TR based on class I (symptomatic) indications versus earlier intervention (asymptomatic severe TR with RV dilation and/or dysfunction, thus without a class I indication). All patients undergoing isolated surgery for severe TR without other concomitant valve surgery at a single center between 2004 and 2018 were consecutively analyzed. The primary outcome was mortality. The study included 159 patients (91 women [57.2%]; 115 for class I indication, 44 for early surgery) with a mean age of 59.7 years, of whom 119 (74.8%) underwent surgical repair. The mean follow-up was 5.1 years. Overall operative mortality was 5.1% (8 patients) (7.0% for class I indication, 0.0% for early surgery; $p = .107$). Additionally, class I patients exhibited higher composite morbidity compared to early surgery (35.7% [n = 41] versus 18.2% [n = 8]; $p = .036$). Cox proportional hazards model analysis indicated that class I indication versus early surgery (hazard ratio [HR], 4.62; $p = .04$), age (HR, 1.03; $p = .046$), and diabetes (HR, 2.50; $p = .024$) were independently associated with higher mortality during follow-up.

In conclusion, the authors argue that patients meeting class I indications for isolated tricuspid valve surgery exhibited lower survival than those undergoing earlier surgery before reaching class I indications. Early intervention may improve outcomes in these high-risk patients.

COMMENTARY:

In this highly valuable study, Wang et al. present a retrospective investigation analyzing 159 patients who underwent isolated tricuspid valve surgery for severe TR at a single center over 14 years, attended by 17 surgeons. After an average follow-up of five years, class I patients showed higher mortality rates, especially those of advanced age and with diabetes. Surprisingly, the early surgery group exhibited significantly lower short-term mortality (0% vs. 7%) and higher long-term survival, even after adjusting for confounding factors. It is noteworthy that although the initial clinical characteristics differed, with class I patients being older, more symptomatic, and presenting higher NYHA class, these results deliver a clear message: waiting until patients develop right HF symptoms is unadvisable. The study raises a rare paradox that should prompt reconsideration of current surgical guidelines. Typically, class I recommendations are associated with greater clinical benefits, both symptomatic and survival-related, compared to class II recommendations, yet this study contradicts that assumption in the findings of Wang et al.

It is essential to recognize that TR should not be underestimated as a benign valvulopathy. Multiple studies indicate nearly 50% mortality at four years in patients with moderate or severe untreated TR, even in the absence of PH or RV dysfunction, highlighting TR as an independent negative predictor. The concept of operating on valvulopathies before reaching decompensation is intuitive and partially applied to aortic and mitral surgeries. In this study, the authors demonstrated the clear advantages of early surgery for isolated tricuspid valve disease, supporting a more proactive intervention strategy for these patients. Furthermore, they emphasize the importance of opting for repair over replacement of the tricuspid valve, which has also shown to enhance survival. Recent developments in percutaneous approaches, such as the “edge-to-edge” device, and promising results from the TRILUMINATE clinical trial (also discussed in a previous blog post) in terms of quality-of-life improvement and TR reduction in select patients open new treatment possibilities for this still poorly defined disease.

The TRI-SCORE risk scale, a recently validated tool, provides valuable information for decision-making in isolated tricuspid surgery. It identifies patients at higher surgical risk, offers clues as to which patients should not undergo surgery, and even opens the door to transcatheter therapies in certain cases. However, the truly intriguing and beneficial advancement would be a scale to predict which patients with severe TR might benefit from surgery before symptoms or structural changes develop, impacting prognosis and limiting repairability as ventricular remodeling and tethering progress.

Another critical aspect is the applicability of these findings from Cleveland Clinic and other high-volume centers to other hospitals. Although early surgery for asymptomatic patients with severe TR is reasonable, in more routine practice, it is more likely that such patients will already present symptoms when seen in specialized centers (class I indication). Often, asymptomatic patients with severe TR are either not properly diagnosed or, if they are, it may be an incidental finding. Over half of these patients present with PH, over a third with RV dysfunction, three-quarters with atrial fibrillation, and over half with other significant comorbidities when referred for surgery. Therefore, it is essential that asymptomatic patients with TR undergo thorough echocardiographic follow-up by experts to detect early RV dilation and/or dysfunction, a challenging task. Early detection would allow timely surgical referral. However, a general trend among cardiologists and surgeons is to delay surgery until symptoms become clear, typically in advanced NYHA functional stages, leading to worsened patient status at surgery and poorer prognosis.

In any case, definitive conclusions cannot be drawn solely from the results of a small group of 44 patients operated on by 17 surgeons over 14 years with notable baseline group differences. Given the rarity of this surgery, assembling larger and more detailed databases remains a challenge. Nonetheless, these results contribute valuable knowledge to the sparse literature on this topic. In my view, we now have a stronger foundation for deciding between surgical intervention or close follow-up for patients with severe TR, even in the absence of class I indications.

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Elio Martín Gutiérrez

Rightward Shift in Valve Surgery

An analysis by the Cleveland Clinic of isolated tricuspid valve surgery outcomes, focusing on etiology and associated clinical and analytical parameters.

Right-sided heart failure, right ventricular dysfunction, and tricuspid insufficiency (TI) have become focal points in recent structural heart disease treatment studies, both percutaneous and surgical. Previous blog posts analyzing key studies affirm this trend. These three entities, while often occurring together, are complementary and can present independently. In line with this, the authors propose diverse clinical scenarios, likely to inspire future right heart failure classifications, as seen with left heart failure. Initially, they outline a scenario involving patients with preserved right ventricular function, where congestive symptoms may be absent or mild (fully reversible) or, alternatively, more pronounced congestion may be present (potentially reversible condition). At the other end of the spectrum, there are patients with right ventricular dysfunction, again either with mild (potentially reversible) or severe (end-stage heart disease) congestion.

The reversibility of right-sided heart failure largely depends on the efficacy of medical treatment and TI correction, whether achieved through depletive-tonic therapy and/or invasive techniques. Due to the unique nature of the tricuspid valve, its insufficiency follows distinct pathophysiology and mechanisms that, in my view, align well with Carpentier's classification without necessitating additional classifications, which are also imperfect. Notably, Shah modified this classification to include mechanisms of mitral insufficiency, such as anterior systolic motion, while El Khoury adapted it to classify mechanisms of aortic insufficiency. For TI, the mechanisms are as follows:

- Isolated: corresponding to Carpentier type I mechanism due to annular dilation without excessive or restricted movement, typically caused by atrial dilation from atrial fibrillation (AF) or persistent intracardiac shunts.

- Primary: aligned with Carpentier types I (perforation of various etiologies, whether traumatic or endocarditic), type II (excessive movement causing prolapse or flail from congenital, traumatic causes, or complications from endomyocardial biopsy or pacemaker lead extraction), and type IIIA (commonly rheumatic disease, congenital, or movement restriction from pacemaker leads).

- Secondary: linked to type IIIB mechanism, involving systolic restriction from right ventricular dysfunction without intrinsic valve disease but often associated with Carpentier type I mechanism due to annular dilation under right-sided volume overload.

Cleveland Clinic reports on their experience with tricuspid valve surgery in patient subgroups mentioned above, characterized by potentially reversible right-sided heart failure: either with concomitant right ventricular dysfunction and mild congestion or without right ventricular dysfunction but severe congestion. Over seven years, they gathered data on 62 patients undergoing isolated tricuspid surgery (excluding infective endocarditis; 73% had prior valve surgery, 19 with previous tricuspid valve procedures; 45% in preoperative AF; 16 with trans-tricuspid pacemaker leads). Initially, the small sample size stands out, as even a high-volume center like Cleveland Clinic operated on fewer than nine patients per year. Moreover, congenital patients were not included, nor was the rejection rate disclosed before selecting these 62 patients.

A crucial aspect in understanding this study is the dichotomy of TI into “functional” or “structural” categories. The first comprises the mechanisms described for "isolated" and "secondary," while the second entirely covers the "primary" category.

The authors conducted a thorough systematic collection of clinical and echocardiographic variables and performed multidimensional statistical analysis, combining various clinical, echographic, and hemodynamic variables grouped into clusters. Despite the sophistication of this approach (evidencing the influence of EH Blackstone), the authors acknowledge that some analyses may have been compromised due to the limited sample size. Key findings are summarized below:

1. Upon comparing the two forms of tricuspid insufficiency, significant demographic, clinical, hemodynamic, and morphological differences in right ventricular function were observed. Patients with functional TI were generally older, had greater right atrial dilation, and higher MELD-sodium scores. Clinically, they exhibited higher degrees of jugular venous congestion, dependent edema, and elevated right and pulmonary artery pressures. Echocardiographically, they showed greater annular dilation with lower TAPSE values; however, other parameters for right ventricular function (fractional area change, ejection fraction, right ventricular systolic and diastolic pressures, systolic excursion velocity, free wall strain) and ventricular diameters did not differ between TI etiologies. These findings indicate a prevalence of "secondary" etiology over "isolated" in the cohort with "functional" TI.

2. Independent of the tricuspid valve etiology, right-sided heart failure severity was better characterized by morphological parameters (primarily volume) than functional metrics. In their discussion, the authors highlight that the International Right Heart Foundation Working Group considers ventricular dilation as the earliest marker of right ventricular failure over function parameters. This association with higher AF rates and congestion symptoms (ascites, edema) further supports this point. Despite these patients exhibiting advanced coagulopathy, post-surgical recovery was comparable to those without dilation or significant congestion.

3. Postoperative outcomes were similarly favorable for both etiologies, with a 0% hospital mortality rate in the "structural" group and 3.2% in the "functional" group. Prosthetic replacement was more common in "structural" cases (55%), whereas repair was predominant in "functional" cases (84%). Postoperative morbidity was similar across groups, though the "functional" group required more blood transfusions and experienced longer hospital stays. Long-term survival over eight years was notably poorer in the "functional" group, a trend that persisted even after propensity matching the two cohorts.

The authors conclude that the cluster analysis of right-sided heart failure characteristics in patients undergoing isolated tricuspid valve surgery identifies two distinct patient profiles. Despite excellent immediate postoperative outcomes, they suggest expanding treatment indications to include earlier-stage patients, particularly those with functional etiology and right ventricular dysfunction/dilation.

COMMENTARY:

This study serves as a renewed call for early intervention in TI, challenging the misconception of its benign nature. Previous blog posts support this stance, with this study providing further evidence.

Simultaneous intervention with other procedures, particularly left-sided valvular or congenital heart disease in adults, should be a standard in patients with right ventricular and tricuspid annular dilation, even in the absence of significant insufficiency. Additionally, the referral of patients with isolated disease for invasive therapies may become more common in coming years. Treatment indications should be based on risk, outcomes, and the corrective potential of the two main approaches: surgery (with its extensive technical options) and edge-to-edge therapy (TriClip® and Pascal®), pending further experience with other devices and prototypes in development for annuloplasty (Millipede®, Cardioband®, DaVingi®, TriCinch®) and percutaneous prostheses (TricValve®, TriCentro®, etc.).

For timely intervention, it will be essential to redefine parameters for evaluating right ventricular function, as dilation alone is a more sensitive prognostic marker than current measures of dysfunction. Right ventricular physiology may differ substantially from that of the left ventricle, suggesting that diagnostic parameters applied to the left may not fully apply to the right. Continued evidence aggregation will advance our understanding of right ventricular mechanics, potentially leading to its consideration as a unique entity rather than merely a weaker counterpart to the left ventricle.

Regarding TI, Carpentier type IIIB mechanisms, “secondary” or “functional” etiology, stand out for their especially poor prognosis, where early intervention—even in a preclinical phase—may improve outcomes. The findings clearly indicate that symptom-based correction, while beneficial, results in lower survival rates compared to patients with "organic" or "primary" etiologies.

In summary, this evidence-generating study sheds light on the timing of intervention, though questions remain on the choice of repair versus replacement and the appropriate specialist (in a simplified, pessimistic view, and one hopefully inaccurate, the dichotomy between surgery/surgeon versus interventional cardiologist). The era of tricuspid valve intervention has only just begun.

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Mónica García Bouza

Should a permanent epicardial pacemaker be routinely implanted in cases of tricuspid valve replacement?

This study analyzes the outcomes and implications of the implantation of definitive epicardial systems in patients undergoing tricuspid valve replacement.

Tricuspid valve replacement (TVR) is among the least frequent interventions in cardiac surgery, presenting unique challenges, not only due to its rarity but also the inherent difficulties. Traditionally, these procedures are performed on high-risk surgical patients, as previously addressed in prior blog entries. Furthermore, TVR is associated with an increased risk of conduction disorders, with an estimated need for a permanent pacemaker ranging from 22% to 32%. Therefore, it may be worth considering a preventive approach by implanting a permanent pacemaker during the same procedure, thereby proactively addressing potential conduction complications.

A recent article by a French team at Bichat Claude Bernard Hospital in Paris explores the prophylactic implantation of permanent epicardial pacemakers in TVR cases. This center decided on routine implantation due to the high incidence of conduction disorders requiring pacing, not only postoperatively but also in the long term. The study aimed to evaluate the risks and benefits of this practice and identify factors associated with conduction disorders following TVR. A total of 80 patients who underwent TVR with bioprosthetic valves between March 2014 and December 2018 were retrospectively included. Patients with preexisting pacemakers or ICDs were excluded. Electrodes were implanted on the diaphragmatic surface of the right ventricle, with the generator placed in a subcostal epigastric location. The mean age was 57±16 years; 70% were women, 35 cases (44%) were reoperations, 19 (24%) of which involved left-sided valve disease, and 24% of patients presented moderate to severe right ventricular dysfunction. TVR alone was performed in 28 patients (35%), alongside mitral valve replacement in 29 patients (36%), aortic valve replacement in 11 patients (14%), and other combinations in 12 patients (15%). A single electrode was implanted in 41 patients (51%), while two electrodes were used in the remainder. Eleven patients (14%) died postoperatively, and 10 (12.5%) were lost to follow-up, leaving a sample of 59 patients for analysis. The mean follow-up duration was 36 months. Nearly half (46%) of patients required pacing after the procedure; however, after the first year, this need decreased to around 5%. Another 9 patients died during follow-up. Notable device-related complications, potentially life-threatening, occurred in 2 patients (2.5%). One patient experienced cardiac arrest secondary to inappropriate pacing, while another developed a generator pocket infection, necessitating device explantation. Additional complications included electrode dysfunction in 3 patients and the need to switch to resynchronization therapy in 4 patients. No cases of premature battery depletion were observed.

The primary limitation of this study is its retrospective, single-center design, which may limit the generalizability of these findings. Nevertheless, the authors conclude that after TVR, nearly half of the patients required permanent pacing due to postoperative atrioventricular conduction disorders. This high incidence, along with an acceptable safety profile, supports a prophylactic epicardial pacing strategy for patients undergoing TVR.

COMMENTARY:

After TVR, one of the consequences of annular suturing may be dysfunction, caused by either permanent injury or temporary inflammation/traction of the atrioventricular node located at the apex of Koch's triangle, adjacent to the septal leaflet. Techniques to reduce

this phenomenon include anchoring the suture in this area on the leaflet itself, reinforced with pericardium or Teflon, or ventricularizing this annular segment, placing the prosthesis on the atrial level outside of this annular segment. Despite these measures, the need for a pacemaker remains high. The presence of a prosthesis in the tricuspid position contraindicates electrode passage through it, due to concerns about dysfunction and a high risk of future endocarditis. Therefore, placing the pacemaker electrode during the same procedure—considering the high incidence of conduction disorders and the traditional use of epicardial systems—avoids the need for another surgical intervention under general anesthesia by addressing the pacemaker implantation in the same act.

Although this study shows higher rates of pacemaker requirement compared to other series, it is essential to consider the high number of concomitant procedures, which may increase the risk of injury/dysfunction to the conduction system. However, as demonstrated, the permanent pacemaker implant is not complication-free, which raises doubts about the appropriateness of prophylactic implantation, even if the authors deem it to have an “acceptable” risk/benefit profile. The reality is that adding an extraordinary surgical procedure may increase the risk of complications, simply by including an additional intervention. Thus, the optimal approach would be to reserve each intervention as needed and consider alternative options.

Several pacing approaches can be considered for these cases. Options include the paravalvular placement of pacemaker electrodes during valve implantation, leadless pacemakers (discussed in previous blog posts), and electrode placement in the coronary sinus. Each alternative has its own balance of risks and benefits. Paravalvular endocavitary systems implanted during the primary surgery are less common and involve trapping the electrode, precluding its removal if dysfunction or, worse, endocarditis occurs. However, they do not interfere with the prosthesis and allow for dual-chamber pacing if the patient remains in sinus rhythm. Leadless systems are still under development with limited experience. They can be positioned in the ventricle, but postoperative implantation would involve transprosthetic catheter manipulation, which is not feasible with mechanical prostheses and is more complex with bioprosthetic valves. Experience with dual-chamber leadless systems is even more limited. Coronary sinus electrodes offer a convenient endocavitary solution; while they also allow dual-chamber pacing, these electrodes tend to have poorer long-term stability and initially stimulate the left ventricle.

With the epicardial option, electrodes can be implanted without connecting them to the generator, leaving them in the left hypochondrium until permanent pacing is necessary, which appears to be the prudent solution. This secondary intervention could be performed under local anesthesia, should pacing be needed, with the only inconvenience being the implantation of unused epicardial electrodes. A significant drawback of the epicardial approach is the higher pacing thresholds compared to endocavitary systems and the need for more frequent generator replacements. Additionally, we must consider the current trends towards minimally invasive surgery, percutaneous approaches, and hybrid strategies that may offer better solutions for these challenges by redefining how we approach our future patients.

The high percentage of patients who do not require long-term pacing further emphasizes that early post-operative pacemaker implantation often yields suboptimal results. In this study, prophylactic implantation was carried out immediately postoperatively, yet a notable number of patients undergoing various procedures (arrhythmia ablation, valve surgeries, sutureless prosthesis implantation) experienced spontaneous recovery within the first two weeks post-surgery.

Therefore, as surgeons, our approach should be to perform TVR only when repair is not feasible, minimize damage to the conduction tissue, and establish a consensus strategy with cardiology teams for managing atrioventricular block complications, adapted to each unit's workflow. Nevertheless, prudence suggests any procedure should be reserved for well-established indications, however straightforward it may seem.

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Irene Toribio García

The Evolution of Tricuspid Regurgitation: From Secondary Actor to Co-star

Review on tricuspid regurgitation, explaining the characterization of this valvulopathy, the new five-grade severity classification, and medical, surgical, and percutaneous treatment options.

The tricuspid valve and the pathologies linked to it have remained in the background until recently, when the evidence on the diagnosis and treatment of tricuspid regurgitation (TR) was updated. Traditionally, mitral valve disease was considered the primary valvulopathy, rendering the tricuspid valve relatively insignificant in therapeutic decision-making, with its repair being an addition to the main surgery. Subsequently, it has become known that severe TR is an entity associated with high morbidity and mortality and that diagnostic delay has major consequences. Available treatments have traditionally been scarce and limited to diuretics and subsequent surgery. However, isolated TR surgery presented a high perioperative mortality rate, and given the limited evidence on its long-term effectiveness, the risk-benefit balance has been considered, at the very least, questionable. This was due to the fact that many interventions were carried out in advanced stages of valvulopathy, often as reoperations following previous left valve surgeries. In this context, the growing interest in TR treatment has been accompanied by the development of edge-to-edge transcatheter repair techniques as a potential alternative to tricuspid valve surgery, which has also been suggested for earlier and more frequent treatment of TR.

The comprehensive review conducted by Hahn et al. provides a complete breakdown of TR as follows:

Epidemiology: It is undeniable that the prevalence of this disease increases with age, particularly in women. Female sex is an independent predictor of severity and progression in TR assessment scales. Other predictive factors include atrial fibrillation, elevated pulmonary artery systolic pressure, and left atrial dilation. The importance of these factors is such that they have been routinely included in studies conducted in recent years; specifically, two studies indicated that after adjusting mortality results by age and sex, a 2-fold and 3.2-fold increase in risk was observed, respectively.

Valvular Anatomy: The tricuspid valve has been described as the largest heart valve of the four. Anatomically, it typically has three leaflets of different sizes. However, it is now known that the number of leaflets in the healthy general population is variable. These leaflets are supported by chordae tendineae anchored to the larger anterior papillary muscle and one or several smaller posterior papillary muscles. According to anatomical variants, each papillary muscle more frequently supplies chordae tendineae to one leaflet or another, achieving an adequate seal along the coaptation zone. As for the tricuspid annulus, it is a fibrous structure composed of collagen, with a three-dimensional shape and dynamic behavior. It is estimated, based on model results, that adaptability to closure is such that only 40% of annular dilations would lead to significant valve regurgitation compared to the mitral valve. Knowledge of the anatomical relationships of the tricuspid valve, particularly with respect to the right coronary artery and the atrioventricular node, is of special interest, as some surgical and percutaneous annular correction devices may involve these structures with the consequences that this entails.

Clinical Presentation:

The most frequently reported symptoms include dyspnea, lower limb edema, and abdominal enlargement due to ascites. These symptoms progress in more advanced

stages, culminating in multi-organ failure, including renal, hepatic, and coagulation issues, as well as signs of low cardiac output. Specifically, heart failure-induced liver dysfunction (or cardiohepatic syndrome) is an independent predictor of increased mortality or hospitalization for heart failure (HF) in patients with tricuspid regurgitation after one year of transcatheter therapy.

Diagnosis:

The assessment of structural heart disease begins with a transthoracic echocardiogram. The traditional three-grade severity classification has transitioned to a multiparametric assessment, leading to an extended classification of five grades: mild [+1], moderate [+2], severe [+3], massive [+4], and torrential [+5]. Color Doppler study is not recommended for assessing TR due to its frequent association with underestimation of the condition. Given the extensive limitations of transthoracic echocardiography, transesophageal echocardiography, cardiac magnetic resonance imaging, and cardiac computed tomography have been incorporated into the diagnosis of TR. Another test of special interest in TR is invasive diagnosis through right heart catheterization, particularly for associated comorbidities such as pulmonary hypertension (PH), with a Class I recommendation.

Medical or Conservative Treatment:

Various classes of diuretics, particularly loop diuretics and mineralocorticoid receptor antagonists, constitute the pharmacological arsenal available for the treatment of TR, with a Class IIa recommendation. Initially, the response to this treatment is usually adequate, but neurohormonal activation and perpetuation of systemic response (tissue edema, increased distribution volume, distal nephron hypertrophy) often lead to frequent diuretic resistance. For this reason, medical treatment ends up being insufficient in the advanced stages of the disease. Additionally, it is essential to establish targeted treatment in cases of secondary regurgitation (left ventricular dysfunction, atrial fibrillation, or concurrent mitral regurgitation).

Invasive Treatment: The Future of the Disease:

1. Surgery:

   Large series attribute in-hospital mortality rates of 10-20% to isolated tricuspid valve replacement for tricuspid regurgitation. As previously mentioned, the historical intervention of these patients in advanced stages of valvulopathy has significantly contributed to these results. The procedure of choice is repair, often through isolated annuloplasty, preferably over valve replacement. In cases involving leaflet tenting, tissue deficiency, or extreme annular dilation (>44 mm), additional techniques for anterior leaflet extension with a pericardial patch may be necessary. Surgical treatment for severe TR is recommended at a Class I level when a left-heart intervention is planned, and at a Class IIa level when TR is moderate or, regardless of grade, when annular dilation exceeds 40 mm or 21 mm/m². In cases of isolated surgery on the tricuspid valve in patients with symptomatic severe TR or those where medical treatment has failed, the recommendation class remains at IIa. This is feasible as long as the patient does not have additional PH, in which case each case should be assessed individually. Finally, Class IIb is limited to those who present with asymptomatic primary TR with associated right ventricular dilation and/or dysfunction. As mentioned in previous blog entries, these recommendations may not be sufficiently updated and may require future review.

2. Percutaneous Intervention:

In recent years, the development of transcatheter devices has been accelerated. Although options are currently extensive, edge-to-edge repair or clip devices represent the fastest-growing treatment in developed countries. Currently available tricuspid valve-specific devices on the market include the TriClip® and Pascal®. Transcatheter valves available for mitral valvulopathy are also beginning to be used. In this context, the TriValve registry has emerged as a multinational study aimed at more accurately describing the characteristics of patients undergoing these treatments. Baseline characteristics identified in the TriValve registry have been shown to be reproducible and consistent across different series. Furthermore, short- and long-term outcome predictors are influenced by the type of patient, as the sample of individuals undergoing these treatments is highly heterogeneous. Similar to valve repair surgery, isolated transcatheter annuloplasty is more useful in patients with annular dilation without significant tenting. Patients eligible for edge-to-edge therapy have more extensively studied criteria, enabling more specific selection and higher device success rates. Clips can reduce TR to moderate or less in 80-85% of patients and to mild or lower in 30-50%, with the statistical conclusions to be further analyzed later. Given the constant research in this field, it has been suggested that orthotopic transcatheter valves may become the most effective device for reducing TR severity in the near future. A milestone of the past year was the publication of the TRILUMINATE study, a pivotal study involving patients with severe TR, comparing two groups of patients: those who underwent surgical treatment and those who received medical treatment. Three study objectives were established: all-cause mortality or tricuspid valve surgery, HF hospitalization, and quality-of-life improvement in standardized questionnaires. After one year of follow-up, no significant differences were observed in the secondary endpoints between both groups; however, these differences were found in the quality-of-life measure according to the KCCQ questionnaire (12.3±1.8 points in the transcatheter therapy group versus 0.6±1.8 points in the control group). We will further analyze the dichotomy of these results in the following section.

COMMENTARY:

This article systematically reviews TR, addressing the latest therapeutic options incorporated into routine clinical practice. The first takeaway from this review is the importance of early identification of patients with TR to initiate the indicated treatment as soon as possible for each specific situation. To support appropriate clinical practice, the article includes illustrative summary figures of the different types of TR and specific treatment options that facilitate decision-making. The significance of this can be readily understood when we consider tricuspid valvulopathy as having the highest all-cause mortality rate compared to other valvular diseases, according to comparative studies. The new five-grade severity classification, along with the emphasis on atrial, annular, or ventricular origins of TR, has transformed the understanding of tricuspid regurgitation in recent years, shedding light on some of the major questions surrounding this valvulopathy.

The TriValve registry was established to promote an adequate understanding of the disease in patients undergoing transcatheter interventions. It should be noted that the sample presented discordant data: individuals who were not of very advanced age, who showed no signs of advanced right-sided HF with low prevalence of ascites, and who had lower proBNP levels compared to those usually observed in clinical practice or in classic surgical series; versus more congruent data: a predominance of female patients, prior cardiac surgery involving left-heart structures, high rates of previous hospitalization

in the last six months, or a prior diagnosis of atrial fibrillation. While the consistency of baseline characteristics has been assured in subsequent studies, at this time, it would be prudent to interpret these data with caution and continue with an individualized approach.

Delving into the different types of TR, in the case of primary TR, it is important to note that the incidence of endocarditis associated with this valve is rising in the United States in parallel with increasing antibiotic resistance, the growing number of implanted devices with leads, and, to a lesser extent, parenteral drug use. Updated literature is available to guide decision-making on the optimal timing for lead explantation in these cases to minimize comorbidity in a severe and complex disease (Nappi F., et al.; J Am Heart Assoc 2020). Another entity to emphasize, despite its low prevalence (20%), is TR post-cardiac transplantation, as it is often associated with allograft vasculopathy and damage caused by endomyocardial biopsies.

In secondary TR, although it is thoroughly categorized in supplementary material tables within the main text, it is worth noting that distinguishing between atrial and ventricular forms has implications for prognosis and treatment, given that mortality and complication rates are clearly higher in the ventricular etiology of TR.

Finally, device-related TR represents a group that has gained its own significance due to the increasing frequency of these interventions. Moderate-to-severe regurgitation is observed in up to 27% of patients following device implantation, a notably high figure considering the associated pacemaker rates (25-29%), excluding other devices.

One emphasized point is the importance of recognizing that the presence of morphological factors associated with certain clinical entities may indicate an increased risk of TR progression:

For patients with PH, predictors to consider include right ventricular dilation, increased sphericity, annular dilation, and increased tenting area of the valve leaflets.

In patients with AF, increased annular diameter, right ventricular remodeling, valve tenting, and increased left atrial volume are additional factors.

Other factors of rapid progression inherent to any patient with TR include previous pacemaker or defibrillator implantation, moderate regurgitation, or association with another valvulopathy requiring surgical intervention. Annular dilation of the tricuspid valve is mentioned again, underscoring the importance of its measurement in assessing right-heart pathology.

Age and female sex have also been proposed as independent risk factors in various published studies.

Regarding medical treatment, it is a developing field where proper assessment of TR type and degree, the presence of PH, left ventricular function, and AF diagnosis are crucial. This is important because directed treatment for secondary TR should be implemented early to modify the disease's natural course; however, these cases represent a minority, and there is no recent solid evidence supporting a significant change in clinical practice.

To conclude, within interventional management, I would like to focus on edge-to-edge or clip therapies, which are novel devices that have facilitated advancements in TR treatment and are currently supported by recently reviewed literature suggesting a potential shift in the treatment of choice for TR. Specifically, the pivotal TRILUMINATE study, presented at the recent ACC/AHA congress, has yielded promising results regarding TR treatment and progression. This study was analyzed in previous blog

entries. The sample indeed presents considerable biases that favor positive results in the primary composite outcome; conversely, no statistically significant differences were observed in the remaining objectives.

Furthermore, discrepancies are noted in participant profiles:

The sample selection was based on TR severity (most cases being severe, massive, or torrential), functional class (usually II), and lower hospitalization rates (in essence, more stable patients despite the severity). Additionally, the impact of the COVID-19 pandemic should not be overlooked.

The surgical risk selection of the sample was performed subjectively by the research team rather than blindly. Notably, there was a lack of data on the etiology of TR or predominant pathophysiological mechanisms, which is striking, as several previous studies have shown that the primary etiology of TR determines its prognosis and that the pathophysiological mechanism also directly affects outcomes after a specific percutaneous repair technique.

It is interesting to note that to achieve the proposed sample size of 350 patients, up to 795 patients were excluded due to screening failure, confirming that a significant percentage of patients with significant TR, presumably with a higher severity profile, were not represented in this study.

In conclusion, TR is a pathology that is currently gaining ground in clinical practice and invasive treatment fields due to the implications of its severity. Percutaneous repair is solidifying as a viable option in routine clinical practice and is strengthened by recent studies. Further analyses will be needed to ascertain the true differences between surgical and percutaneous techniques and the results of new devices that are continually being developed.

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Elio Martín Gutiérrez

TRI-SCORE: better intention than result

Analysis of the foundational work of the TRI-SCORE scoring system, designed to assess the risk-benefit balance of invasive treatment options versus conservative management in patients with significant isolated tricuspid regurgitation (TR).

The growing interest in tricuspid regurgitation (TR) treatment from a percutaneous approach represents the natural progression of edge-to-edge therapy as implemented in mitral clipping. Unlike the mitral valve, the tricuspid valve pathology predominantly presents as functional insufficiency, primarily classified under Carpentier's type I and IIIB mechanisms. These correspond to isolated and primary forms, respectively, in the recently published reclassification, which we reviewed in a prior blog post. The prevalence of TR is considerable in the general population, contradicting the long-held assumption in clinical cardiology that TR is a benign condition suitable for medical treatment only, with invasive intervention reserved for cases of refractory and advanced-stage heart failure (HF), as discussed in previous blog entries.

The surgical community was prompted by Dreyfus's work to move tricuspid valve treatment forward to scenarios with annular dilation (septo-lateral diameter >40 mm echographically, and antero-posterior >70 mm intraoperatively), independent of TR grade, preferably with semi-rigid prosthetic rings. These findings have reshaped the perspective that tricuspid valve improvement could follow left-sided valve repair, positioning early TR intervention as an opportunity to enhance the prognosis in surgically treated HF patients. However, a significant subset of patients with isolated tricuspid disease, whether primary or secondary to left-sided valvular disease repair (rheumatic disease, irreversible pulmonary hypertension, atrial fibrillation), remains under conservative care with pharmacological treatment, primarily diuretics, lacking alternative treatment options.

In this context, the TRI-SCORE scoring system emerged from an initiative to analyze data from the TRIGISTRY registry, which collected clinical and echographic variables in patients with significant isolated TR. This was an altruistic, non-sponsored project involving 33 centers across 10 countries, including those from Europe (Spain included), the US, Canada, and Israel. Data from a total of 2,413 patients were analyzed over a two-year survival period, of which 1,217 received conservative management, 551 isolated tricuspid valve surgery (excluding any concomitant procedures, and incorporating both repair and replacement techniques), and 645 percutaneous treatment (without concomitant procedures and exclusively using edge-to-edge techniques, excluding other device implants).

Without delving into methodological aspects (which we will discuss below), invasive therapy, both surgical and percutaneous, demonstrated a survival benefit over conservative treatment in patients with low TRI-SCORE scores (≤3 points): 93% surgery, 87% percutaneous, and 79% conservative; $p = .0002$. There were no significant differences among groups for intermediate (4-5 points) or high (≥6) scores. Only 3% of the surgical group failed to achieve successful TR correction (≥2+ residual grade) and were thus excluded from a subanalysis on successful repair. However, in the percutaneous group, there was a benefit over conservative treatment for intermediate scores when adequate repair was achieved (two-year survival 81% vs. 71%, $p = .009$). The high-score category continued to show no therapeutic benefit from invasive treatment over conservative, even with successful repair.

The authors conclude that the TRI-SCORE system shows good alignment with isolated TR survival rates and that, compared to conservative management, early correction with

surgical or percutaneous treatment improves two-year survival in patients with low and intermediate scores when residual TR is ≤ grade 2+.

COMMENTARY:

In developing commonly used surgical risk assessment systems (EuroSCORE II and STS-PROM score), TR patients were not adequately represented. As a result, the STS system would not be applicable, and EuroSCORE would only equate risk to other isolated procedures, excluding aortic surgery or coronary revascularization. This has led to a poor fit for these systems in categorizing TR patients by risk and a lack of predictive power regarding actual surgical risk. Thus, a new tool to manage these patients effectively has long been awaited. The TRIGISTRY registry was a first approach, gathering various data, including mortality rates of approximately 2%, 9%, and 16% for low, medium, and high TRI-SCORE scores, far from the 20-40% average mortality of classic series when patients were operated in advanced HF stages.

Given this background and other risk stratification systems, TRI-SCORE shows good calibration, i.e., patient scoring matches clinical outcomes and, therefore, established risk categories. Nevertheless, despite its described merits, several critiques can be made, which we can discuss based on findings that will soon populate cardiology and cardiac surgery literature:

1. The sample size in the score system's creation is limited. Only around 2,400 patients were included, in contrast with over 22,000 for EuroSCORE II or the more than 7.5 million cases in the STS database. This reduces statistical power, limiting the ability to identify statistically significant differences. This limitation is exacerbated by the fact that half the patients received conservative treatment, leaving each invasive alternative with just a quarter of the sample. While recruitment may have been challenging due to the limited casuistry of isolated TR treatment, this restricts the tool's utility, developed to provide alternatives to conservative management. Also, the two-year maximum follow-up limits its utility in long-term therapeutic decision-making.

2. The apparent goodness of fit results from an overly simplistic design. This is due to the limited sample volume used. Typically, score systems are developed in two phases: an initial development phase using half the sample, followed by a validation phase using the other half to test its fit. TRI-SCORE was directly developed on the TRIGISTRY registry, which could present significant validity issues. The authors do not report patient characteristics across treatment groups and note lower morbidity in the surgical group than in conservative and, especially, percutaneous options. It is logical to expect a good fit on the sample used for development; however, this may not be representative (high-level centers, selected patients, etc.), potentially limiting the tool's generalizability.

3. The eight variables include: age (cut-off at 70 years), NYHA functional class (III-IV threshold), right HF signs, daily furosemide dose (125 mg threshold, equivalent to 40 mg torasemide), glomerular filtration rate (cut-off at 30 ml/min), total bilirubin (threshold at the high normal limit), left ventricular ejection fraction (60% threshold), and right ventricular function. Each variable contributes cumulatively with a score of 0 to 12 points, where variables such as right HF signs, furosemide dose >125 mg, GFR <30 ml/min, and elevated bilirubin score 2 points, with the remaining variables weighted at one point

each. In an excess of statistical confidence, they assign each score a hospital mortality risk based on TRIGISTRY data, which is inadequate due to previously noted validity and sample size limitations. Thus, it becomes an additive score without factoring in exponential clinical effects.

4. Variable selection also warrants a note. Risk scoring systems typically derive from a multivariate analysis, as the basis for the predictive model. Variables with a significant independent relationship with the outcome (two-year mortality in this case) are included, each weighted according to relative significance. However, TRI-SCORE development lacks transparency on method selection, implying that the model was built using the eight TRIGISTRY variables. Furthermore, biases associated with data collection (variable definition, interobserver variability in echocardiograms, etc.) produce paradoxical examples, such as right ventricular function having less weight than other clinical variables; hypertension not included, nor atrial fibrillation or therapy techniques; or redundant variables like right HF signs and NYHA functional class, among other crucial considerations for TR treatment.

Thus, once again, haste and pressure to generate evidence have negatively impacted a well-intentioned initiative. Rather than aiding decision-making for TR patients, TRI-SCORE likely serves as a call to consider invasive treatment early in the disease, before organ damage from right HF raises procedural risks and influences prognosis, even post-valve repair. Thus, two-year survival results suggest early intervention, improving reparability and, in surgical cases, achieving outcomes superior to percutaneous (93% two-year survival vs. 87%; $p = .0002$). Further research is imminent.

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Elio Martín Gutiérrez

VARC criteria for tricuspid valve insufficiency treatment: the game board

Definition of Framework Criteria of the Valve Academic Research Consortium for Characterizing Tricuspid Regurgitation and Setting Outcomes in Subsequent Studies on Its Invasive Treatment

The criteria established by the Valve Academic Research Consortium (VARC) — whether we like them or not — represent the rules of engagement for studies addressing structural heart disease treatment. These guidelines define the criteria for a successful procedure and provide a framework for grading the severity of developed complications. This is critical because it establishes a benchmark for determining which "suboptimal" outcomes might be acceptable and which are not. Additionally, these criteria enable quality and outcome comparisons across different procedures by following a common and objective standard. While VARC guidelines have traditionally been more intervention-focused, they also allow for comparisons between surgical techniques and transcatheter procedures. Initially, these criteria were introduced for aortic stenosis treatment, with three updates solidifying their role. Criteria for mitral insufficiency have since been published, and in this analysis, we focus on tricuspid regurgitation (TR).

As with previous editions, this publication includes contributions from both cardiologists and surgeons from renowned international institutions. The article is organized into two sections, which we will summarize to outline the essentials needed to critically assess the controversy surrounding the interventional versus surgical management of TR — at both the individual patient level and in anticipation of the wave of studies soon to flood the literature.

1. Characterization of Tricuspid Regurgitation

The first aspect to address is the characterization of tricuspid regurgitation (TR). This involves multiple concepts, many of which are essential when considering the treatment of TR. We will outline each below with a brief description of key knowledge points:

1.a) New Etiological Classification of TR

The relationship of this new classification with Carpentier's classification has been previously introduced in the blog. Carpentier's classification was functional; however, given that over 80% of TR cases stem from secondary causes (predominantly mechanisms I and IIIB), a reformulation was warranted. Primary etiology (5-10% of cases) involves intrinsic leaflet pathology due to degenerative, congenital, or acquired causes (e.g., tumors, trauma, carcinoid syndrome, rheumatic disease, radiotherapy). Secondary etiology includes two subclassifications: "ventricular," which encompasses left ventricular dysfunction affecting the right side, precapillary/parenchymal pulmonary hypertension, and right ventricular dysfunction itself, with coexisting Carpentier type I and IIIB mechanisms to varying degrees. The second subclassification, "atrial," considers atrial dilation due to atrial fibrillation (AF) and annular dysfunction, as well as atrial enlargement resulting from hypertensive cardiopathy, age, or heart failure with preserved ventricular function (Carpentier type I). Lastly, a third classification involves transvalvular device leads, which can be subdivided into type A if the lead directly contributes to TR or type B if the lead simply passes through the valve without affecting function.

The core of this new classification lies in distinguishing the prevalence of the "ventricular" versus "atrial" phenotypes in secondary TR, or, more specifically, how much annular dilation (type I) or systolic restriction in leaflet movement (Carpentier type IIIB) predominate. This distinction, with prognostic implications for edge-to-edge therapy, is equally applicable in surgical technique and should be required in preoperative studies. Relevant parameters include tenting analysis, with cut-off points of 9 mm for tenting height, 2.1 cm^2 for tenting area, and 2.5 cc for tenting volume. Furthermore, right ventricular dilation with an indexed end-diastolic volume cut-off at 80 cc/m^2 and end-systolic volume at 21 cc/m^2 differentiates between an "atrial" versus "ventricular" phenotype, with values below and above these thresholds, respectively. Lastly, a simple yet highly intuitive parameter is the right atrium-to-ventricle area ratio with a cut-off of 1.5. Values at or above this ratio indicate an "atrial" phenotype, whereas those below suggest a "ventricular" phenotype.

1.b) New Morphological Characterization

The tricuspid valve could more aptly be renamed the "right atrioventricular valve," as seen in the congenital heart disease field. This is due to the fact that, in many cases, we cannot accurately describe the valve as having three cusps. The most common morphology (54%) is type I, featuring the traditionally described three leaflets. Type II (5%) involves fusion of the anterior and posterior leaflets, creating a bicuspid valve. Type III, subdivided into three subtypes, features an indentation dividing one of the leaflets. In type IIIA (3%), the anterior leaflet divides into A1 and A2; type IIIB, the second most common (32%), involves the posterior leaflet dividing into P1 and P2; and type IIIC (4%) involves the septal leaflet dividing into S1 and S2. By convention, the closest scallop to the atrioventricular node is labeled as A1, P1, or S1, with the most anterior scallop designated for the posterior leaflet. Lastly, type IV (2%) involves two indentations, with divisions in the anterior (A1 and A2) and posterior leaflets (P1 and P2), leaving the septal leaflet intact.

1.c) New Severity Classification of TR

Like mitral regurgitation, TR was initially graded into three categories: mild, moderate, and severe. This classification primarily uses semiquantitative parameters, such as the PISA radius (<5.4 mm^2, 5.5-8.9 mm^2, and ≥9 mm^2, respectively) and vena contracta width (<3 mm^2, 3-6.9 mm^2, and ≥7 mm^2, respectively). Given the significance of severe TR, three additional gradations were created, forming a five-level scale. Although initially controversial, this extended scale gained support due to the unique nature of the right heart. Right-sided regurgitant volumes that cause systemic venous congestion are manageable in the right heart but would be unmanageable in the left heart due to pulmonary edema and postcapillary pulmonary hypertension incompatible with sustained circulation. This extended grading scale has demonstrated prognostic implications, with worsened survival correlating with each step up in severity. The selected parameters for classifying severe, massive, and torrential TR include quantitative metrics such as PISA-derived regurgitant orifice area (40-59 mm^2, 60-79 mm^2, and ≥80 mm^2, respectively) and 3D vena contracta area (75-94.9 mm^2, 95-114.9 mm^2, and ≥115 mm^2, respectively), although vena contracta width remains a useful semiquantitative parameter (7-13.9 mm^2, 14-20.9 mm^2, and ≥21 mm^2, respectively). This classification also has technical implications: one main limitation for edge-to-edge or isolated annuloplasty techniques is the presence of a significant leaflet gap (>1 cm). Given the strong dependency of right heart hemodynamics on preload, afterload, and respiratory dynamics, these

parameters should be measured at end-expiration in spontaneously breathing patients and in a state of euvolemia, stable diuretic therapy, and normalized blood pressure.

1.d) Assessment of Right Ventricular Function and Right Ventricular-Pulmonary Artery Coupling

One primary concern in addressing TR is assessing whether the right ventricle (RV) can sustain cardiac output after residual TR is minimized or eliminated. Evaluating RV function pre-procedure is challenging, as it may be masked by regurgitation, which acts as a relief valve. RV function assessment should encompass multiple parameters since a single definitive measure remains elusive. The evaluation should include traditional measurements, such as tissue Doppler wave S (mild dysfunction, 9-11 cm/s; moderate, 6-8 cm/s; and severe, <6 cm/s), TAPSE (mild dysfunction, 14-17 mm; moderate, 10-13 mm; and severe, <10 mm), global strain (mild dysfunction, 18-21%; moderate, 14-17%; and severe, <14%), and free wall strain (mild dysfunction, 20-23%; moderate, 15-19%; and severe, <15%), with the more precise but complex three-dimensional ejection fraction (mild dysfunction, 45-50%; moderate, 35-45%; and severe, <35%). This RV functional assessment should also consider pulmonary afterload using the right ventricular-pulmonary artery coupling concept, which describes the hemodynamic conditions where the RV can maintain forward pulmonary flow. Suggested indices include TAPSE/pulmonary artery systolic pressure, though no definitive cut-off exists. Alternatively, the indexed RV stroke volume relative to end-systolic volume can be measured using 3D echocardiography, CT, or MRI. This measure does not depend on pulmonary artery pressure but, while intuitive, lacks standardization.

1.e) Characterizing the Risk of Invasive Procedures

This aspect will be discussed in future blog entries, though it is worth noting that the effects of systemic venous congestion warrant a multimodal assessment across organs and systems, rather than focusing solely on cardiac disease and related morbidities, as is typical in conventional risk-scoring systems. This unique profile has led to the development of tricuspid valve-specific risk scores, such as TRI-SCORE, among others.

2. Characterization of Outcomes in Invasive Procedures

The VARC panel's guidelines on outcomes criteria for future studies and grading the impact of complications or suboptimal results are notably less biased than those used for aortic and mitral valves. There are no significant biases that would disadvantage surgical outcomes relative to interventional ones. In fact, some points are particularly striking, including:

2.a) "Technical success" requires proper device implantation, with reduction of TR to mild or lower (optimal outcome) or moderate or lower (acceptable outcome), absence of tricuspid stenosis, and absence of major complications. A cut-off for tricuspid stenosis is set at a valve area >1.5 cm^2 or indexed >0.9 cm^2/m^2 (>0.75 cm^2 if BMI >30 kg/m^2) with a mean gradient <5 mmHg. Tricuspid stenosis is less common with edge-to-edge tricuspid repair than with mitral, as the tricuspid valve is physiologically 20% larger. However, prosthetic replacement, particularly percutaneous, may carry this risk.

2.b) A “clinical success” criterion is added, requiring no adverse events (e.g., bleeding, AKIN stage II or III renal dysfunction, heart failure, embolism) from 30 days post-procedure to one year, with no re-hospitalizations, improvement in dyspnea class, improved functional capacity (6-minute walk test increase by 50 meters), and/or improved quality of life as measured by at least a 5-point increase on the KCCQ scale.

2.c) Follow-up for different devices must be sufficient to confirm effectiveness, with a minimum threshold of five years, especially for newly introduced devices.

2.d) Device-related complications are categorized and graded, including phenomena like thrombosis (HALT) or leaflet mobility impairments.

2.e) Results on all-cause mortality and re-hospitalization are required. Only secondary outcomes categorize cause-specific mortality or re-hospitalization, with heart failure-related readmissions as especially relevant.

2.f) Post-procedure hemodynamic studies should be conducted in a stable medical treatment context. Increased diuretic therapy in control groups, as seen in the Triluminate study, or pre-transcatheter therapy to reduce leaflet gap could skew results. Reporting medical therapy is essential, as it may serve as a major confounding factor.

COMMENTARY:

Surgery pioneered valve treatment, and percutaneous intervention, currently expanding, attempts to replicate surgical concepts with transcatheter devices and techniques. As surgeons, we must ensure this exchange of knowledge flows both ways. The cardiology community's interest in TR and valvular diseases has spurred innovation in the past two decades. Surgeons should embrace and integrate this knowledge, holding it to the same standard in our procedures. Although VARC’s tricuspid criteria seem intervention-focused, they present a neutral scenario for the surgical alternative without any biases. By doing things right and knowing what we’re doing, we can compete effectively in this emerging arena of debate.

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Elio Martín Gutiérrez

Tricuspid Valve Surgery: How to Assess Surgical Risk

This single-center study examines the role of the MELD scoring system, traditionally applied to advanced liver disease, in assessing surgical risk for isolated tricuspid valve surgery. This study contrasts MELD with conventional risk scoring systems, such as EuroSCORE II and STS score.

If the early 2000s marked the advent of interventional procedures on the aortic valve (e.g., the first TAVI in 2002) and the following decade saw focus on the mitral valve (notably, with Abbott's acquisition of MitraClip® technology in 2009 and its FDA approval in 2009), the 2020s appear to be witnessing renewed interest in the tricuspid valve. Much has been written about tricuspid regurgitation (TR), though with varying perspectives. From being labeled as a valvular condition with poor prognosis, in line with current trends, to prior publications proposing prophylactic surgery in early, non-severe stages when annular dilation is present; and even earlier, teachings considered TR nearly benign and reversible following correction of left heart disease. This diversity of perspectives has left cardiac surgeons and cardiologists facing a multitude of views, ultimately leading to disorganized approaches in interpreting tricuspid valve disease.

One key misinterpretation lies in equating the right atrioventricular valve's pathophysiology to that of its left-sided counterpart, the mitral valve. However, the tricuspid valve's unique features, such as leaflet anchoring independent of papillary muscles (particularly at the septal level), its three-dimensional annulus, anatomical variations of its leaflets, location within a low-pressure and high-capacitance environment, and dependency on pulmonary vascular resistance (partly intrinsic, partly passively transmitted from the left side), make it a singular valve with distinct characteristics. Many of these factors have been previously discussed on this blog.

Despite the clear surgical indications outlined in clinical guidelines, tricuspid valve surgery remains underutilized, particularly in isolated cases. This is likely due to longstanding conceptual confusion and the apparent efficacy of medical management, leading to the current situation. It's challenging to pinpoint the origin of this vicious cycle, but it likely stems from the traditional under-referral of TR patients for surgery, either due to a misperception of benignity or the reluctance of surgical teams to address cases where the valvular disease is considerably advanced and "ventricularized." This resistance may have discouraged referrals for surgical intervention. However, the rise of interventional procedures has shifted focus to this patient group, spurring research not only in percutaneous but also in all invasive approaches, including surgical. Enhanced understanding, the development of novel surgical techniques (e.g., subvalvular repair procedures), and improved risk stratification have now opened doors to treating many patients previously relegated to maintenance therapy. Given their ineligibility or lack of knowledge (with the exception of cardiac transplantation) on the use of ARNI, SGLT2 inhibitors, mechanical support, or resynchronization therapy, the outlook for these patients in the therapeutic horizon now attracting attention was bleak.

With this large pool of potential candidates awaiting clinical trials (beyond the Triluminate trial and with no recent surgical trials) to establish the indications for percutaneous therapy, effective risk stratification is essential for determining patient eligibility for either surgical or percutaneous treatment and identifying those for whom the risk would be prohibitive or for whom invasive treatment would likely be futile. In line with the growing interest in tricuspid valve disease, several options have emerged that will likely need refinement over the next few years:

1. TRI-SCORE: This risk scoring system is currently the most suitable for stratifying patients based on conservative versus invasive treatment options, including both surgical and percutaneous procedures. It has also been validated in surgical cohorts, demonstrating good fit and predictive capacity. A previous blog post highlighted that, for TRI-SCORE values of ≤3, surgery yielded superior outcomes to interventional treatment, and this in turn to conservative management, with no group differences for intermediate scores (4-5 points) or high scores (≥6). However, in invasive treatment, benefit over conservative management was observed for intermediate scores when adequate repair with residual TR ≤2+ was achieved. For high scores, there remained no therapeutic benefit of invasive over conservative management, even with successful repair, suggesting a futility threshold for surgical or percutaneous treatment.

2. Conventional Risk Scores: Given that tricuspid valve surgery is ultimately a surgical procedure, traditional risk scoring systems may still play a role, although tricuspid pathology is not adequately represented in EuroSCORE II (only the number of procedures is considered, with most tricuspid surgeries performed in conjunction rather than as isolated procedures) and is not specifically addressed in different versions of the STS score.

3. Disease-Specific Prognostic Factors: The prognosis for tricuspid valve surgery is influenced by factors beyond right ventricular-pulmonary artery coupling (previously discussed in the blog), including organ damage from systemic congestion. Various biomarkers are recognized, though many are not yet incorporated into risk scoring systems or lack established cut-off points for accurate stratification. Nevertheless, these markers should still be evaluated when considering tricuspid valve disease management. These include NT-proBNP, BUN, creatinine, glomerular filtration rate, albumin levels, transaminase levels, bilirubin levels, INR, and platelet count, as well as CA-125, which is overexpressed in congestion. Thus, scoring systems like MELD (Model for End-stage Liver Disease) could play a role in predicting risk in tricuspid valve surgery patients.

Consequently, the authors propose a study including all consecutive patients who underwent isolated tricuspid valve surgery at their institution (Jena, Germany) between 2011 and 2020. Patients with intrinsic tricuspid pathology, functional or primary, were selected, excluding carcinoid, traumatic, congenital, or tumor cases but including those with infectious endocarditis (16%). The MELD score for each patient was analyzed and compared with EuroSCORE II and the STS score (the aortic valve replacement model was used due to the lack of a specific model).

In a sample of 181 symptomatic patients (NYHA class III-IV, TR grade 3+ or higher), more than 75-80% exhibited these criteria. Over 60% had atrial fibrillation, more than 30% had a transvalvular pacemaker/defibrillator electrode, and over 50% had moderate to severe pulmonary hypertension. More than one-third had undergone previous surgery, with 10% having undergone myocardial revascularization, 8% aortic valve surgery, 15% mitral valve surgery, and 13% prior tricuspid procedures. Surgery was performed with a minimally invasive approach via right minithoracotomy in 90% of cases without cardioplegic arrest. The authors emphasized ensuring adequate venous drainage using vacuum assistance and cannulation of both venae cavae. Optimal repair was achieved in 95% (residual TR ≤1+) and acceptable repair (residual TR ≤2+) in 5% of cases. The revision rate for bleeding was notably high (15%), though not discussed by the authors,

and other notable complications included stroke (4%) and renal replacement therapy (15%). Several cases required laparotomy due to visceral perforation, abdominal compartment syndrome, mesenteric ischemia, and acute abdomen (not directly related to the surgical procedure).

Thirty-day mortality was 8.9% in the overall series, reaching 65% at maximum follow-up (median 4.4 years). The mean EuroSCORE II was 7.2%, and the mean STS score was 4.9%. The MELD system's discriminative ability was strong, showing good fit similar to traditional perioperative risk scores. For low MELD scores (<10 points), observed mortality was 4%, with EuroSCORE II and STS scores both predicting 5%. For intermediate MELD scores (10-20 points), observed mortality was 5%, with an average prediction of 8% by EuroSCORE II and 6% by STS. However, predictability varied significantly for high MELD scores (>20 points), where observed mortality reached 31%, well above the 10% and 11% predicted by EuroSCORE II and STS, respectively. This discrepancy may represent a futility threshold for surgical treatment, consistent with previous work discussed on the blog evaluating Child-Pugh (9 points) and MELD (20 points) thresholds as indicative of prohibitive risk in patients with primary hepatic dysfunction undergoing cardiac surgery. The ROC curve yielded a 77% result for STS score and a close 74% for MELD.

The authors conclude that classic risk stratification systems are not highly predictive for isolated tricuspid valve surgery, especially in the presence of secondary liver dysfunction. The MELD score may prove useful in risk stratification for these patients.

COMMENTARY:

This study is of special interest for its originality and pioneering nature, applying existing tools to stratify risk in patients undergoing isolated tricuspid valve surgery. This all-corners study yields ostensibly modest but excellent results, as it includes high-risk patients. Rather than establishing any risk score system as a reference, this study hints at the need for a risk assessment focused on right-sided pathophysiology, similar to the TRI-SCORE initiative. Left-sided pathophysiology principles are not fully applicable, and the positive outcome with a risk scoring system geared towards liver pathology underlines the significance of systemic congestion on surgical risk, an aspect that classic risk scoring systems fail to assess. Future research, possibly aided by big-data and registry analysis, will likely be necessary to develop a new risk scoring system integrating the aforementioned factors. Until then, caution, observation, and common sense are advised... and among the few existing resources, TRI-SCORE (≤3 points) suggests surgical treatment is preferable to intervention.

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Marina Combarro Eiriz

Percutaneous Tricuspid Repair: The Definitive Treatment for Moderate- or High-Risk Surgical Patients?

This is a multicenter, randomized clinical trial evaluating outcomes of transcatheter edge-to-edge tricuspid valve repair compared to optimized medical management in 350 patients with severe tricuspid regurgitation.

Historically, tricuspid valve disease has often been overlooked, frequently presenting alongside left-sided valve diseases and thus receiving lower priority for intervention. However, it is now recognized that significant tricuspid regurgitation (TR) is an independent predictor of adverse clinical outcomes in these patients. TR is also associated with the development of heart failure (HF) and a deterioration in patients' quality of life. Furthermore, isolated surgical treatment for TR is challenging, primarily due to other factors that elevate surgical risk in these patients, such as right ventricular dysfunction, hepatorenal impairment, pulmonary hypertension, and a history of previous cardiac surgery, which is common in this pathology. According to large North American registries, mortality for this type of surgery is approximately 8–10%.

In recent years, transcatheter tricuspid valve repair (TTVR) with edge-to-edge devices has emerged as a safe and potentially effective alternative for specific cases of TR. Recent studies have shown that TTVR can successfully reduce the degree of valvular insufficiency and alleviate patient symptoms. However, it remains undetermined whether TTVR is superior to optimized medical therapy.

The TRILUMINATE study discussed in this review was a randomized clinical trial conducted across 65 centers in the United States, Europe, and Canada. It included 350 patients with symptomatic severe TR (NYHA functional class II–IV), a systolic pulmonary artery pressure below 70 mmHg, stable HF medication for at least 30 days prior to enrollment, and classified as moderate- or high-risk surgical candidates, excluding conditions necessitating surgical intervention. The study aimed to demonstrate a clinical benefit of TTVR compared to pharmacological treatment over a one-year follow-up. For all patients assigned to the tricuspid repair arm, the TriClip® device was used, introduced via a 25 Fr catheter through femoral venous access, enabling clip placement on the tricuspid leaflets with transesophageal echocardiographic and fluoroscopic guidance. All procedures were performed under general anesthesia.

The study's primary outcome was a hierarchical composite including all-cause mortality, tricuspid valve surgery, HF hospitalizations, and quality-of-life impact assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ). Additional evaluated outcomes included renal failure development, endocarditis, procedure-related complications, reduction in TR severity, and the six-minute walk test performance.

The enrolled patients had an average age of 78 years, with a slight predominance of females, and 94% presented functional TR associated with right ventricular dilation. Left ventricular function was preserved in both groups, with 70% of patients showing massive or torrential TR severity. There were no significant procedure-related complications, such as device embolization, major bleeding, significant tricuspid stenosis, or intraprocedural or periprocedural mortality. Patients undergoing the procedure were discharged after an average stay of one day, with an average of two clips per patient.

Results were analyzed using the win ratio method, which enables treatment superiority assessment by ranking events in a pre-established hierarchical order by importance. The win ratio result for the primary outcome favored the tricuspid repair group with TriClip®

(1.48, *p*=.02). However, this outcome was primarily achieved through KCCQ score improvement, without demonstrating superiority in terms of mortality, surgical need, or HF hospitalizations. At 30 days, 87% of the percutaneous group showed less than moderate-severe TR compared to 4.8% of the control group (*p*<.001).

The authors conclude that edge-to-edge TTVR for severe TR reduces TR severity and is associated with improved quality of life.

COMMENTARY:

Given that patients with severe TR frequently present high surgical risk, developing new minimally invasive techniques for tricuspid repair has become essential. With the advent of edge-to-edge devices like TriClip®, a range of options opens up for certain patients who otherwise would rely increasingly on diuretics as their sole therapy. Current evidence reinforces that, in carefully selected patients, this is a safe and effective technique with a significant TR reduction sustained over follow-up.

Based on the findings of this study, comparing percutaneous intervention in severe TR patients with conventional pharmacologic management, the technique appears beneficial for quality of life. Although superiority in “hard” clinical events (mortality, intervention necessity, or HF decompensation admissions) was not demonstrated, the symptomatic burden of cardiopathy—and thus, patient quality of life—should always be a priority for healthcare providers interacting with these patients. However, on closer examination of study results, an intriguing detail arises: the objective quantification of functional capacity (six-minute walk test) did not reach statistical significance between the treatment groups, contrasting with the subjective improvement perceived by study participants via the KCCQ. Given the nature of the intervention and the open study design, where patients knew their treatment arm and no placebo or simulated intervention was performed, patients undergoing interventional treatment may have perceived an erroneous subjective improvement, which could explain the lack of correlation with the six-minute walk test results. If true, this would represent a significant design bias.

Despite its limitations, this is among the first prospective, randomized studies assessing this type of percutaneous device in treating severe TR, demonstrating its potential as a viable treatment alternative for this valvulopathy. Further studies with larger sample sizes and longer follow-up periods are required to reach more robust conclusions on the true benefit of this technique. Similarly, it would be interesting to see results comparing percutaneous repair with surgical approaches for tricuspid pathology in different populations, such as those with low surgical risk.

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Section V D:

Other valvulopathies

Elio Martín Gutiérrez

Valve Bioprostheses: Resilient Over Time

Five-year results and preliminary seven-year data from the COMMENCE study on Edwards® RESILIA® bovine pericardial tissue in aortic position bioprostheses.

The evolution of cardiac valve bioprostheses is a medical milestone we encounter daily. Reflecting Cooley's maxim, "apply, simplify, modify," certain surgeons, aided by engineers and biophysicists, have significantly advanced these devices, which are now implanted in hundreds of thousands worldwide annually.

Cardiac bioprostheses emerged following the experience with mechanical devices, aimed at avoiding anticoagulation and its associated complications. In 1966, Carpentier described a method to reduce inflammatory reactions on biological tissue by using glutaraldehyde to chemically treat porcine valves. By creating cross-links between collagen molecules, this treatment protected the tissue from denaturation and immunologically inactivated it through surface antigen modification. Later, by mounting the entire porcine valve on a stent, an appropriate three-dimensional spatial relationship between the leaflets was achieved, simplifying implantation and enhancing the device's functionality and durability. In 1971, Ionescu mounted artificial bovine pericardial leaflets on a stent, a concept quickly adopted by the newly established Edwards Lifesciences® for the development of their well-known bioprostheses.

Since then, the emergence of new devices and refinement of existing ones shaped clinical practice over the last three decades of the past century, leading up to the advent of TAVI. Essentially, these changes focused on three aspects: First, the choice of biological tissue, including the porcine aortic valve (whole or fragmented, discarding the leaflet bearing the muscular moderator band as in the Medtronic Mosaic® or the Abbott Epic®) or animal pericardium. The latter incorporates equine, porcine, or bovine origins, providing an increasing level of hemodynamic flow and mechanical stress based on a better ratio of collagen and elastic fibers. Second, the assembly of biological tissue, either mounted inside or outside the stent, as well as the flexibility of the stent itself. Notably, the promising Mitroflow®/Crown® design with pericardial sheets mounted outside the stent encountered significant challenges; although the St. Jude Trifecta® resolved stent deformability issues and preserved pericardial coverage on leaflet-stent contact surfaces, results remained suboptimal regarding structural degeneration. Third, tissue fixation continued to rely on glutaraldehyde, augmented with various, often proprietary, anticalcification treatments.

During the rebranding of Mitroflow® to Crown®, a new anticalcification treatment (PRT: phospholipid reduction treatment) was introduced, while Abbott® employs Linx®, Medtronic® uses AOA®, and platforms like Livanova Perceval Plus® incorporate FREE (formaldehyde-free aldehyde storage). These treatments focus on minimizing phospholipids, derived from the glycocalyx of cell membranes on the biological tissue surface, and covering free aldehyde radicals after tissue fixation, as both are known sites for calcium ion deposition in the bloodstream, promoting structural degeneration of the leaflets.

Edwards Lifesciences® introduced RESILIA® pericardial tissue in 2014, a new fixation concept based on three principles. The most significant was a washing process that removed many active radicals responsible for oxidation and calcium deposits. Furthermore, the remaining radicals were covered, acting not only on aldehydes but also on similar agents. Lastly, glycerolization, which replaces water in biological tissue with alcohols (ethanol and glycerol), enables sterilization with ethylene oxide and

preservation in a dry atmosphere, eliminating the need for a liquid solution or aldehyde. The initial experience was published in a comparative series of mitral valve implants in sheep, using both conventional pericardium and RESILIA® tissue. Although the results showed significantly lower degeneration rates and greater durability compared to the traditional platform, clinical results were necessary to validate these findings.

The EU Feasibility Trial was the first study that obtained CE marking for RESILIA® tissue, investigating its safety and performance in aortic valve replacement prostheses. Subsequently, the COMMENCE trial expanded the patient population from the previous study, and along with the RESILIENCE trial (ongoing, for patients under 65 years), aims to broaden the indications for these bioprostheses by examining their long-term durability. The benchmark set by Bourguignon et al. with the series of long-term results for the Carpentier Edwards Perimount/Magna® prosthesis represents the gold standard of cardiac bioprosthesis performance, a goal that both surgical and transcatheter platforms seek to surpass.

The COMMENCE study recruited patients between 2013 and 2016, including 698 patients in a prospective, non-randomized, uncontrolled, international study with 27 participating centers. The results have been reported in successive updates, with the current analysis completing the 5-year follow-up. This study stands out for its transparency in follow-up, with 190 losses, 69 due to mortality and the remainder due to patient choice, except for only 26 cases where no justification was found. At 5 years, there are 499 patients with complete follow-up, with 37 patients for whom data were unavailable at the time of publication. The 5-year results are excellent, with an overall survival rate of 89%, valve-related event-free survival of 97%, and reoperation-free rate of 98.7%. No thrombosis cases were recorded, with an endocarditis rate of 2.2%, significant paravalvular leakage rate of 0.5%, and no registered cases of structural degeneration.

Recently, at the STS congress, results for the 195 patients with 7-year follow-up data from the initial recruitment were presented, showing a survival rate of 85.4%, reoperation-free survival of 97.2%, 15 endocarditis cases (rate of 2.7%), and 2 cases of structural degeneration (rate of 0.7%). These last two cases were resolved with a TAVI-in-valve procedure in the first and reoperation with mechanical prosthesis replacement in the second. Throughout the follow-up, mean gradients of the bioprostheses remained stable between 11.1 and 9.4 mmHg, covering all available sizes from 19 to 29 mm.

With these results, the authors conclude that the safety and mid-term hemodynamic performance of the aortic prosthesis with RESILIA® tissue are encouraging, justifying continued follow-up and promoting its use extension to other bioprosthesis platforms.

COMMENTARY:

As Bavaria himself stated, “all previous bioprosthesis trials have shown structural deterioration beginning around five years, with rates between 1.5% and 5%. Therefore, we can conclude that the five- and seven-year structural deterioration curve is exceptionally favorable in the COMMENCE study. Although we must await ten-year data, these results are highly encouraging for the RESILIA® tissue platform. Furthermore, the stable maintenance of the mean gradient, the virtually insignificant levels of paravalvular aortic insufficiency, and the relatively low rates of adverse events like endocarditis and thrombosis all indicate no concerning signals in these areas compared to historical trial outcomes of other cardiac valves.”

Given the findings presented, it appears reasonable to expand the clinical use of RESILIA® tissue. This could be applied to various scenarios, such as aortic valve implantation in patients aged 55 to 65 years, who have a long life expectancy, and who

reject or have contraindications to oral anticoagulation (provided they are adequately informed). In addition, it would incorporate Edwards INSPIRIS® support for future TAVI-in-valve procedures. This could also apply to Bentall-De Bono procedures in analogous contexts, utilizing a valved graft with a bioprosthesis or, when available, the eagerly awaited Edwards KONECT RESILIA® valved conduit in Europe. For atrioventricular valves, the Edwards MITRIS RESILIA® bioprosthesis may also be an option, supported by its corresponding COMMENCE mitral study, now with four-year follow-up, although with a smaller sample size of 82 patients (98.7% structural degeneration-free survival and stable mean gradients between 3.8 and 4.3 mmHg).

While the clinical superiority of RESILIA® tissue cannot be confirmed until at least ten years of follow-up are completed, it is worth noting one of the limitations of the COMMENCE study. The structural degeneration criteria used do not align with those established by Capodanno et al. in the widely accepted VARC criteria, applicable to percutaneous devices and increasingly used for surgical bioprostheses. The COMMENCE study's more lenient criteria consider structural degeneration due to dysfunction or deterioration, excluding degeneration from thrombosis and/or endocarditis, either necessitating reintervention or discovered at autopsy. As such, most structural degeneration cases detected would derive from new valve procedures (surgical or percutaneous) and may have been underestimated, as some patients may not have been considered candidates for reoperation or TAVI-in-valve. The authors justified the deviation from the VARC criteria to the FDA commission that approved the trial, noting that VARC criteria, in their 2017 version 3, define valve dysfunction in four ways: structural, non-structural, thrombosis, and endocarditis. For structural dysfunction, VARC includes morphological criteria, which are debated, as well as functional criteria such as:

- An increase in mean gradient compared to post-implant baseline >10 mmHg for moderate degeneration and >20 mmHg for severe degeneration.

- Moderate or severe intraprosthetic regurgitation (depending on the degree of degeneration), new or worsening of known previous regurgitation.

- Mean gradient >20 mmHg for moderate grade or >40 mmHg for severe grade, without specifying the time of detection.

This last criterion should be reviewed, as it suggests a prosthesis-patient mismatch situation (non-structural dysfunction) typically defined by effective valve area proportion in relation to body surface area (<0.65 cm^2/m^2 for severe grade and <0.85 cm^2/m^2 for moderate grade).

To conclude, we welcome efforts to enhance surgical devices in a changing world where significant investment is directed towards transcatheter therapies. We should not assume that, with durability concerns in mind and awaiting long-term TAVI results, surgery will not again become a testing ground for interventional approaches should long-term outcomes fall short of expectations. While it is conceivable that an "Edwards SAPIEN RESILIA®" will soon be introduced (presumably to be named Edwards SAPIEN 3 Ultra®), we hope that beyond the remarkable properties of this "miraculous" tissue, preservation of the leaflet architecture on commissural posts and avoidance of crimping damage to pericardium will differentiate surgical from percutaneous prostheses. Until then, we can only wait.

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Beatriz Vera Puente

The dilemma with dialysis patients: implantation of biological or mechanical prosthesis

Long-term outcomes in a Japanese cohort of dialysis patients undergoing aortic valve replacement with biological and mechanical prostheses.

Severe aortic stenosis (AS), when coexisting with chronic kidney disease (CKD), is associated with a faster progression of valvular disease and consequently a poorer prognosis. Aortic valve replacement (AVR) has shown a reduction in mortality compared to conservative treatment. In Spain, CKD affects approximately 10% of the population, and in its terminal stage, patients require renal replacement therapy, with a prevalence around 149 individuals per million inhabitants in 2021. The survival rate for severe AS patients in advanced CKD stages is significantly lower than for those without nephropathy (35% vs. 70%).

This study aims to compare the long-term outcomes of mechanical vs. biological AVR in dialysis patients. It is a retrospective analysis using data from the Japanese Cardiovascular Surgery Database, including dialysis patients who underwent AVR (isolated or combined with annular enlargement, mitral valve surgery, or coronary revascularization) between 2010 and 2012, excluding transcatheter interventions (TAVI) and aortic surgery. An additional period from 2019 to 2020 was designated to gather data on dialysis duration and clinical outcomes. A comparative analysis of mortality, cerebral infarction, cerebral hemorrhage, gastrointestinal bleeding, and prosthetic valve failure was conducted. The analysis included a total of 1,016 patients, evenly split into two groups (n = 508) after propensity score matching. The maximum follow-up period was 8 years.

No significant differences were found in 5-year survival (49% for bioprosthesis vs. 53% for mechanical prosthesis) per the Cox regression model ($p = .318$). Secondary event comparisons showed no significant differences between mechanical and biological prostheses in cerebral infarction ($p = .747$) and prosthetic valve failure ($p = .09$). However, the incidence of cerebral ($p = .002$) and gastrointestinal bleeding ($p = .0005$), necessitating admission, was higher in patients with mechanical aortic prostheses. Study data indicate that the number of dialysis patients undergoing AVR increased by nearly 20% (from 2,369 procedures in 2014 to 2,834 in 2016), with a corresponding reduction in mortality from 11.7% to 10.7% during this period.

The authors conclude that the average survival for dialysis patients undergoing AVR is approximately 50%, regardless of whether a mechanical or biological prosthesis is used. Although survival does not differ, bleeding complications are more common in patients with mechanical prostheses.

COMMENTARY:

The choice of prosthesis type (mechanical or biological) remains a point of contention in the treatment of severe AS in dialysis patients. Traditionally, it has been considered that valve degeneration in biological prostheses is higher in these patients. This may involve the same pathophysiological processes that cause greater degeneration and calcification of the native valve, although the exact mechanisms behind this degeneration are not fully understood. The durability timelines of biological prostheses in this subgroup of patients are also not well-defined, as most studies have short follow-up periods. Although historically, American guidelines recommended mechanical prostheses for such patients (class II indication), this recommendation was later removed from subsequent valvular disease guidelines without issuing specific guidance. However, choosing a mechanical

prosthesis entails a higher bleeding risk due to anticoagulation and the coagulopathy that accompanies CKD. The benefits of durability must be weighed considering the reduced survival rate of dialysis patients compared to the general population.

This article provides useful findings; however, limitations exist due to its retrospective nature and reliance on national database data, which may be incomplete and make extrapolation to other populations challenging. Additionally, the lack of stratification based on concomitant surgeries may introduce bias. For example, patients who undergo mechanical mitral valve replacement, requiring a higher anticoagulation range and with a greater likelihood of bleeding complications, could skew study results. Furthermore, data on quality of life and echocardiographic data on bioprosthetic degeneration, which could guide decision-making, are missing.

In treating AS with AVR in dialysis patients, prosthesis choice should be individualized and discussed with the patient, taking into account not only age but also other conditions associated with their renal disease, such as life expectancy or kidney transplant eligibility. It is crucial to assess how these factors will impact patient quality of life, with the patient's informed opinion being integral to the decision-making process.

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Bunty Ramchandani

Bioprostheses in the current era

A retrospective study of a national database in Taiwan that examines durability outcomes for all bioprosthetic valves implanted in the aortic and/or mitral position from 2001 to 2017.

Over the past decade, biological prostheses have become increasingly used in the mitral and especially the aortic positions. Selecting the type of prosthesis is not a trivial decision and requires a calm discussion with the patient regarding the advantages and disadvantages. During this conversation, it is crucial to mention the shorter durability compared to mechanical prostheses and the benefits related to fewer bleeding and/or thromboembolic events. Indicating a bioprosthesis should not be based solely on the patient's age, as various clinical factors like comorbidities, life expectancy, frailty, and preoperative treatment should also be considered. Likewise, assessing personal aspects is equally essential, such as quality of life, reproductive desires, occupation, and treatment adherence, among many other factors. Considering these elements, it is vital to recognize the inevitability of bioprosthetic degeneration and to develop a future management plan (reintervention and/or potential solutions via percutaneous intervention).

Clinical guidelines differentiate two age thresholds based on the position of bioprosthesis implantation. They recommend bioprostheses for mitral valve replacement (MVR) in patients over 65 years of age and for aortic valve replacement (AVR) in those over 50 years (ACC/AHA guidelines). However, as stated previously, age is merely one factor in the decision-making algorithm, and these guidelines, as their name suggests, are meant to guide rather than dictate. The choice of prosthesis type will always be an individualized and shared decision.

The current study aims to assess, on a population level, the long-term durability of bioprostheses in the aortic, mitral, and mitro-aortic positions. The Taiwanese national health insurance database was utilized to evaluate all cases of MVR, AVR, and mitro-aortic valve replacement (MAVR) from 2001 to 2017, with reoperation as the primary event. Two experimental designs were employed: a between-subject design and a within-subject design (for MAVR cases). For the former, a propensity score-matched analysis was performed to compare AVR with MVR.

A total of 10,308 patients were analyzed; 5,462 underwent AVR, 3,901 underwent MVR, and the remaining 945 received MAVR. After applying the propensity analysis, 2,259 patients were matched for AVR and MVR comparison. With a mean follow-up of 4.2 years (range from 1 day to 17.9 years), they found a reoperation rate of 3.5% for MVR compared to 2.6% for AVR (HR 1.41; $p<.05$). Similarly, MVR was associated with higher all-cause mortality (36.5% vs. 32.6% for AVR) with an HR of 1.21 ($p<.05$). In patients with MAVR using the same type of bioprosthesis, aortic-positioned prostheses showed a lower reoperation incidence.

The authors concluded that aortic-positioned bioprostheses present better outcomes in terms of durability, long-term mortality, and perioperative morbidity compared to those implanted in the mitral position. They foresee expanded indications for these prostheses due to enhanced durability resulting from advancements in anticalcification treatment for valve leaflets and the evolution of percutaneous interventions, which may delay/avoid future reinterventions.

COMMENTARY:

The results of this study, at first glance, do not seem to offer new insights beyond what we already know about bioprostheses. We know that aortic-positioned bioprostheses last longer than those in the mitral position, leading to more frequent reinterventions for mitral valves. It is also known that mitral valve surgery and re-surgery are more complex, with a more fragile patient profile, contributing to the higher morbidity and mortality of these procedures. This background knowledge aligns with the recommendations of clinical practice guidelines in developed countries, which suggest delaying biological mitral valve replacement until 65 years of age. However, this knowledge is based on personal and collective experiences from peers, societies, and the few published studies that directly compare bioprostheses in these two positions. Available studies are generally small, single-center, and limited in the range of models studied, often lacking sufficient statistical power and riddled with various biases. Despite the limitations of the current study, as discussed later, an analysis of a national database encompassing over 10,000 patients with various types of bioprostheses is a gem.

Like any gem, it must be polished to reveal its brilliance rather than be mistaken for an ordinary stone. The general data on reoperation and mortality consolidate and validate our experience regarding bioprostheses. The most interesting findings lie in the various subanalyses. When evaluated globally and independently of implantation position, no differences were found regarding the different models available on the market. However, for aortic-positioned bioprostheses, the Carpentier-Edwards Perimount/Magna® valves showed fewer reoperations—a finding not observed in the mitral position. Additionally, no differences in durability and reoperations were found between porcine and bovine bioprostheses. There were also no differences in infectious endocarditis rates based on the position of the bioprosthesis. Finally, none of the usual comorbidities (renal failure, prior heart failure admission, etc.) correlated with an increased reintervention risk, except for age.

The limitations of this type of study have been mentioned in various blog entries. As it is an administrative database of the national health insurance system, we lack access to laboratory or echocardiographic data. This study only considers reoperations and not prosthetic degenerations that would require echocardiographic data for diagnosis. This limitation may introduce bias, potentially overestimating the actual durability of the prostheses, as some patients may be indicated for reoperation but are inoperable due to age or comorbidities. Additionally, case identification relied on ICD-9 classification codes, with inherent coding errors. Lastly, an average follow-up of 4.3 years warrants caution with such low reintervention data.

In conclusion, the article by Chen et al., based on a valuable database, provides a contemporary view on the use of bioprostheses in aortic and mitral positions, offering a snapshot that confirms our perception of these outcomes.

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José Manuel Martínez Comendador

Vegetation size, multiplicity, and position in patients with infective endocarditis

This retrospective study aims to determine whether vegetation size, multiplicity, and position in patients with infective endocarditis (IE) pose a risk factor for cerebral embolism and long-term mortality.

Despite medical advances, IE remains a disease with high morbidity and mortality. Cerebral embolism is one of the most common and devastating complications of IE. Early surgery for patients with surgical indications aims to avoid this complication. Recent ACC/AHA and ESC/EACTS guidelines emphasize that surgery should not be delayed once a surgical indication has been established. However, when addressing vegetations, these guidelines consider only the size of vegetations as a criterion for surgical indication. Furthermore, other factors, such as the location of the vegetation, a history of prior stroke, or the type of microorganism causing IE, may also contribute to the mechanism of cerebral embolism. Additionally, the 10 mm vegetation size threshold has persistently been used to assess embolic risk in IE patients, yet variables such as multiple vegetation locations or the importance of the affected valve have never been adequately examined.

The purpose of this study was to assess the size, multiplicity, and position of vegetations and their association with cerebral embolism and long-term mortality in IE patients. A total of 419 patients with IE admitted to a single institution from November 2005 to August 2017 were retrospectively reviewed, of whom 273 underwent surgery. The primary endpoint was all-cause mortality, and the secondary endpoint was cerebral embolism. Cox regression analysis and logistic regression were performed to identify risk factors for 30-day mortality, long-term mortality, and cerebral embolism. Age (HR = 1.02), renal failure (HR = 4.21), surgery (HR = 0.31), and a high APACHE II score (HR = 1.08) were associated with increased long-term mortality. However, vegetation size, multiplicity, and position were not significantly associated with long-term mortality. Still, a mitral vegetation size greater than 10 mm (OR = 2.25) was an independent risk factor for cerebral embolism.

The authors conclude that mitral vegetation size over 10 mm is a risk factor for cerebral embolism, and for this group, early surgery could be considered to prevent cerebral embolism.

COMMENTARY:

Today, IE remains one of the greatest challenges faced by different medical specialists, not only due to its diagnostic difficulty from its varied clinical presentations but also due to the complexity of its medical and surgical treatment. The in-hospital mortality rate of IE ranges between 15% and 20%, with one-year mortality close to 40% in many series. These figures contrast with the excellent outcomes in this study by Song et al., with a 30-day mortality of 8.8% and long-term mortality of 29.1% after a mean follow-up of 61.5 months. In the last decade, the trend has leaned towards earlier surgical intervention in patients with IE who meet the appropriate criteria. The three main reasons for early surgery are heart failure, uncontrolled infection, and embolism prevention. Scientific evidence supporting early surgery for IE with large vegetations to improve survival is limited, mainly based on a small randomized study and a recent meta-analysis.

Song et al., through their study of 419 IE patients with a mean follow-up of over five years, shed light on the implications of certain vegetations for cerebral embolism and long-term mortality. Interestingly, the increase in these complications was not associated with multiple vegetation locations or vegetations on the aortic valve. However, mobile

vegetations larger than 10 mm located on the mitral valve posed a significant risk of stroke. The latest ACC/AHA and ESC/EACTS guidelines for IE precisely use the criteria of a vegetation >10 mm, mobile vegetation, and particularly involvement of the left heart chambers to decide on an indication for early surgery. The results of this study align with these societies' recommendations, thereby adding evidence to define which patients might benefit from early surgery for IE.

One limitation of the study, aside from its retrospective nature, is the unknown incidence of subclinical cerebral embolism, as brain imaging was only performed for patients presenting neurological symptoms.

As often, reality is far more complex than theory, and an individualized study of each case is essential to decide which patients to operate on and, more importantly, when. Numerous variables must be considered before determining which patients to intervene early, including associated comorbidities; patient frailty and baseline status; surgical risk; time since antibiotic initiation; absence of heart failure or valve destruction; surgical factors such as aortic calcification, coagulation status, and other factors. In fact, 51 patients meeting surgical criteria per guidelines were not operated on due to reasons such as multiorgan failure or severe comorbidities. From now on, however, the finding of a large, mobile vegetation, especially on the mitral valve, should be more heavily weighed in our mental algorithm for decision-making in patients with IE surgical criteria.

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José Manuel Martínez Comendador

Reoperations in cardiac valve surgery: a review of major considerations

This review article provides an exhaustive analysis of perioperative considerations and essential techniques in cardiac valve reoperations.

We present an in-depth review article that tackles a topic of growing interest for cardiac surgeons: cardiac reoperations, specifically valve reoperations. This article is structured into two clearly defined sections. The first section focuses on the preoperative evaluation of patients in this context, emphasizing the importance of surgical risk assessment and interpretation with the help of a multidisciplinary team to facilitate informed decision-making. Additionally, the importance of recommended complementary imaging tests before performing reoperations on these patients is directly addressed. To conclude this first section, an overview is provided of various surgical strategies that must be planned in advance to maximize successful outcomes.

The second section of the review specifically addresses reoperations on the aortic, mitral, and tricuspid valves. It offers recommendations on surgical approaches and techniques based on individual circumstances, providing valuable information to optimize overall outcomes in valve reoperations.

The number of cardiac valve reoperations is experiencing exponential growth, mainly due to the aging population and the increase in bioprosthetic implant procedures, both surgical and percutaneous. This rise leads to a correlating increase in cases of endocarditis and structural deterioration of these bioprostheses. This trend is expected to continue in the near future, especially with the imminent introduction of percutaneous aortic valve implants (TAVI) in low-risk patient groups. In this context, possessing the necessary knowledge and technical skills to perform successful reoperations in these patients has taken on unprecedented importance in the modern era of cardiac surgery.

Cardiac reoperations demand an even higher level of expertise than the first intervention. Technical complexity is largely influenced by the presence of pericardial and mediastinal adhesions, which become more pronounced with more recent surgeries and an increased number of prior interventions. Additionally, patients requiring reoperations often present with a higher burden of comorbidities and frailty, factors that inevitably influence a less favorable prognosis.

Screening and surgical risk assessment

The Heart Team approach is central to the evaluation of patients anticipated to require a reoperation. In decision-making, both clinical and anatomical considerations of the patients are given equal weight.

Although traditional surgical risk scores, such as EuroSCORE II or the STS scale, continue to be useful in predicting outcomes for reoperated patients, controversy remains regarding which scale is most appropriate for mortality prediction. Individual risk factors, like the NYHA functional classification, remain pertinent, demonstrating a mortality rate of 1.6% in functional class I and 20.8% in functional class IV. Scheduled procedures reflect a mortality rate of 1.4%, while urgent and emergency cases increase this figure to 8% and 37.5%, respectively, underscoring the critical importance of performing surgery before clinical deterioration occurs.

In the context of valve reoperations, concomitant procedures, such as additional coronary surgery, have shown a negative impact on outcomes. Therefore, current trends lean towards percutaneous revascularization whenever possible. All recognized

comorbidity parameters that increase surgical risk in a first operation, such as low ejection fraction, liver or renal dysfunction, also impact reoperations.

The complexity of surgery is also influenced by other specific surgical factors. These include the number of previous operations, the degree of paravalvular or infected tissue calcification, the presence and location of patent grafts, and the proximity of mediastinal structures to the sternum in anticipation of a re-sternotomy.

Lastly, but no less importantly, the surgeon's skill and experience play a critical role in achieving successful outcomes in these procedures. Multiple studies have shown a volume-dependent correlation between surgical experience and outcomes in high-complexity surgeries.

Preoperative assessment

Today, two imaging tests are essential for thorough preoperative evaluation in any patient undergoing a valve reoperation: transesophageal echocardiography (TEE) and electrocardiography-synchronized computed tomography (CT).

TEE provides a detailed visualization of valve morphology and dysfunction mechanisms, which is crucial for decision-making. For instance, it allows determining if a cardiac reoperation is necessary for significant paravalvular leakage or if a transcatheter valve-in-valve procedure is more suitable in cases of transvalvular insufficiency. Another benefit of TEE is its ability to distinguish between thrombus, pannus, and vegetation, which can be critical in treatment planning. In cases of endocarditis, TEE is absolutely essential, as it not only enhances valve and vegetation visualization but also detects abscesses and fistulas with high precision. Furthermore, positron emission tomography (PET/CT) can be valuable in cases of prosthetic endocarditis, adding substantial diagnostic value.

Synchronized CT is another highly recommended test for this patient group, providing essential information to enhance safety in any reoperation procedure. The risks of damage to various structures during a re-sternotomy are considerable. CT provides reference points for the location and proximity of critical structures such as the aorta, innominate vein, right heart chambers, and previously placed grafts. Additionally, it provides details on the degree of aortic calcification, the type and location of paravalvular tissue, and heart rotation. It is estimated that in nearly 20% of cases, CT information prompts a modification in the surgical approach and strategy. For instance, when mediastinal structures are too close to the sternum, peripheral cannulation and initiation of cardiopulmonary bypass (CPB) before sternotomy may be preferred. In mitral or tricuspid surgery cases, even a right minithoracotomy may be considered. Meticulous planning of the surgical strategy and preventive maneuvers have been shown to reduce intraoperative complications, clamping and CPB times, myocardial infarction episodes, and ICU stays.

In patients with a history of coronary surgery, coronary angiography becomes necessary. However, if the risk of coronary disease is low, synchronized coronary CT may suffice for a complete assessment.

Perioperative management and technical considerations

Primarily based on CT findings, different cannulation alternatives for initiating CPB can be considered. If femoral cannulation is chosen, percutaneous ultrasound-guided cannulation can be performed if familiar. External defibrillator pads should be placed in all patients before starting the intervention, as dense pericardial adhesions will likely prevent the use of internal defibrillation paddles. In high-risk anatomical scenarios, it may be prudent to initiate CPB before opening the chest to prevent potential ruptures,

although this measure may increase bleeding. Throughout the procedure, meticulous hemostasis must be practiced, with the use of antifibrinolytic agents and coagulation factor replacement as needed to control excessive bleeding.

Planning the myocardial protection strategy is crucial. Cold cardioplegia should be administered following recommended doses and timings. In cases of aortic insufficiency or patent coronary grafts, retrograde cardioplegia may be suitable.

A fundamental practice is to carefully review prior surgical reports. When feasible, the option to modify valve implantation techniques should be considered to simplify surgery. This may involve implanting prostheses in previously placed Dacron conduits, using percutaneous valves in open-heart surgery, or opting for sutureless prostheses. Automated knot-tying devices can also be highly beneficial for reducing surgical times in these cases.

Reoperations on the aortic valve

Reoperations on the aortic valve account for approximately 10% of all procedures related to this valve structure. Published series indicate that this type of reoperation can achieve results comparable to those of primary surgeries. However, due to the particular technical complexity associated with aortic valve reoperations in patients with prior TAVI implants, the mortality rate is higher compared to removing surgically implanted bioprostheses, as detailed in previous blog articles.

Reasonable alternatives to sternotomy may include minimally invasive access routes, such as superior partial sternotomy or anterolateral thoracotomy. These approaches reduce the need for pericardial dissection, decrease the risk of damaging coronary grafts, and preserve sternal integrity. Ultimately, these factors contribute to a higher likelihood of early extubation and lower risk of mediastinitis.

For over a decade, the TAVI valve-in-valve procedure has been used to treat dysfunctions in aortic bioprostheses across various patients, demonstrating safety and rapid post-intervention recovery. However, certain considerations should be noted. Potential drawbacks include higher rates of aortic insufficiency and patient-prosthesis mismatch. These complications have shown an association with higher short-term mortality in high-risk patients compared to conventional reoperations. Nonetheless, understanding long-term outcomes remains limited due to the retrospective nature of studies and limitations in clinical follow-up.

Reoperations on the mitral valve

Achieving proper exposure of the mitral valve during this type of reoperation is crucial. The most commonly used approach is the left atriotomy through the Sondergaard groove. However, due to the firm adhesions that typically develop, the dissection necessary for adequate exposure is not straightforward. Alternatively, the right atrial transseptal approach provides excellent mitral valve exposure and requires less dissection to expose the left atrium. This approach has gained prominence as the predominant choice in mitral reoperations.

When close proximity of vital structures to the sternum prevents standard access, right thoracotomy may be a valid alternative. However, this option is limited in cases of aortic insufficiency exceeding a moderate degree due to ventricular dilation resulting from cardioplegia. Additionally, for concomitant surgeries other than tricuspid surgery, careful evaluation should be performed before selecting this approach.

In cases of severe mitral annular calcification (MAC), the risk of complications is greatly amplified. In scenarios requiring partial or total decalcification of the annulus, the risk of

atrioventricular sulcus rupture can be minimized by using a patch of autologous pericardium sutured to the left ventricle, annulus, and left atrium. This patch provides support to the prosthesis. In certain cases, and increasingly when specific anatomical criteria are met, percutaneous prosthesis implantation during open-heart surgery or even percutaneous mitral valve implantation via a transcatheter procedure may be considered. Both techniques have been discussed recently in other blog entries.

If paravalvular leakage is the reason for surgery, various solutions are available. These include using percutaneous closure devices, direct surgical closure, applying a pericardial patch to close the defect, or even implanting a new valve, depending on the size and location of the dehiscence.

In experienced hands, as we have previously detailed, the so-called "Commando" technique can be applied. This involves artificially creating a new mitroaortic curtain using a pericardial patch. In cases of patent grafts, mitral surgery can be effectively performed with the heart in ventricular fibrillation, avoiding graft manipulation and damage.

The most common reasons for mitral reoperation are structural dysfunction and endocarditis. In cases of dysfunction arising after previous mitral repair, usually due to mitral ring dehiscence or neochord rupture, re-repair may be attempted. However, the likelihood of success is lower in a re-repair, although success rates are higher in cases of early dysfunction.

Reoperations on the tricuspid valve

In the absence of the need for concomitant surgery, a right thoracotomy approach may emerge as a valuable alternative. This approach can be performed without requiring aortic clamping, allowing the heart to beat throughout the procedure.

In terms of primary etiology, the two main reasons for this reoperation are bioprosthetic dysfunction and endocarditis. In particular, endocarditis recurrence is more frequent among individuals with endocardial electrodes and those who abuse intravenous drugs (ADVP).

A significant proportion of patients requiring tricuspid reoperation have high surgical risk and limited life expectancy. Therefore, we emphasize the importance of multidisciplinary evaluation and appropriate risk scale application, such as the TRI-SCORE, to support clinical decisions. As highlighted in previous review articles on this blog, timely referral of these patients is essential, before complications associated with right heart failure fully manifest. Severe pulmonary hypertension (PH) is widely recognized as an independent predictor of poor prognosis. Currently, the consideration of the aortopulmonary pressure ratio is emphasized, as it has shown superior predictive value even compared to isolated PH.

COMMENTARY:

This article underscores a fundamental message: assessing the risk associated with cardiac valve reoperations is a complex challenge that must be addressed with an individualized and detailed approach. This is because the risk depends not only on patient parameters but also on the nature of the procedure required. In particularly complex cases, collaboration with a multidisciplinary team can be highly beneficial in ensuring informed and accurate decision-making.

The second core message of the text is that, through rigorous preoperative evaluation, careful perioperative approach, and continuous advancements in surgical techniques, in certain cases, valve reoperation should no longer be considered an automatic predictor

of mortality. Surgery remains a highly effective option, especially for patients at low or moderate risk, who need to undergo a valve reoperation.

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Section VI:

Miscellaneous

José Manuel Martínez Comendador

Early lead extraction for infected implanted cardiac electronic devices

This review, published in JACC, addresses the global impact of infections in implanted cardiac electronic devices (CIEDs), providing treatment recommendations and potential improvements in application.

Implanted cardiac electronic devices (CIEDs) play an invaluable and growing role in managing cardiac arrhythmias and preventing sudden death. However, CIED infections (CIED-I) are increasingly common, presenting a significant public health challenge worldwide. In this context, the early extraction of CIED leads may offer an effective solution to minimize the impact of these infections. This updated review examines the impact of CIED-I, provides treatment recommendations, and discusses potential improvements in their implementation:

1. Epidemiology of CIED-I and Clinical and Economic Impact

The annual incidence of CIED-I is estimated between 1.2% and 3.4%. Studies like WRAP-IT and registries such as POINTED have significantly demonstrated that CIED-I negatively impacts quality of life and survival. Known risk factors, such as renal failure and immunosuppression, are highlighted, as well as less evident factors, such as being younger or receiving oral anticoagulant treatment.

The economic impact of CIED-I varies significantly depending on the geographic region. Globally, the average cost of a CIED-I can range from 15,000 to 60,000 USD, with most expenses attributable to hospital care.

2. Clinical Outcomes

Optimal treatment for CIED-I includes antibiotic therapy and complete extraction of the infected device. Numerous studies have shown a high procedural success rate exceeding 95%, with complication rates below 4% and mortality rates under 1%. Conversely, antibiotic treatment without device extraction increases 30-day mortality sevenfold, and annual mortality nearly triples (40% compared to 14% when extraction is performed).

Furthermore, early device extraction has been associated with higher one-year survival rates compared to delayed extraction following antibiotic treatment failure, with survival rates around 15% for early extraction compared to 35% for delayed extraction. It is essential to note that patient cohorts with delayed extractions often include older individuals, those with frailty, or even those with terminal conditions, potentially complicating result interpretation. Finally, reinfection incidence is substantially lower when a complete system extraction is performed (1% compared to 50%).

3. Clinical Guidelines and Real-World Practice Patterns

Current clinical guidelines, including those from the American Heart Association, the British Heart Rhythm Society, the European Society of Cardiology, the Heart Rhythm Society, and EHRA, recommend the complete extraction of the infected device in cases of local or systemic infection, bacteremia, or endocarditis, considering it a Class I indication. Additionally, three of these guidelines explicitly suggest early and complete CIED extraction upon infection diagnosis. However, U.S. Medicare data shows that over 80% of patients do not receive the recommended complete system extraction per Class

I indication. Other relevant studies from Europe, covering a four-decade experience, indicate that just over half of patients undergo system extraction upon confirmed CIED infection.

4. Barriers to Proper Guideline Adherence

A 2020 survey conducted by EHRA/ESC identified three main barriers limiting proper adherence to clinical guidelines for CIED-I management. First, inadequate identification or diagnosis of device infection, reflecting a lack of knowledge and skills among general practitioners to effectively diagnose this condition. Second, the difficulty of referring patients to appropriate centers due to distance or lack of access to reference centers. Lastly, it is crucial to highlight the barrier of assessing the feasibility of system extraction, especially in patients with multiple comorbidities, advanced age, or leads implanted many years ago. This situation creates an inappropriate perception of both the procedure risk and associated mortality, potentially leading to dismissal of cases that could be eligible for extraction.

5. Strategies to Address Challenges in Proper CIED-I Management

One strategy involves incorporating an alert system in the patient's electronic health record, enabling responsible physicians to activate the necessary mechanisms early and thus comply with guideline recommendations. Additionally, creating expert multidisciplinary teams, including specialists in infectious diseases and trained professionals for device extraction, is essential. This approach allows comprehensive management of CIED-I, enhancing the treatment's efficacy and safety for these patients.

COMMENTARY:

This article focuses on reviewing the epidemiology, clinical, and economic impact of CIED-I on health systems. Some of the most relevant and clear findings from this review are the high success rate of early extraction procedures, as well as their low mortality and major complication rates, provided that the procedure is performed promptly and with the necessary resources. However, it also highlights the low adherence to guideline recommendations among healthcare professionals involved in CIED-I management. This issue is mainly due to difficulties in diagnosing CIED-I, inadequate patient referral to reference centers, and misconceptions about device extraction. It is crucial for all professionals involved in managing CIED-I to be informed and updated on best practices to ensure patient safety and treatment efficacy.

In Spain's National Health System, we have solutions to optimize CIED-I management, as mentioned in this review. In most autonomous communities, electronic health records are available to facilitate early diagnosis and expedite referral for prompt extraction. Furthermore, many tertiary hospitals across the country have specialists dedicated to this pathology, facilitating referral from hospitals not equipped to perform extractions with maximum safety.

A previous study conducted at our hospital, published by Mosquera et al. several years ago, demonstrated the remarkable efficacy and safety of excimer laser-assisted transvenous lead extraction in high-risk patients, supporting the outcomes described in this review. This was only possible due to meticulous perioperative patient assessment and joint evaluation by all involved services (cardiologists, infectious disease internists, electrophysiologists, and cardiac surgeons), allowing for early detection and extraction in most cases. Additionally, a strict institutional protocol with a pre-established rescue surgical plan and comprehensive intraoperative invasive monitoring was implemented

for each patient to minimize response time in case of major complications. Finally, all procedures were conducted in an operating room equipped for open or endovascular surgery, led by an experienced operator with immediate availability of extracorporeal circulation (ECC) surgery. These aspects are crucial to ensure the safety and effectiveness of the procedure in patients with CIED-I.

Although infected device extraction is a highly effective procedure, we must not overlook that, in some high-risk surgical patients—such as those with leads implanted for over eight years, significant frailty, or limited life expectancy—chronic antibiotic therapy may be an acceptable and effective option. Given the aging population and the projected increase in device implantations in the coming years, careful case-by-case evaluation will be essential, considering all available options before making the drastic and difficult decision not to extract the infected device in certain patients.

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Pablo Fernández de Aspe

The latest in pacing: leadless dual-chamber pacemaker

A study on the first experience with transcatheter implantation of a leadless dual-chamber pacemaker in humans.

Conventional pacemakers are antibradycardia pacing systems consisting of a pulse generator connected to transvenous leads. Although these devices are highly effective, they are associated with complications related to the pocket housing the generator and the leads themselves (infection, hematoma, lead dysfunction, venous thrombosis, tricuspid valve injury, etc.).

Totally intracardiac leadless pacemakers, implanted via transcatheter, were developed to overcome these limitations and represent an excellent option for specific patient profiles, such as those who have experienced an infection with a prior pacing device, are at high risk of infection, have developed fractures in conventional pacemaker leads, or present with subclavian vein thrombosis, complicated venous access, tricuspid valve disease, or bioprosthesis at that level.

To date, only a single-chamber leadless pacemaker for right ventricular pacing was available, which neither allows atrial pacing nor achieves optimal atrioventricular (AV) synchrony, making it suboptimal for patients with sinus node dysfunction or those requiring nearly 100% AV synchrony. In this context, the leadless dual-chamber pacing system emerged.

The AVEIR DR™ i2i™ (Abbott™, Chicago, Illinois, USA) study is a prospective, multicenter, single-group trial evaluating the safety and efficacy of the leadless dual-chamber pacemaker. The study included 300 patients with conventional indications for dual-chamber pacing and an age of ≥18 years. Patients with mechanical tricuspid prostheses, inferior vena cava (IVC) filters, or preexisting leads were excluded. The primary safety endpoint was freedom from device- or procedure-related complications at 90 days. The primary efficacy endpoint was a combination of adequate atrial capture threshold (≤3 V/0.4 ms) and sensing amplitude (P wave ≥1 mV) at 90 days. The secondary efficacy endpoint was AV synchrony of at least 70% at 3 months. As there was no control group, outcomes were compared against prespecified safety and efficacy targets.

A total of 300 patients were included, with a mean age of 69 years, and 62% were male. The primary indications for implantation were sinus node dysfunction (63%) and atrioventricular block (AVB) (33%). The implantation procedure was successful (both leadless pacemakers implanted with proper function and communication) in 98.3% of cases.

The primary safety endpoint (absence of device- or procedure-related complications at 90 days) was achieved in 90.3% of patients, surpassing the prespecified target of 78% ($p < .001$). A total of 35 device- or procedure-related complications occurred in 29 patients, spanning a wide severity range (from cardiac tamponade to urinary retention). Among the 35 complications, notable events included 9 episodes of atrial fibrillation, 2 pericardial effusions related to atrial pacemaker implantation (one requiring pericardiocentesis), 6 intraprocedural pacemaker dislocations (5 atrial and 1 ventricular), and 5 postprocedural atrial pacemaker dislocations (all displaced pacemakers were retrieved percutaneously). There were no device- or procedure-related deaths.

The primary efficacy endpoint (adequate atrial capture threshold and atrial sensitivity amplitude at 90 days) was achieved in 90.2% of patients, surpassing the prespecified

target of 82.5% ($p < .001$). The median atrial pacing threshold was 0.82 ± 0.70 V at 0.4 ms, and the median P-wave amplitude was 3.58 ± 1.88 mV. This criterion was not met in 22 patients with inadequate P-wave sensing and 6 patients with an inadequate pacing threshold.

AV synchrony of at least 70% was achieved in 97.3% of patients, exceeding the prespecified target of 83% ($p < .001$).

The authors conclude that the leadless dual-chamber pacemaker met the primary safety endpoint and provided atrial pacing and adequate AV synchrony during a 3-month follow-up period post-implantation.

COMMENTARY:

For over half a century, cardiac pacing for bradycardia has been achieved with systems comprising a subcutaneous pulse generator connected to one or more transvenous leads. While effective, these systems are associated with serious complications related to the pocket and leads, particularly infections and lead dysfunction, which can affect up to 1 in 6 patients with transvenous systems after 3 years of follow-up.

Leadless pacemakers overcome the limitations of conventional pacemakers and are an excellent option for patients at high risk of infection, those with prior lead dysfunction, or those with challenging venous access, among others. However, until now, no leadless pacemakers capable of achieving nearly 100% AV synchrony have been available.

The AVEIR DR™ i2i™ study offers the first human experience with a fully intracardiac, percutaneously implanted dual-chamber leadless pacemaker system. This system retains the benefits of existing leadless pacemakers by eliminating pocket- and lead-related complications, while overcoming their limitations by offering atrial pacing and AV synchrony, making it an appealing alternative for select patients.

Nevertheless, this study has several limitations, most notably the lack of a control group, so outcomes were compared to prespecified targets. To date, no randomized clinical trial has directly compared leadless pacemakers with conventional pacemakers (comparisons have been made with historical cohorts). Despite these limitations, published studies and accumulated clinical experience support their use given demonstrated functionality, electrical performance, and safety.

Other limitations include the small sample size and short follow-up, which limit conclusions regarding long-term complications, battery longevity, and management at battery depletion. Several questions will need to be addressed in the future: Is extraction or abandonment preferred upon battery depletion? Is it possible to implant a new leadless pacemaker in parallel? Is the implantation of multiple devices in the atrium feasible and safe?

In conclusion, this study presents a promising leadless dual-chamber pacing system that offers the advantages of avoiding pocket- and lead-related complications and expands its indications by providing atrial pacing and nearly 100% AV synchrony. Nonetheless, further data are needed before integrating it into routine clinical practice. A randomized trial with a control group is also essential to compare this new pacemaker system with conventional dual-chamber pacemakers and to provide longer-term follow-up to assess the stability of electrical parameters, battery longevity, and optimal management at battery depletion. Finally, optimizing implantation technique and device technology will be crucial to improve safety, particularly regarding the number of dislocations.

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Raquel Vázquez García

Hybrid Ablation: A Strategy Against Persistent Atrial Fibrillation?

A review paper published in JACC on the available evidence regarding hybrid ablation in patients with persistent atrial fibrillation.

Atrial fibrillation (AF) is the most common tachyarrhythmia in adults and is associated with high morbidity and mortality. Its estimated prevalence is between 2-4% and is expected to increase progressively in the coming years. The benefits of rhythm control in these patients include not only a significant improvement in quality of life but also reduced hospitalizations and mortality, particularly in patients with ventricular dysfunction. Ablation techniques generally focus on isolating the pulmonary veins (PVs), as they represent the most common arrhythmogenic substrate. The efficacy of endocardial ablation in patients with paroxysmal AF is approximately 70-80%; however, in persistent AF, this efficacy is more modest, reaching a success rate of 40-70%, with approximately 1 in 3 patients requiring a repeat procedure. Additionally, the complex pathophysiology of persistent AF necessitates exploring substrates beyond electrical isolation of the PVs.

To improve these outcomes and address new electroanatomic substrates, hybrid ablation was developed. This is a novel technique that combines a surgical epicardial approach with conventional endocardial catheter ablation. The epicardial surgical access can be achieved through thoracoscopy, subxiphoid approach, or minithoracotomy. Lesions are created (using various available radiofrequency devices) to isolate the posterior atrial wall through one of three methods: PV isolation and connecting lines between each pair of veins at the atrial roof and floor; posterior “box” isolation; or posterior wall ablation. In the first approach, a clamp device (e.g., Atricure® Isolator Synergy®) is applied around the PVs, followed by creation of roof and floor lines. The second approach is technically simpler, as two specific devices (Estech® COBRA Fusion® and Medtronic® Cardioblate Gemini-S®) jointly encircle the antrum of the four PVs. In the third approach, a single access is used to perform ablation with the Atricure® EPi-Sense® device, applying radiofrequency to the posterior atrial wall. Additionally, some groups perform accessory lesions at other levels, and epicardial left atrial appendage exclusion using a clip (AtriClip® Pro®, Pro-2®, and Pro-V®) is recommended as standard. Subsequently, endocardial ablation assesses the zones blocked through the epicardial approach, with any detected gaps being re-ablated. Procedures can be simultaneous or staged, beginning with epicardial application, followed by endocardial ablation after 1-3 months. No studies compare these two strategies; however, a staged approach allows for detection of reconnections following the formation of the definitive epicardial scar, making endocardial ablation a rescue step.

A significant limitation of hybrid ablation is lesion durability. Long-term data following both procedures is lacking, and the high heterogeneity of observational studies limits interpretation of their results. This is compounded by the variability in surgical approaches, technologies, and procedural intervals, resulting in a wide range of reconnection rates (7-80%) across studies. The carina between PVs and the atrial roof line are the most common sites of reconnection.

Regarding procedural efficacy, this article compiles results from various observational studies. The percentage of patients free of tachyarrhythmias at 1 year, depending on whether procedures were performed sequentially or simultaneously, is 83% (95% CI: 68%-94%) and 71% (95% CI: 68%-75%), respectively. However, these results should be interpreted cautiously due to several limitations. One limitation is the varying definition of tachyarrhythmia and its monitoring across studies. In most cases, the goal was to

detect 30 seconds of any type of atrial arrhythmia, but detection methods varied, with some studies using a subcutaneous Holter monitor and others using serial ECGs, the latter of which have a lower detection capability and may overestimate procedural success. Another major limitation previously mentioned is the heterogeneity in lesion types, approaches, devices, and procedural intervals, preventing standardized action and outcome comparison. Moreover, the external validity of these studies is limited; although they included patients with persistent AF, they generally excluded patients with dilated atria (common in patients with longer AF duration due to atriopathy progression) or ventricular dysfunction (groups in which rhythm control has demonstrated mortality reduction).

In 2020, a meta-analysis of 34 observational studies demonstrated higher success rates with hybrid ablation (70%) compared to conventional ablation (50%). That same year, the CONVERGE study was published—the only randomized trial with 150 patients comparing hybrid and conventional ablation in patients with persistent and long-standing persistent AF (>12 months), including those with more advanced atrial pathology and an average AF duration of 4 years. After one year of follow-up, hybrid ablation increased the percentage of patients free from atrial arrhythmias (67% vs. 50%) and significantly reduced arrhythmic burden.

Despite these positive outcomes, it is known that hybrid ablation is a more invasive technique, inevitably increasing complication risks. To date, this risk is 3-7 times higher than with conventional interventional ablation, mainly due to the surgical procedure. Possibly, standardization of these techniques could optimize and reduce these figures.

COMMENTARY:

It is clear that new approaches are needed to address the complex pathophysiology of persistent AF. Hybrid ablation offers both benefits and challenges. Current evidence is limited and highly heterogeneous, but it points to the potential benefits of this technique, even in patients with more advanced disease stages, albeit with an increase in adverse effects.

The FAST study provides some information on one of the main gaps in this technique. This study found that exclusive epicardial ablation in AF patients was superior to conventional interventional ablation in maintaining sinus rhythm over 7 years of follow-up. Therefore, it might be expected that if a single procedure provides this durability, even better results could be achieved with both approaches. However, the reality is that we currently lack data beyond one year following the two procedures. Another relevant detail is that we are comparing a procedure that involves two ablations with a single endocardial procedure, which logically could overestimate the effect of hybrid ablation, and the ongoing incorporation of new technologies in endocardial approaches will likely enhance the performance of this technique in the future.

We should also note that, at present, there is insufficient evidence supporting ablation (at least endocardial) of substrates beyond the PVs. Posterior wall ablation has sparked interest in this patient group due to its embryologic origin shared with the PVs, heterogeneous fiber orientation that facilitates micro-reentry formation, and rich autonomic innervation— all possible pathophysiological mechanisms of persistent AF. Endocardial ablation at this level is technically complex with a risk of esophageal perforation of 0.5-0.6%, so epicardial ablation could facilitate more durable transmural lesions at this site. Based on this, could epicardial ablation demonstrate the need to ablate these extrapulmonary substrates? This is still an open question, and new clinical trials are needed to answer it.

In conclusion, many questions remain to be answered before standardizing this therapy. The 2020 European Society of Cardiology guidelines recommend (Class IIa) hybrid ablation for patients with symptomatic persistent AF following failed rhythm control with antiarrhythmic drugs and/or endocardial interventional ablation. Its application as first-line treatment for symptomatic persistent AF patients with risk factors for recurrence has yet to prove efficacy, with guidelines offering only a Class IIb recommendation based on expert opinion. Upcoming clinical trials will shed more light on this technique, potentially providing a new therapeutic option for these patients with a complex approach.

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Adrián Muinelo Paúl

Late incidence and recurrence of new-onset atrial fibrillation after isolated aortic valve replacement surgery

This multicenter retrospective cohort study investigates the occurrence of atrial fibrillation after isolated aortic valve replacement (AVR), examining the recurrence of the arrhythmia and associated complications during long-term follow-up.

Atrial fibrillation (AF) is a known complication of cardiac surgery, with incidence rates varying significantly across series and centers. The incidence is recognized to be higher following AVR compared to other interventions. Nonetheless, several questions remain concerning its prognostic implications in the medium and long term.

The primary objective of this work by Björn et al. is to provide evidence on the recurrence of atrial fibrillation during postoperative follow-up and complications associated with new-onset atrial fibrillation (NOAF) occurring during the same admission. A retrospective cohort of 1,073 patients undergoing AVR was analyzed, recruited across four hospitals in Finland. After excluding patients with a history of preoperative AF, 529 patients with biological prostheses and 253 with mechanical prostheses were included. The median follow-up was 5.4 years. During hospitalization, 333 patients (42.6%) experienced NOAF, and 250 (32%) had AF post-discharge. Among those with mechanical prostheses, 64 (25.4%) had NOAF during hospitalization, and 74 (29.2%) developed AF after discharge. Meanwhile, in the bioprosthetic cohort, 269 (50.9%) experienced NOAF during hospitalization, and 176 (33.3%) post-discharge. Patients with NOAF during hospitalization had an increased risk of AF during follow-up in the combined cohort (HR = 3.68; $p < .001$) as well as in both individual cohorts. Patients with mechanical prostheses (HR = 2.05; $p = .025$) and bioprostheses (HR = 1.63; $p = .004$) showed a higher risk of death during follow-up.

The study concludes that NOAF during hospitalization is associated with a 2- to 4-fold increase in risk of AF during follow-up and a 1.6- to 2-fold higher risk of all-cause mortality post-AVR.

COMMENTARY:

AVR remains one of the most performed cardiac surgeries in Western centers, with AF as one of the most frequent complications cardiac surgeons encounter during the immediate postoperative period. This study not only provides evidence of the incidence of this significant postoperative complication but also emphasizes its long-term prognostic role.

The authors themselves recognize limitations, including the retrospective nature of the study and the fact that AF diagnosis was based solely on electrocardiogram (ECG) readings during follow-up appointments and in symptomatic cases caused by the arrhythmia or other factors. This is notable as it's possible that many asymptomatic paroxysmal AF episodes went undiagnosed post-discharge. Additionally, a more detailed collection of variables would have been beneficial. Knowing which intraoperative variables could predispose patients to NOAF could greatly impact the prevention of this complication. For instance, could the incidence of arrhythmic events vary based on the prosthesis type? It is well-known that AF rates are lower following TAVI compared to AVR, which raises the question of whether certain bioprosthetic options, such as sutureless prostheses, which involve less manipulation of the surgical field, were used and if their usage correlated with different AF incidence rates. Similarly, AVR can now be performed via various surgical approaches (traditional median sternotomy, mini-sternotomy, mini-thoracotomy). Determining whether surgical approach impacts the

development of postoperative AF would be highly relevant, especially in patients with predisposing factors for arrhythmia.

The difference in all-cause mortality during follow-up between patients with NOAF in both groups deserves attention. The cohort treated with bioprostheses shows a higher mortality rate than those with mechanical prostheses. However, within the mechanical cohort, the mortality curves between patients with and without NOAF are more distinctly separated compared to the bioprosthetic cohort. This observation raises the question of whether new-onset AF is a complication that impacts medium- and long-term prognosis, influencing mortality, or if it merely reflects greater frailty and comorbidities in these patients, thus serving as a prognostic marker for identifying those at increased risk of mortality during follow-up.

The central takeaway from this study, with a large sample size and robust statistical analysis, is that NOAF following AVR predisposes patients to AF recurrence during follow-up and is associated with higher long-term mortality. Future studies should focus more on identifying perioperative variables that could decrease the incidence of postoperative AF, ultimately aiming to reduce medium- and long-term mortality following AVR.

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Elio Martín Gutiérrez

Postoperative atrial fibrillation: risk factor or marker of adverse outcomes in the evolution of patients undergoing cardiac surgery?

A comprehensive meta-analysis investigating the impact of postoperative atrial fibrillation (POAF) on various postoperative complications, incorporating 57 studies and 246,340 patients.

Postoperative atrial fibrillation (POAF) has traditionally been considered a minor complication with limited impact on patients undergoing cardiac surgery. Its incidence varies depending on the series and the underlying heart disease treated, ranging between 40-60% for valve surgery patients and 10-30% for patients undergoing myocardial revascularization. Given its frequent reversibility—either through therapeutic measures or spontaneously within two months post-surgery—a definitive causal link with other postoperative complications has yet to be established. However, numerous studies have explored this association beyond the logical connection with increased mortality and a higher incidence of cerebrovascular accidents in the short and medium term.

This meta-analysis represents the most extensive review to date on this topic, encompassing 57 studies over a broad time frame from 1997 to the present (analyzed to determine temporal trends) and including multiple nationalities (although 13 potentially eligible studies were excluded solely for not being in English). Altogether, this study compiles data on 246,340 patients in an analysis with ample statistical power, considering, for the first time, mortality and five additional adverse events in the early postoperative phase of cardiac surgery, as well as mortality and two more adverse events during follow-up. The meta-analysis design is sound from all formal aspects of bias control, though an excessive permissiveness in model heterogeneity stands out—a limitation that authors and reviewers should have acknowledged.

The main findings reveal that POAF is significantly associated with increased postoperative mortality (OR = 1.92), incidence of cerebrovascular events (OR = 2.17), perioperative myocardial infarction (OR = 1.28), postoperative renal failure (OR = 2.74), and a prolonged hospital stay, both in general and in intensive/critical care. During follow-up, POAF was significantly associated with higher mortality rates (RR = 1.54), incidence of cerebrovascular events (RR = 1.21), and persistent/permanent AF (RR = 4.73). In the analysis of temporal trends, the association between POAF and increased postoperative mortality remained stable regardless of the period from which the studies originated. The method of diagnosing POAF, whether through a single ECG or continuous telemetry monitoring, also did not influence its impact on early postoperative mortality. However, POAF was associated with higher early postoperative mortality in patients undergoing myocardial revascularization surgery (OR = 2.4), without reaching statistical significance in combined valve and coronary surgery or isolated valve surgery, although statistical power was more limited in the third subanalysis.

The authors conclude that POAF has a significant association with mortality and the development of complications in the short and long term following cardiac surgery. However, causality for some of these associations remains to be determined in future studies.

COMMENTARY:

This is the most comprehensive review to date on POAF, both in terms of the number of included studies and its statistical power, as well as in its novel investigation of POAF's association with other complications previously suggested in individual studies.

POAF represents the most common cause of secondary AF. Its development involves various factors: preoperative (e.g., hypertension and, particularly, underlying ischemic or structural/valvular heart disease), perioperative (e.g., surgical trauma, local inflammation, fluid balance alterations, ionic disturbances), and postoperative (e.g., use of inotropic and vasoactive agents, lack of atrial pacing, respiratory complications). Given its high incidence and its demonstrated association with increased perioperative morbidity and mortality and extended hospital stays, the implementation of preventive measures could become one of the most efficient strategies in enhanced recovery recommendations for cardiac surgery patients.

The association between AF and increased perioperative morbidity and mortality, as found in this study, is also a matter of debate. The authors highlight the need to establish causal relationships that could substantiate the observed statistical significance. The pathophysiological link between AF and the increased incidence of cerebrovascular events is undeniable, which, combined with its association with other adverse events and postoperative morbidity, would justify its connection with extended postoperative stays and mortality. Moreover, the presence of a perioperative arrhythmogenic substrate could easily explain why these patients develop higher rates of persistent/permanent AF during follow-up, leading to further cerebrovascular events and mortality. Mortality during follow-up may also be justified by the association between AF and progressively worsening heart failure. However, the associations with renal failure or perioperative myocardial infarction are less clear, suggesting that AF might be a concomitant, non-causal factor, serving instead as a marker rather than a risk factor.

It is also noteworthy to distinguish de novo POAF, which occurs postoperatively, from undiagnosed paroxysmal AF at the time of surgery. This distinction could explain the survival impact in the group of patients undergoing myocardial revascularization surgery compared to those undergoing valve surgery, where silent paroxysmal AF might not have been considered and could act as a confounding factor. Lastly, the lack of superiority of continuous monitoring systems for POAF over daily ECGs is also notable. If continuous monitoring had shown superiority, it alone would have identified the statistical association with the adverse event, in this case, perioperative mortality.

The study by Caldonazo et al. will serve as a reference for future research, particularly to answer some of the questions raised by their analysis: What anticoagulation policy should be followed for patients developing POAF, given its association with future persistent AF, increased stroke risk, and follow-up mortality, as well as the better safety profile of new direct-acting oral anticoagulants? Could a subanalysis of the included studies help develop scoring models to identify patients at higher risk of developing POAF? Should protocols for the prevention of POAF be reviewed and applied systematically or selectively in high-risk patients? Finally, would reducing postoperative AF ultimately have a significant impact on short- and long-term mortality? This would ultimately confirm whether POAF acts as a factor or simply a marker of risk.

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Elio Martín Gutiérrez

Unclosed Appendage, a Missed Opportunity

This review paper updates the evidence regarding indications, techniques, and outcomes of concomitant left atrial appendage (LAA) closure in atrial fibrillation patients undergoing cardiac surgery.

The motivation for this work stems from a commentary on the results of the LAAOS III study, published mid-2021, which led to the inclusion of a class IIa recommendation in the 2021 European guidelines on valvular heart disease, advocating LAA closure during cardiac surgery in patients with a CHA2DS2VAsc score of 2 or higher. This work focuses on a nonsystematic review of the literature, emphasizing anatomical and technical aspects to optimize procedural outcomes, concluding with a review of current evidence and future perspectives.

The authors emphasize that the perspective on LAA closure should shift. Rather than considering it a minor or accessory procedure with a questionable risk-benefit balance due to potential complications and uncertain utility, it should be viewed as a valuable opportunity during cardiac surgery. LAA closure is a simple, safe procedure that significantly and permanently reduces the long-term stroke risk.

COMMENTARY:

We have all heard aphorisms like, “never trust the appendage of an eighty-year-old lady” or “the roof of the left atrium has no friends” during procedures. These phrases originated at the Cleveland Clinic and highlight the care taken in the mitral approach, as they reference two of the most fragile cardiac structures. Given that a surgeon’s experience is forged through complications, whether their own or others’, the lack of evidence supporting LAA closure relegated it for a long time to a class IIb recommendation, where the preferred option was “leave it alone” unless combined with an ablation procedure.

In nonvalvular atrial fibrillation, over 90% of emboli originate in the LAA, and in cases of AF associated with rheumatic valve disease, the rate is between 50% and 75%. In valvular, non-rheumatic AF, the rate lies between these two percentages. In structural heart disease, a minority of emboli originate from sites other than the LAA due to endocardial changes caused by regurgitation jets or inflammatory processes associated with rheumatic disease, creating thrombotic substrates.

Interest in structural interventions for percutaneous LAA closure in nonvalvular AF revived interest in a previously undervalued procedure. Once again, competition with interventional cardiology prompted surgeons to reconsider its importance. Devices like Watchman® and Amplatzer® Amulet® entered the market, and we adopted a classification of the LAA into four morphological types requiring some imagination: chicken wing, cactus, windsock, and cauliflower. Although many of us have seen appendages that do not fit these types, they relate to embolic risk and technical approach.

LAA anatomy includes the ostium, neck, and trabeculated region, which forms and retains clots in AF patients. The four LAA morphologies are classified based on total length and the angle/shape of the trabeculated portion and neck. Morphologies >4 cm include chicken wing and windsock, while <4 cm are cactus and cauliflower, with shorter morphologies carrying higher embolic risk. Longer shapes may have an angle <100º (chicken wing) or >100º (windsock), with smaller angles offering protection against emboli. The cactus and cauliflower types differ in lobule configuration: multiple around a main stem (cactus) or small, unbranched (cauliflower). Thus, in decreasing embolic risk,

these morphologies rank as cauliflower, cactus, windsock, and chicken wing, inversely correlated to their frequency in patients: 3%, 19%, 30%, and 48%, respectively.

The goal of LAA closure is to isolate circulation via neck manipulation, leaving a stump <1 cm from the ostium with continuous sealing of the trabeculated area. During this procedure, interference with adjacent structures, particularly the circumflex vessels in the left atrioventricular groove, should be avoided.

Suggested LAA closure techniques are highly variable, likely affecting outcome consistency. Basic techniques include linear suture (simple or double, endocardial or epicardial, with/without excision), intracavitary patching, circumferential ligature, purse-string suture, and the use of staplers or clips. However, endocardial double-suture line or epicardial clip exclusion or excision with subsequent suture line have shown the best results. Although considered equivalent, each approach has pros and cons. The endocardial technique provides sealing close to the ostium but carries a high risk of recanalization. Epicardial exclusion is suitable for any LAA type, is often combined with ablation, and ensures sealing; however, it is more complex and increases bleeding risk, requiring supportive bands and sealants. The AtriClip® has simplified epicardial approaches with open or minimally invasive designs (Pro®, Pro-V®, Pro2®), achieving >95% implant success. Failures primarily involve a residual stump >1 cm, which is preferable to failure from permeability in suture-line closure. In cases of LAA recanalization (endocardial suture or percutaneous closure), the outcome worsens as systemic coagulation increases in the LAA cul-de-sac. Stroke risk rises, not due to an embolus from a millimeter-wide opening but to thromboemboli originating elsewhere or local atherothrombosis in patients with advanced cardiovascular risk and CHA2DS2VAsc scores. For optimal clip positioning, particularly with concomitant ablation, severing the Marshall ligament, which runs between the lateral face of the LAA and the left pulmonary veins, is recommended.

The literature review highlights the work of Friedman et al., the first to demonstrate the benefit of concomitant LAA closure, and Whitlock et al. (LAAOS III), which consolidated guideline recognition. LAA closure almost halved the risk of new ischemic stroke, reducing stroke incidence by 2%. A meta-analysis from our center, also cited in the 2021 European guidelines, demonstrated LAA closure's protective benefit in patients with bioprosthesis/mechanical prosthesis/valve repair, those undergoing surgical ablation, or following various anticoagulation regimens. Even with continued anticoagulation, LAA closure offers synergistic protection during subtherapeutic anticoagulation periods, especially with vitamin K antagonists. Additionally, LAA closure provides a permanent benefit and reduces the need for interventional procedures if anticoagulation is suspended.

Finally, two controversies arise:

1. The authors question whether excluding the LAA alone is worthwhile without concurrent ablation, given the limited success of concomitant ablation in valvular heart disease AF. They conclude that there is insufficient evidence to make this claim, as no studies specifically address it. Ablation includes LAA exclusion, and while both reduce embolic risk, each has its target and indications, likely making them complementary. Patient selection for ablation plus LAA closure or LAA closure alone is necessary.

2. The LAA serves as a sensor for hypervolemia/volume overload, distending to release atrial natriuretic peptide. Although beneficial effects in AF patients are well-documented, where endocrine function is impaired,

recent studies suggest closure benefits for patients in sinus rhythm. Cardiac surgery patients have an increased risk of early or long-term AF development, heightening stroke risk. However, no randomized evidence supports systematic closure. The AtriClip® ATLAS study will address this question. Currently, no recommendation can be made, but for patients losing the LAA, diuretic therapy should be continued short- to mid-term postoperatively until neuroendocrine mechanisms readapt following correction of cardiopathy.

In any case, we can no longer view the LAA as a trivial appendix. It should be a therapeutic target in any AF patient undergoing surgery, providing a clear clinical benefit. The benefit will be permanent and complementary to cardiopathy correction. For example, in mitral insufficiency, the prothrombotic state increases after correcting atrial washout by eliminating regurgitation jets after valve repair or replacement. This is further reason not to leave the appendage open.

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Manuel Carnero Alcázar

Stand-alone surgical ablation for atrial fibrillation: expert opinion

Expert opinion by Dr. M. Carnero on the state of the art of stand-alone surgical ablation for atrial fibrillation (AF).

In 1987, JL. Cox described one of the most effective treatments for rhythm control in AF: the maze procedure or Cox-maze technique. This procedure aimed to isolate or disrupt all electrical mechanisms underlying AF, enabling sinus impulses to activate the entire atrium in an orderly manner. This isolation was achieved through a "cut and sew" technique on specific atrial regions identified in prior animal studies.

Iterations aimed at reducing block risk led to the development of Cox-maze II and Cox-maze III. Despite its high efficacy, the maze surgery was complex and not without risk due to the cut-and-sew nature of the procedure. Alternative energy sources emerged, allowing lesion sets to be created using radiofrequency and/or cryoablation (Cox-Maze IV), thus reducing risks associated with cut and sew and broadening indications.

In the 1990s, Haïsaguerre et al. found that radiofrequency catheter isolation of the pulmonary veins could interrupt paroxysmal AF, leading to a rise in percutaneous techniques. Meanwhile, atrial arrhythmia surgery, due to its invasiveness, was limited to procedures where it could be performed concomitantly with surgery for another structural or coronary condition.

In the last decade, however, reports of high recurrence following catheter ablation for persistent and long-standing persistent AF have emerged. Concurrently, new minimally invasive thoracoscopic approaches have renewed interest in stand-alone atrial arrhythmia surgery. For example, the latest European guidelines recommend stand-alone thoracoscopic AF surgery (IIa/B) for patients with paroxysmal or persistent AF refractory to antiarrhythmics who have a recurrence or high recurrence risk after catheter ablation.

Thoracoscopic stand-alone AF ablation relies on two principles: left atrial posterior wall isolation and electrical/mechanical exclusion of the left atrial appendage. Additionally, depending on AF substrate, patient characteristics, team technical expertise, or the setting (hybrid operating room vs. standard OR), additional lesions may be made in the right atrium, the coumadin ridge (a normal variant separating the superior left pulmonary vein ostium from the LAA), or the left atrial isthmus.

Unipolar or bipolar radiofrequency is used in thoracoscopic AF ablation. Technologies for electrically isolating the left atrial posterior wall include:

The classic box lesion (posterior wall and pulmonary vein isolation) with the Cardioblate Gemini™ (Medtronic™, Minnesota, USA)or combining Isolator Sinergy Clamp™ bipolar radiofrequency clamps (AtriCure™, Minnesota, USA) for the pulmonary veins and Coolrail™ linear pen (AtriCure™, Minnesota, USA) for left atrial posterior wall roof and floor lesions. This procedure electrically disconnects the left atrial posterior wall and pulmonary veins and ablates the coumadin ridge and Marshall ligament. Depending on devices and techniques, this lesion set can be achieved with a unilateral or bilateral approach using three ports. Compared to percutaneous ablation, the effectiveness is significantly higher. For instance, the FAST trial by Castellá et al. reported a 56% recurrence rate at 7 years for thoracoscopic patients versus 87% for catheter-based approaches. Stand-alone posterior wall ablation with the Episense™ system (AtriCure™, Minnesota, USA). This technique involves unipolar radiofrequency isolation of the posterior wall via a subxiphoid approach. It requires percutaneous pulmonary vein ablation, thus considered part of a hybrid rather than a stand-alone approach. One-year

AF survival with this technique was 68%, versus 50% for catheter ablation, as shown in the randomized CONVERGE trial.

In all cases, surgical exclusion of the LAA reduces thromboembolic complications. Methods for LAA occlusion include automatic staplers and clips (AtriClip™, AtriCure™, Minnesota, USA), though clips appear safer with more reproducible implant success. Surgical LAA exclusion not only prevents thrombus formation but also achieves electrical isolation, unattainable with catheter-based devices, significantly reducing arrhythmia recurrence.

Decision-making in symptomatic, refractory AF or high-risk patients post-optimal medical therapy and pulmonary vein catheter ablation is complex. Emerging technologies, such as pulsed-field ablation, show promise, though the effect of mechanistic approaches, such as “driver” ablation, remains undetermined. In this context, thoracoscopic AF surgery should be considered an additional step in patient management rather than an alternative. Hybrid programs combining percutaneous and minimally invasive surgical ablation in high-expertise centers may provide effective solutions for persistent or long-standing persistent AF patients, for whom medical or catheter treatments yield poor outcomes.

At the 2023 European Heart Rhythm Association Congress, results from the CEASE AF trial (available at https://esc365.escardio.org/presentation/265325) were presented, comparing hybrid surgical and percutaneous approaches versus percutaneous-only ablation in AF patients with no previous ablations. The principal investigator (Nicholas Doll, Schüchtermann Clinic, Bad Rothenfelde, Germany) reported an 83% relative risk reduction in AF recurrence with the hybrid arm versus catheter alone.

In Spain, AF surgery (stand-alone or concomitant) is underutilized compared to other European countries and the United States. This may be due to advanced AF stage at referral, economic constraints, lack of training, or limited awareness of the technique within the cardiology community. However, given the current scientific evidence, available technology, and growing demand for symptomatic AF treatment, there are increasingly more reasons—and fewer excuses—to support atrial fibrillation surgery.

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Elio Martín Gutiérrez

Concomitant Ablation of Atrial Fibrillation: No Longer or Why Not?

Comparison of perioperative and long-term outcomes in patients undergoing cardiac surgery with and without concomitant af ablation in a national registry from Taiwan.

The role of surgical ablation for atrial fibrillation (AF) has experienced a re-evaluation, similar to other procedures in recent years, due to a shift in focus on how certain heart conditions are perceived. Tricuspid regurgitation and left atrial appendage closure, also associated with AF, have followed a similar trajectory, leading to an overestimation of potential treatment candidates and blurring the lines between clinical utility and futility—all in the interest of generating case series. While ablation was never entirely abandoned, it thrived more decades ago, later facing a phase of disenchantment where recurrent arrhythmia cast it “more as a means to understand AF than as a true cure.”

Earlier periods allowed the development of concomitant AF ablation, including the description of cut-and-sew lesion patterns, the emergence, refinement, and selection of energy-based devices, surgical team training, and eventually integration into minimally invasive approaches, extending its application to isolated AF ablation. This growing case volume improved identification of candidates with lower recurrence rates (non-rheumatic valve disease, left atrial diameter <50 mm, non-permanent AF, and other markers of lesser atrial remodeling), avoidance of mistakes such as discontinuing oral anticoagulation (even when left atrial appendage was closed, and sinus rhythm remained stable), or limiting the excessive prolongation of extracorporeal circulation times and associated morbidity. European guidelines thus provided class IIa indications for symptomatic AF and IIb for asymptomatic cases considering concomitant ablation with other cardiac surgery. In American guidelines, concomitant ablation is class IA for mitral valve surgery and IB for aortic valve and/or coronary procedures. Despite high recurrence rates, the largest meta-analysis by McClure et al., including 23 clinical trials, revealed that concomitant ablation offers benefits in maintaining sinus rhythm, though it lacks survival impact.

Cheng et al. conducted an analysis of Taiwan's national health database from 2001 to 2016. They included 11,495 patients with preoperative AF undergoing diverse cardiac surgeries, of whom 3,255 had concomitant ablation, while 8,204 did not. After propensity score matching in a 2:1 ratio, comparisons were made between 2,828 patients with concomitant ablation and 4,106 without ablation. Radiofrequency was used in 71.2% of cases, and cryoablation in 28.8%. No differences were observed in hospital mortality (ablation 5.4% vs. 6.7%) or pacemaker implantation need (4.3% vs. 4.2%) among other analyzed perioperative complications. Likely related to prolonged surgical times and increased technical complexity, the ablation group showed higher rates of re-exploration due to bleeding (2.9% vs. 2.6%; $p = .0029$). With a mean follow-up over five years, mortality was significantly lower in the ablation group (5.7% vs. 7.7%, $p < .0001$), as were ischemic stroke (1.8% vs. 2.5%, $p = .0013$) and readmission rates (25.2% vs. 27.9%, $p = .0095$). There were no differences in pacemaker implantation need during follow-up (approximately 1.4%) or gastrointestinal bleeding (around 1.6%).

The authors conclude that concomitant AF ablation is safe and does not significantly increase perioperative complication rates, providing greater long-term benefits compared to isolated cardiac surgery without concomitant AF ablation, particularly in terms of improved patient survival.

COMMENTARY:

The study by Cheng et al. is one of the few in which concomitant AF ablation demonstrates a survival benefit. This work boasts strong statistical power, a major limiting factor in previous studies, though the aggregated evidence in McClure et al.'s meta-analysis similarly could not establish such an effect.

Given these results, one question arises: How is this outcome possible? Various explanations could account for this finding, though the retrospective design introduces limitations and potential biases. First, the authors do not precisely describe preoperative AF characteristics, lesion patterns applied, or success rate in restoring sinus rhythm with/without antiarrhythmic support and effective atrial transport function (a-wave >0.3 m/s). This might have resulted in abnormally favorable outcomes, stemming from a sample with a high representation of paroxysmal AF and/or lower degrees of remodeling, essentially a selected population. In fact, alongside unequal follow-up and methods used (from spot ECG to implantable Holter), these factors account for the vast differences in rhythm restoration rates across studies (<40% to >80%). Second, left atrial appendage closure invariably contributes to clinical benefits. Its closure rates surpass those in patients not undergoing ablation. Although this procedure is inherent to ablation, it is a classic confounding factor, particularly now recognized as an independent protector against stroke and other major cardiovascular events. Finally, lack of randomization allows for preprocedural candidate selection bias, which may have included patients in poorer health, more advanced cardiac disease, or morbidities not accounted for in the propensity analysis, ultimately impacting survival outcomes. Neither antiarrhythmic nor anticoagulant protocols (including the adoption of direct-acting anticoagulants within the study period) are analyzed, both pivotal in influencing morbidity and mortality in AF patients.

Regardless, surgical AF ablation is experiencing a renaissance, particularly in the field of isolated ablation but also in concomitant procedures. For the latter, lessons learned may lead us to consider candidate selection as crucial, particularly for cases with difficult rate control, typically symptomatic and paroxysmal in nature. For many such patients, if not a cure, at least AF burden reduction (time in AF during the day) likely contributes to symptom relief and the prevention of future complications with prognostic impact, such as stroke, functional valve regurgitation (mitral and tricuspid insufficiency), or tachycardiomyopathy. For cases with low success probability, technical complexity, and/or high surgical risk, adequate exclusion of the left atrial appendage remains an alternative to reduce stroke risk. Years ago, we perhaps over-abated or ablated poorly, and recently, we may have ablated too little. Concomitant surgical AF ablation is still seeking its role, its position, and its level of acceptable outcomes. It is clear that the time has not yet come to abandon it, but rather to improve candidate selection.

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Bunty Ramchandani

Posterior left pericardiotomy: does it prevent postoperative atrial fibrillation?

A post hoc analysis of the PALACS trial (Posterior Left Pericardiotomy for Prevention of Atrial Fibrillation After Cardiac Surgery) examining the characteristics of atrial fibrillation and the influence of posterior pericardiotomy on its prevention.

Postoperative atrial fibrillation (POAF) is a minor and transient complication, occurring in one in three patients undergoing cardiac surgery. Initially viewed as a benign adverse event, numerous studies have shown that it increases hospital stay by 1 to 6 days and raises the incidence of postoperative and long-term stroke. The exact mechanism triggering this arrhythmia remains unclear, although it is associated with a combination of preoperative and postoperative risk factors. These range from degenerative changes in the atrial myocardium due to age and the patient's inherent lesion mechanisms to postoperative changes that promote POAF, including left atrial refractory period dispersion, increased phase 3 depolarization, heightened automaticity, extended interatrial conduction time, reduced conduction velocity, transmembrane potential alterations, and various electrolyte imbalances.

The study analyzed in this article aims to evaluate POAF characteristics and outcomes, as well as the effect of posterior pericardiotomy on its prevention. Using PALACS study data, a post hoc analysis was performed, describing clinical and hemodynamic characteristics, including data on onset, duration, rapid ventricular response (>100 bpm), antiarrhythmic use, electrical cardioversion, and systemic anticoagulation.

Among the 420 patients analyzed, 25% developed POAF. The median time to arrhythmia onset was 50.3 hours, with 71% of cases occurring within the first 3 days. More than half of the cases presented with a rapid ventricular response, and in 8.7% of patients, POAF led to hemodynamic instability. The majority of patients (97%) received some form of antiarrhythmic therapy; 20% required electrical cardioversion, and 40% received oral anticoagulation. The median duration of POAF was approximately 24 hours, with 71% resolving within the first 36 hours. This accounted for around 16% of the patient's total hospital stay. All patients showed sinus rhythm at follow-up. Experiencing POAF extended hospital stay by one day ($p < .001$) without a clear increase in morbidity or mortality. Posterior pericardiotomy reduced the incidence of POAF by nearly half (17.7% vs. 31.3%; $p < .001$), with this effect observed after the second postoperative day. Age was confirmed to be associated with POAF, while female sex, coronary artery bypass grafting, beta-blocker therapy, and posterior pericardiotomy provided protection against it.

The study authors concluded that, despite advances, POAF remains a common postoperative complication. Although rarely causing hemodynamic instability, it frequently presents with a rapid ventricular response requiring electrical cardioversion. The arrhythmia typically resolves within the first month post-surgery, with posterior pericardiotomy notably reducing POAF incidence, especially beyond the second postoperative day.

COMMENTARY:

The PALACS study was a single-center, prospective, randomized trial aimed at assessing the efficacy of posterior pericardiotomy in preventing POAF. Patients were randomized into groups with and without posterior pericardiotomy. The study included patients undergoing coronary artery bypass grafting, aortic valve replacement, ascending aortic repair, and combined surgeries. Mitral and tricuspid valve surgeries were excluded. Continuous postoperative telemetry monitoring was employed, with

POAF defined as an irregular rhythm without detectable P waves lasting more than 30 seconds. The duration of POAF episodes was recorded to calculate total time in POAF if multiple episodes occurred. An independent committee comprising two cardiologists and a cardiac surgeon evaluated all arrhythmic events. The clinical trial demonstrated that posterior pericardiotomy significantly reduced POAF incidence (OR 0.44; $p < .005$).

The quest for an effective drug or maneuver to prevent POAF is longstanding in cardiac surgery. Various agents, such as beta blockers, sotalol (a class III antiarrhythmic with beta-blocking activity), amiodarone, atrial pacing, and even antioxidant vitamins, have been used with varying success. Many other drugs, like digoxin, class I antiarrhythmics, calcium channel blockers, intravenous magnesium, ACE inhibitors, statins, N-acetylcysteine, colchicine, naproxen, and glucocorticoids, have proven ineffective. Posterior pericardiotomy is particularly appealing as a relatively simple procedure with minimal side effects compared to the extensive list of medications attempted.

A major strength of the PALACS study is its precise definition of POAF and the use of telemetry for its diagnosis. Despite its frequency, POAF has multiple definitions depending on the source—be it the Society of Thoracic Surgeons, the Heart Rhythm Society, or the American Association for Thoracic Surgery. This lack of consensus complicates the comparison of findings across different studies. Moreover, many studies rely on clinical diagnoses, underestimating the true incidence of the arrhythmia.

Posterior pericardiotomy creates a communication between the pericardial cavity and the left pleura. Its association with reduced POAF incidence provides insight into the pathophysiology of this arrhythmia and its relationship with postoperative pericardial effusion. POAF occurring within the first 48 hours is more likely linked to the patient's preexisting arrhythmogenic substrate. Given the minimal invasiveness of added left posterior pericardiotomy, this procedure could be considered in all patients undergoing median sternotomy.

The findings from this post hoc analysis should be interpreted cautiously. These results stem from a single-center study with a relatively high POAF incidence, even in low-risk patients, and are not generalizable to patients with mitral or tricuspid pathology. Potassium and magnesium levels at POAF onset were not recorded, nor was the number of episodes per patient, with only cumulative arrhythmia time provided. There is no data beyond 30 days post-discharge, limiting late-onset POAF analysis.

In summary, this study provides intriguing and promising insights into POAF characteristics and how posterior pericardiotomy might influence its onset. Future studies are warranted to explore the pathophysiologic underpinnings of this frequent complication.

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Santiago Varela Jaramillo

Postoperative Atrial Fibrillation: Etiologic Factor or Prognostic Marker?

This retrospective study evaluates and describes short-, medium-, and long-term outcomes in patients with postoperative atrial fibrillation (POAF) compared to those without this arrhythmia.

POAF is the most frequent arrhythmia in patients undergoing cardiac surgery, with a prevalence exceeding 30%, especially in elderly patients, those undergoing valve procedures, and notably in combined procedures. Etiological factors contributing to its pathogenesis include atrial distention from perioperative volume overload, pericardial inflammation, hypoxia, tissue acidosis, and electrolyte imbalances.

In addition to its frequency, POAF is a complication with rising incidence linked to comorbidities such as COPD and diabetes mellitus, increasingly common in the patient population. While POAF might seem benign, it can result in various short-, medium-, and long-term postoperative complications, including heart failure and stroke. Due to the associated high morbidity and mortality, as well as healthcare costs, various management and prevention strategies have been implemented, although with variable results.
Bianco et al. conducted a single-center retrospective study including 12,227 patients who underwent cardiac surgery from 2011 to 2018, both elective and urgent cases. Exclusion criteria were a history of AF, surgical ablation procedures like Cox-Maze, heart transplant, or ventricular assist device implantation. Diagnosis relied on a 12-lead electrocardiogram and continuous telemetry monitoring in the early postoperative period, with follow-up every six months.

Patients were divided into two cohorts based on POAF presence, with an additional subanalysis according to surgery type (coronary revascularization, isolated valve, or combined procedures). Initial univariate analysis followed by logistic regression allowed for the calculation of a POAF propensity score based on preoperative characteristics, enhancing homogeneity and comparability between groups.

Baseline characteristics: Among the 12,227 patients, 7,927 showed no evidence of POAF, while the remaining 4,300 (35.2%) developed POAF. Additionally, 0.76% exhibited atrial flutter, and 2% had combined AF and flutter. Postoperative outcomes: No significant differences in mortality, mediastinitis, or stroke were observed between groups. However, POAF patients showed significantly higher rates of reoperation, transfusions, sepsis, prolonged mechanical ventilation, and dialysis requirement ($p <$ .001). The POAF group also had an increased need for intra-aortic balloon pump support ($p =$ .003). Concerning surgery type, independent associations with POAF were found for aortic root replacement ($p =$ .001), CABG combined with mitral valve surgery ($p <$ .001), double mitral-aortic valve replacement ($p <$ .001), and triple-valve surgery ($p <$ .022). Female gender was associated with reduced POAF risk ($p <$ .001). A total of 1,538 patients (36.6%) were discharged with AF. Among these, only 27% were discharged on anticoagulation due to POAF occurrence. Warfarin was more frequently prescribed (66%) compared to Xa inhibitors (5%; $p <$ .001), with 46.2% of patients discharged on amiodarone. One- and five-year survival rates were higher in the non-POAF group ($p <$ .001). Patients with POAF had a higher incidence of long-term AF ($p <$ .001). There was no difference in ischemic or hemorrhagic stroke risk between groups ($p =$ .385 and $p =$ .946, respectively). POAF was associated with increased mortality risk ($p <$ .001), especially among patients with preoperative COPD, dialysis requirement, and combined CABG with right-sided valve surgery. The POAF cohort showed a high readmission risk,

particularly for COPD, diabetes, or prior heart failure decompensation, especially in patients undergoing triple valve surgery or discharged on oral anticoagulation, both at one and five years.

Bianco et al. concluded that multiple-valve replacements and combined procedures have the strongest association with POAF. However, associations were also present in coronary surgery and isolated valve replacement subgroups. POAF correlates with an elevated risk of mortality and hospital readmissions for multiple causes.

COMMENTARY:

Despite extensive research on POAF, this study stands out due to its large sample size and extended follow-up. The findings support associations identified by other researchers regarding POAF and high-risk patient characteristics, such as procedure types, risk factors, and postoperative complications. Novel findings include the association of POAF with increased short- and long-term mortality, underscoring POAF as an independent factor linked to reduced survival. The readmission findings highlight POAF's impact not only in the short-term (30 days) but also at one and five years, including a high risk of readmission due to heart failure.

The results raise a question: Is POAF an etiological factor leading to patient deterioration, resulting in reduced survival, or is it simply a marker of higher disease burden and frailty in patients already predisposed to shorter life expectancy? Addressing this requires considering specific AF types and patient monitoring. Not all AFs are the same; those occurring in patients with perioperative complications like sepsis or inotropic/mechanical support needs differ from transient AF without associated complications. Furthermore, patients with complex postoperative courses might have been monitored more closely, potentially leading to a selection bias that may explain the poorer outcomes in the POAF group.

While it is known that POAF typically occurs within the first 72 hours, Bianco et al.'s work provides a longer perspective, not limited to the early postoperative period. This raises questions about AF types and their impact on survival, readmission, and complications. Despite its value, there remain knowledge gaps in cardiac surgery regarding POAF that future studies with varied parameters could help fill, aiming to improve understanding and prevention.

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Bunty Ramchandani

Direct oral anticoagulants: is it time to make the switch in cardiac surgery?

A meta-analysis of 4 clinical trials and 6 observational studies comparing the outcomes of direct oral anticoagulants (DOACs) with vitamin K antagonists (VKAs) in patients with atrial fibrillation (AF) carrying a bioprosthesis.

Treatment with VKAs has long been one of the most effective strategies for preventing ischemic stroke caused by embolic events in AF. More than half a century passed from the introduction of warfarin to the advent of dabigatran in 2010, marking one of the first direct oral anticoagulants. Over the past decade, substantial evidence has emerged for DOACs, warranting their consideration in specific settings, such as rheumatic valvular disease, bioprosthetic valve carriers, and post-valve repair patients. These clinical contexts were typically excluded from early efficacy and safety trials of DOACs.

This study aims to evaluate anticoagulation management in patients with AF and bioprosthetic valve replacement. The review covered literature up to March 2021, examining outcomes such as all-cause mortality, major bleeding, stroke, and systemic embolism.

Four randomized clinical trials (n = 1,007) and six observational studies (n = 5,084) were identified, totaling 6,405 patients. Of these, patients with AF and bioprosthetic valve replacement were selected, with 1,007 patients in the DOAC group and 1,233 in the VKA group. The combined analysis indicated comparable overall mortality rates without statistically significant differences. However, the major bleeding rate was significantly lower in the DOAC group (HR = 0.66; p = .006), with no significant differences in stroke or systemic embolism rates.

The study's authors concluded that DOACs may reduce the risk of major bleeding without increasing the risk of stroke, systemic embolism, or all-cause mortality in patients with AF carrying a bioprosthetic valve.

COMMENTARY:

The use of DOACs has become more widespread over the past decade. Their advantage lies in the lack of monitoring requirements, diet-independent effect, and fewer drug interactions, which advocates for their replacement of VKAs. Evidence for the safe use of DOACs is accumulating across most oral anticoagulation scenarios, including AF, venous thromboembolism, acute coronary syndrome, peripheral artery disease, and bioprosthetic valves. In fact, European clinical guidelines view DOAC use in patients with AF and bioprosthetic valves as a valid anticoagulant option, provided at least three months have passed since valve surgery. The American guidelines take this a step further, giving DOACs a class IA recommendation based on findings from the RIVER trial (Rivaroxaban for thromboembolism prophylaxis in patients with atrial fibrillation and bioprosthetic mitral valve). This trial provides the most substantial patient contribution to the meta-analysis, highlighting DOACs as a viable option after cardiac surgery. Another study noted a threefold increase in DOAC use for anticoagulation following bioprosthetic valve replacement over the past seven years.

The growing role of DOACs across all facets of anticoagulant therapy also has a commercial dimension. Developing a new drug costs, on average, one billion dollars, a cost pharmaceutical companies recoup within the first six months post-launch. Subsequently, FDA approval grants 14 years of exclusive marketing rights, enabling companies to capitalize on the drug's profitability. Currently, exclusivity periods for

several DOACs are nearing expiration, likely spurring increased use as new clinical trials explore their expanded applications.

Despite the enthusiasm for DOACs, critical evaluation of this meta-analysis's findings is warranted. First, four different anticoagulation regimens were included without evaluating each one's separate efficacy and safety. Additionally, all bioprostheses were analyzed together, whether aortic, mitral, or transcatheter, resulting in a varied patient profile in terms of embolic risk and oral anticoagulation strategies. Potential biases from the six observational studies also warrant consideration. Lastly, the follow-up periods were relatively short, given the chronic nature of these treatments.

In conclusion, the use of DOACs represents an unavoidable reality. It is not far-fetched to anticipate that, in the future, they may fully replace VKAs, at least in patients with AF and bioprosthetic valves.

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José Manuel Martínez Comendador

ENAVLE Study: Efficacy and Safety of Edoxaban After Bioprosthetic Valve Repair or Replacement

A randomized, open-label, prospective trial assessing the efficacy and safety of edoxaban compared to warfarin following bioprosthetic valve replacement or valve repair.

Oral anticoagulation with vitamin K antagonists (VKAs), such as warfarin or acenocoumarol, is indicated with varying degrees of recommendation (ESC/EACTS 2021 guidelines on the diagnosis and treatment of valvular heart disease) in the immediate postoperative period for patients undergoing valve replacement or repair. Direct oral anticoagulants (DOACs), or non-vitamin K-dependent oral anticoagulants, present clear advantages in dosing, monitoring, and drug interactions over VKAs. However, the efficacy and safety of DOACs in the postoperative period following cardiac surgery remain uncertain.

The ENAVLE study was a randomized (1:1), open-label, prospective clinical trial conducted between December 2017 and September 2019, aimed at comparing the efficacy and safety of edoxaban (60 mg or 30 mg once daily) with warfarin during the first 3 months post-bioprosthetic valve surgery (aortic or mitral) or mitral repair. The primary efficacy endpoint was a composite of adverse outcomes including death, clinical thromboembolic events, or asymptomatic intracardiac thrombosis, analyzed as a combined event. The primary safety endpoint was the incidence of major bleeding. Out of 220 participants, 218 (109 per group) were included in a modified intention-to-treat analysis. The primary efficacy outcome occurred in 4 patients (3.7%) in the warfarin group and none in the edoxaban group (risk difference = 0.037; $p < .001$ for non-inferiority). The primary safety endpoint was observed in 1 patient (0.9%) in the warfarin group and 3 patients (2.8%) in the edoxaban group (risk difference = 0.0183; $p = .013$ for non-inferiority).

The study concluded that, as an anticoagulation therapy during the first 3 months following bioprosthetic valve implantation or valve repair, edoxaban is not inferior to warfarin in preventing thromboembolism and is potentially comparable in terms of major bleeding risk.

COMMENTARY:

New DOACs such as apixaban, rivaroxaban, edoxaban, and dabigatran are well-established as the treatment of choice in non-valvular atrial fibrillation (AF) for stroke prevention or in the treatment of deep vein thrombosis. Compared to VKAs, such as acenocoumarol or warfarin, DOACs have the advantage of a quicker onset of action, negating the need for bridging therapy with heparin during the initial days, reduced monitoring requirements for correct dosing, fewer drug interactions, and minimal food-drug interactions. For these reasons, the use of DOACs as an alternative to VKAs after cardiac valve surgery is highly attractive, but unfortunately, the safety and efficacy of DOACs in bioprosthetic valves within the first 3 months post-surgery or percutaneous implantation remain undefined. If we refer to, for example, the latest ESC/EACTS 2021 guidelines on valvular heart disease, oral anticoagulation with VKAs after bioprosthetic implantation in the mitral or aortic position is clearly recommended only if the patient has other indications for anticoagulation (level of evidence I class C); in other cases, it should be considered during the first 3 months, with an alternative option of low-dose aspirin for bioprosthetic valves in the aortic position (level of evidence IIa class B). The recommendation for DOACs is quite different, as they are given a IIaB recommendation

from the third month onward in patients with AF, but may only be considered (level of evidence IIb class C) during the first 3 months in biological mitral valve replacement in patients with AF. In this same guideline, DOACs for mitral or tricuspid repair, or even for TAVI, are not assigned a recommendation level.

The only two clinical trials to date comparing VKAs with DOACs in this context are the RIVER study and this ENAVLE study. The RIVER study (rivaroxaban vs. warfarin) demonstrated non-inferiority of rivaroxaban following mitral valve replacement; however, only 20% of patients were included within the first 3 months. The ENAVLE study results (edoxaban vs. warfarin), the subject of this article, though officially published this month, were already considered in drafting the latest ESC/EACTS 2021 guidelines on valvular heart disease. However, DOACs did not receive a higher level of recommendation or evidence, primarily due to the small number of patients randomized.

Shim et al., in this randomized clinical trial, present impressive results with edoxaban following valve surgery, demonstrating non-inferiority compared to warfarin in stroke prevention and major bleeding incidence. A key but often overlooked aspect of this study, which accurately reflects daily practice with warfarin or acenocoumarol, is the poor control of the international normalized ratio (INR) observed, with patients being out of the target INR range (between 2 and 3) nearly half the time; numbers contrasting with the high adherence observed in the edoxaban group to the DOAC. It is thus unsurprising that, although still outside the guidelines, many cardiac surgeons are opting to anticoagulate their patients with DOACs.

It would have been highly informative to conduct this study with a more homogeneous population, avoiding mixing bioprosthetic valves in the mitral or aortic position with mitral repair, or sinus rhythm with AF, as each of these groups carries distinct thromboembolic risks that deserve separate analysis in future research. Another evident limitation of the ENAVLE study was the low number of patients included. When coupled with the unexpectedly low event rates found (below anticipated levels) and the relatively large non-inferiority margins, caution is advised before extrapolating these results to real-world clinical practice. Larger multicenter, double-blind clinical trials with greater patient numbers are needed before advancing DOAC recommendations in clinical guidelines. In any case, these results represent a major step toward the approval of early anticoagulation with DOACs following valve surgery and pave the way for future studies evaluating their efficacy in TAVI.

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Elio Martín Gutiérrez

New Times and New Anticoagulants: What a Cardiac Surgeon Needs to Know

Literature review on direct-acting anticoagulants: pharmacokinetic and pharmacodynamic characteristics, and their use in various pre- and postoperative contexts of cardiac surgery

The incorporation of direct-acting oral anticoagulants (DOACs) into the cardiological therapeutic arsenal is an increasingly evident reality. Gradually, they have displaced vitamin K antagonists (VKAs) in most indications, given their equivalent or even superior profile in terms of ischemic event prevention, hemorrhagic safety, and patient convenience. DOACs offer predictable therapeutic effects and do not require dosing adjustments, which enhances patient comfort. Currently, the indication for VKA anticoagulation persists only in cases involving mechanical prostheses and rheumatic heart disease. In these contexts, DOACs were shown to be deleterious in the initial RE-ALIGN clinical trial conducted with dabigatran. Following this, subsequent DOAC trials included these as exclusion criteria and have not readdressed them, leaving these as the final frontier in the wide array of DOAC indications.

This evolution makes it essential for us to become familiar with these drugs; rather than "syncing" with traditional treatments, we must "tune in" to this new reality, where expertise in managing these agents becomes almost obligatory for any cardiac surgeon. Accordingly, this work offers a comprehensive update on everything required for daily clinical practice, concluding with a list of best practices for perioperative DOAC management in patients undergoing cardiac surgery.

To begin, it is well-known that four DOACs are currently available: dabigatran (Pradaxa®), which acts at the end of the coagulation cascade on thrombin (activated factor II); rivaroxaban (Xarelto®), apixaban (Eliquis®), and edoxaban (Lixiana®), which exert their effect through the inhibition of activated factor X. This mechanism is also shared by heparins, particularly low-molecular-weight heparins, and heparinoids (fondaparinux). Although all DOACs are indicated for the prevention of thromboembolic events associated or not with non-valvular atrial fibrillation (meaning without concurrent rheumatic disease), it is worth noting that rivaroxaban also has an additional indication for anticoagulation in chronic ischemia, both coronary and peripheral. Concerning contraindications, key ones include reduced renal clearance (<15 cc/min for factor Xa inhibitors and <30 cc/min for dabigatran), mechanical valve prostheses, hemorrhagic diathesis, severe hepatic insufficiency, pregnancy, and antiphospholipid syndrome. Standard dosing information is included in this review. However, there are multiple dosing regimens, with apixaban being the most versatile (2.5 or 5 mg, once or twice daily), making this a notable advantage of this agent. Rivaroxaban's unique indication (20 mg once daily) and dabigatran's potent effect (150 mg twice daily) are suitable for high ischemic risk and low bleeding risk profiles, as seen in young patients with atrial fibrillation, while edoxaban (60 mg twice daily) is seen as the "black sheep" among the options.

In the perioperative setting, cardiac surgeons mainly "withdraw" or "resume" these agents. Typically, most guidelines focus on resumption, but we prefer an approach oriented to surgery.

"WITHDRAW" refers to suspending anticoagulant effect to facilitate surgical intervention. Generally, 48 hours are widely accepted for DOAC effect dissipation post-administration. However, adjustments may be necessary based on patient-specific factors. For elective or urgent situations in stable patients, the 48-hour rule may be extended based on renal

clearance; dabigatran should be withdrawn for 72 hours with clearances of 50–80 cc/min and 96 hours for 30–50 cc/min. For the other three agents, we should extend the withdrawal period to 72 hours for clearances below 30–50 cc/min and to 96 hours for those with clearances <30 cc/min. Given the predictable pharmacology of DOACs, bridging with heparin is generally unnecessary and discouraged unless intervention is delayed, resulting in thromboembolic risk.

For urgent unstable cases, residual anticoagulant effect levels may be measured. Dabigatran's effect is assessed by thrombin time (threshold <21 seconds for cessation), while the other three agents can be measured via anti-Xa factor activity (<30 ng/mL). Heparin or low-molecular-weight heparins can also be monitored, with adjustments necessary for clearance below 30 cc/min. Standard coagulation tests, while less specific, remain options where anti-Xa testing is unavailable, although reliability decreases with clearance <30 cc/min.

“IMMEDIATE NEED” involves emergent or urgent interventions. Residual effects may be evaluated with the tests mentioned. In cases of active pharmacological effect, specific and non-specific antagonistic measures may be implemented:

1. Specific measures include direct antagonists for dabigatran (idarucizumab) or anti-Xa agents (andexanet alfa). Studies cited in this work highlight the success and safety of these agents in cardiac surgery, albeit with some cautionary notes:

    - Dabigatran can be safely reversed with idarucizumab (Praxbind®) at any perioperative phase without significant side effects or interference with extracorporeal circulation.

    - Andexanet alfa (Ondexxa® or Andexxa®) poses greater risk, as its trial (ANNEXA-4) excluded emergent surgeries due to heparin resistance risk. It should be used compassionately, post-cardiopulmonary bypass if feasible, with antithrombin III supplementation as an alternative.

2. Non-specific measures may include transfusion of blood products or coagulation factors, such as activated factor VII, for intra- or post-operative periods to support hemostasis. Hemodialysis has proven effective for dabigatran elimination, given its low plasma protein binding. For Xa inhibitors, hemadsorption using devices like Cytosorb® may be employed, particularly for agents like ticagrelor or clopidogrel, and is effective when combined with extracorporeal circulation.

“RESUME” introduces unique challenges in the postoperative period, with clinical guidelines generally recommending resumption of DOACs one month after surgery if contraindications are absent. Observational studies indicate increasing early adoption of DOACs, with documented thromboembolic protection and hemorrhagic safety.

Special Considerations:

- Valvular AF: Rheumatic heart disease requires VKAs, as surgical correction does not eliminate thrombotic risk.

- Renal Clearance: Dabigatran demands dose adjustments at <50 cc/min, with different doses specified for rivaroxaban, apixaban, and edoxaban based

on renal and clinical profiles. Apixaban is often favorable for elderly patients with multiple comorbidities.

COMMENTARY:

The adoption of new oral anticoagulants before and after cardiac surgery has become a reality. We must adapt to this new paradigm of specific anticoagulation agents, moving beyond traditional therapies. Cardiac surgery outcomes in patients with atrial fibrillation are heavily influenced by their anticoagulation management, which must be carefully established from the initial postoperative phase, discharge, and follow-up.

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José Manuel Martínez Comendador

Temporal association of invasive procedures and infective endocarditis: a new shift in antibiotic prophylaxis?

This retrospective study aims to establish an association between all infective endocarditis (IE) hospital admissions in England over a 7-year period and specific diagnostic-therapeutic invasive procedures (IPs) performed in the 3 months preceding the admission.

For decades, antibiotic prophylaxis was recommended for patients at high risk of IE undergoing specific IPs. Due to the lack of clear evidence supporting its use, recommendations for antibiotic prophylaxis ceased in the mid-2000s, except for high-risk patients undergoing invasive dental procedures (IDPs). This study aims to quantify the association between IPs and IE incidence.

All IE admissions in England from April 2010 to March 2016 were identified through the national admissions register (n = 14731). All IPs performed within the 15 months prior to admission were then identified. To determine whether the odds of developing IE increased within 3 months post certain IPs, the incidence of IPs in the 3 months immediately before IE admission (case period) was compared with the incidence in the preceding 12 months (control period). The odds of IE increased following permanent pacemaker and defibrillator implantation (OR = 1.54; $p < .001$), dental extraction (OR = 2.14; $p = .047$), upper (OR = 1.58; $p < .001$) and lower (OR = 1.66; $p < .001$) gastrointestinal endoscopy, bone marrow biopsy (OR = 1.76; $p = .039$), bronchoscopy (OR = 1.33; $p = .049$), and blood product transfusions (OR = 1.2; $p = .012$).

The study's conclusion indicates a clear association between specific IPs (permanent pacemaker and defibrillator implantation, dental extraction, gastrointestinal endoscopy, and bronchoscopy) and subsequent development of IE. These findings should prompt a necessary reevaluation of current IE prophylaxis recommendations for high-risk individuals.

COMMENTARY:

In developed countries, several factors are contributing to the rising IE incidence observed in the past decade. These include an aging population, increased use of implantable cardiac devices (ICDs), the advent of transcatheter prostheses, more patients on hemodialysis, improved IE detection due to advancements in diagnostic techniques (especially echocardiography), and the guideline change in the early 2000s that discontinued antibiotic prophylaxis for IE in diagnostic-therapeutic invasive procedures that compromise epithelial or mucosal integrity or pose a risk of bacteremia. Pre-2007 and 2009 AHA and ESC guidelines recommended antibiotic prophylaxis for patients at moderate to high risk of IE undergoing invasive procedures. However, due to the lack of evidence at that time linking these procedures with IE (except for dental procedures affecting the gingiva or the pulp and root), and concerns about adverse effects and antibiotic resistance, the AHA and ESC restricted prophylaxis to high-risk patients undergoing IDPs (e.g., those with previous IE, valve prostheses, including transcatheter valves, or unrepaired cyanotic congenital heart defects). Despite studies suggesting a possible rise in IE incidence, the 2015 ESC/EACTS guideline recommendations remained unchanged due to conflicting study results. The 2021 ESC/EACTS guideline on valve disease diagnosis and treatment also did not modify the IE prophylaxis recommendations.

To date, the strongest evidence for an association between IE and IPs comes from a Swedish study conducted in 2018 by Janszky et al. Interestingly, the findings of this study are nearly consistent with those in the current study led by Thornhill MH et al. Both studies found a clear relationship between IE development and certain IPs, such as recent ICD implantation, upper and lower GI endoscopy, and bronchoscopy. Notably, the current study also demonstrates a clear association between IE and IDPs performed within three months, a factor not analyzed in the Janszky et al. study.

Most healthcare systems in industrialized countries ensure specific antibiotic coverage for IDPs, ICD implantation, and bronchoscopy to prevent infections. High-risk patients undergo dental extractions per IE prophylaxis guidelines. Patients undergoing ICD implantation or bronchoscopy also receive antibiotic coverage according to procedure-specific guidelines, such as the 2015 British guideline on ICD infection prevention and the 2013 guideline on flexible bronchoscopy. However, these guidelines do not recommend antibiotic prophylaxis specifically to prevent IE, but rather to prevent procedural infectious complications (e.g., generator infection or pneumonia). Despite these three invasive procedures typically receiving antibiotic prophylaxis, this study showed a significant association with IE within three months post-procedure, suggesting possible incomplete prophylaxis, limited guideline adherence in clinical practice, or ineffective prevention protocols.

Furthermore, there was a strong association between upper and lower GI endoscopy and IE, as demonstrated in Janszky et al.'s Swedish study. However, this was not observed with endoscopic retrograde cholangiopancreatography, likely because these patients already receive intensive antibiotic prophylaxis to prevent cholangitis. It is concerning that routine GI endoscopy, unlike other invasive procedures studied, has no general or IE prophylactic antibiotic recommendation, making it a critical point for future guideline updates.

Regarding hematologic procedures, an association was found between bone marrow biopsy and blood product transfusions (including red blood cells and plasma), though these results must be interpreted cautiously, as these procedures are often performed under a misdiagnosis of hematologic malignancy during the initial diagnostic phase of IE. No association was observed between otorhinolaryngology, dermatology, obstetric procedures, or IE, though the number of these procedures was minimal. Similarly, no association was found with cystoscopy and prostate endoscopic procedures, potentially explained by the frequent use of antibiotics for postprocedural urinary infection prevention.

In conclusion, although this study was conducted using administrative databases with inherent limitations, its results are highly relevant. As in Janszky et al.'s study, a clear association was demonstrated between IPs and subsequent IE development within a short period. The accumulated evidence from these studies necessitates reconsideration of antibiotic prophylaxis for high-risk patients undergoing IPs such as ICD implantation, upper and lower GI endoscopy (notably, the only one lacking routine antibiotic coverage), bronchoscopy, and potentially any other procedure that could induce bacteremia.

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Bunty Ramchandani

Where Should Infective Endocarditis Be Operated?

This is a multicenter retrospective study comparing surgical outcomes for infective endocarditis cases treated at primary valve centers versus specialized hospitals.

Infective endocarditis has a global incidence of 3-10 cases per 100,000 people and an approximate mortality rate of 25%. In a European cohort, the incidence drops to 33.8 cases per million inhabitants with a similar hospital mortality rate of 22.7%. Over the past decade, the incidence of this disease has doubled, and current trends suggest it will continue to rise. In 2019, the *Journal of Thoracic and Cardiovascular Surgery* published a consensus document to optimize the care of patients with valvular disease. This document defined two types of centers: specialized valve centers (SVCs) or level I centers, and primary valve centers (PVCs) or level II centers. It recommended treating endocarditis patients at an SVC due to their experience in managing complex valvular cases. Should endocarditis patients be referred to an SVC?

Today's article aims to provide evidence for this recommendation. It is a retrospective, multicenter study evaluating, from 2014 to 2020, 513 patients operated on for infective endocarditis in 8 U.S. hospitals; 2 classified as SVCs and 6 as PVCs. The study compares the outcomes between these two types of centers after adjusting for propensity scores, taking into account patient characteristics, valve type, and endocarditis status (active or inactive). A multivariable logistic regression was used to identify risk factors for surgical mortality. After propensity score matching, two comparable groups were generated, with similar mean STS/Gaca endocarditis risk scores for each type of center. In cases of aortic root abscess, SVCs showed a higher likelihood of performing the Bentall procedure (60.4% vs 21.7%; $p < .01$). Similarly, SVCs exhibited higher mitral repair rates in cases involving the mitral valve (50.4% vs 26.3%; $p < .01$). Hospital mortality was significantly lower at SVCs (6.2% vs 13.0%; $p = .04$), and multivariable logistic regression analysis suggested that surgery at an SVC was a protective factor, with an OR = 0.39 ($p = .02$). These findings were consistent even when only considering patients with active endocarditis.

The authors conclude that surgery at PVCs is associated with higher mortality compared to SVCs. Therefore, transferring these patients to level I units should be considered.

COMMENTARY:

Consensus documents are valuable resources, based on current scientific evidence, that aim to standardize and optimize the care provided to patients. This was the objective of the 2019 recommendations published by the *Journal of Thoracic and Cardiovascular Surgery* for the treatment of valvular diseases. However, there is no formal process currently to designate a center as either SVC or PVC, nor has such designation been validated. In this study, SVCs were defined as hospitals capable of performing aortic valve-sparing surgeries (no aortic valves were spared in the endocarditis cases), aortic aneurysm procedures, mitral repair, multivalve procedures, reoperations, with a dedicated imaging team and a 24/7 ICU with intensivist coverage. Among the two SVCs, they handle an average of 32 endocarditis cases per year, compared to just 3.2 cases per year at the PVCs. In fact, one SVC reported 6,000 valvular surgeries during the study period, while the other SVC reported 1,300 cases in the same timeframe. Would both hospitals have similar outcomes in endocarditis surgery? We do not know.

We also lack data on the referral network for these hospitals. All eight hospitals belong to the same health care group, and we do not know if any barriers prevented patient transfers to more specialized centers, if patients refused transfers to stay closer to family,

or if coverage issues impacted these decisions. We also do not know if specialized centers accepted referrals based on risk scores, possibly selecting lower-risk patients. Note that the Gaca score has only one variable related to the presence of endocarditis, while the remaining items evaluate prognosis in any cardiac surgery. This results in a generic score, more simplified than the STS score, which is less applicable to actual endocarditis scenarios as it does not evaluate critical factors like native versus prosthetic valve infections, presence of vegetations, or positive blood cultures.

One-year mortality rates were similar between the two types of centers. Despite better 30-day outcomes at SVCs, this advantage was lost after discharge. Therefore, the true benefit of treatment at an SVC versus a PVC remains uncertain.

There are undoubtedly differences between these two types of centers. More human and material resources, along with accumulated experience and dedicated units, improve short-term outcomes for endocarditis surgeries. Does this justify transferring all patients to these centers? Probably not; the key lesson is that extracorporeal circulation should not be performed in centers without 24/7 intensivist availability. Fortunately, such situations are rare in Spain.

Today's article does not clarify if it is better to transfer endocarditis patients to a level I unit, as it does not specify how the consensus document's recommendations were applied to the patients studied and does not evaluate comparable centers. This article is a prime example of comparing apples to oranges.

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José Manuel Martínez Comendador

Clinical Guidelines on Infective Endocarditis ESC 2023: Summary of Key Updates

This blog article summarizes and presents the main updates to the 2023 clinical guidelines on infective endocarditis (IE) by the European Society of Cardiology (ESC).

The long-awaited and much-needed update to the clinical guidelines on infective endocarditis (IE) has finally been published, driven by recent scientific evidence and the obsolescence of the previous 2015 guidelines.

If I had to highlight the most innovative contributions of these new guidelines, two fundamental aspects stand out. First, the long-anticipated reintroduction of antibiotic prophylaxis for procedures beyond dental interventions, reviving a practice that existed prior to the 2009 guidelines. The second highly significant change, paradigm-shifting after the POET clinical trial, is the possibility of oral antibiotic therapy starting from the tenth day of intravenous antibiotic treatment in selected cases, particularly after confirming the absence of complications with transesophageal echocardiography (TEE).

Main Updates

In addition to the above, the guideline introduces a series of highly interesting updates in almost all areas. It emphasizes the importance of a multidisciplinary team in managing complicated IE. Moreover, it provides new indications for prophylaxis and expands and modifies prophylactic antibiotic therapy. In the diagnostic field, it introduces innovations in advanced imaging techniques and presents highly useful algorithms for approaching suspected endocarditis. It underscores the relevance of early surgical intervention and updates embolism prevention strategies. Additionally, it addresses various other aspects, such as introducing recommendations for epicardial pacemaker implantation and proposing new guidelines for diagnostic tests in cases of spondylodiscitis. It also provides guidance on when to avoid preoperative coronary angiography and revises recommendations for surgical indications in endocarditis with right-sided chamber involvement, among other updates.

The core of this guideline lies in a scheme that illustrates, in detail, the patient's flow from the moment IE is suspected until their medical discharge. At the heart of this process, especially for complicated IE, the fundamental role of the specialized multidisciplinary endocarditis team is highlighted. This team is responsible for making crucial decisions in managing the patient. Ideally, this team should operate from a referral center, ensuring the best care and follow-up.

1. **Endocarditis Prophylaxis**

The first recommendation of the guideline advocates the implementation of general prevention measures in patients at intermediate and high risk of developing IE. The identification of high-risk populations remains consistent with the 2015 guidelines. This includes patients with a history of endocarditis, those with cardiac prostheses (whether surgical or transcatheter), as well as patients with cyanotic congenital heart disease—whether unrepaired, repaired with a residual shunt, or completely repaired. For patients with complete repair, antibiotic prophylaxis is required only during the first six months. Notably, the recommendation class has been updated to Class I. Additionally, two new indications for antibiotic prophylaxis have been introduced:

1. **Patients with ventricular assist devices**, with a Class I recommendation.
2. **Heart transplant recipients**, with a Class IIb recommendation.

Regarding procedures requiring antibiotic prophylaxis, the recommendation for patients undergoing dental procedures involving gingival mucosa or the periapical region of the teeth has been upgraded to Class I B. A particularly significant innovation is the inclusion of other diagnostic and therapeutic procedures involving the respiratory, gastrointestinal, genitourinary, skin, and musculoskeletal systems, albeit with a slightly lower recommendation level of IIb C. Thus, antibiotic prophylaxis is no longer limited to dental procedures but extends to other types of interventions, reviving a practice that was in place before the 2009 guidelines. In a recent blog post, we anticipated that this extension was a much-needed measure, finally reflected in the new guidelines due to the abundant accumulated evidence.

For prophylactic antibiotic therapy in patients not allergic to beta-lactams, the recommendation to use amoxicillin or ampicillin is maintained. Options such as cefazolin or ceftriaxone are added. For patients allergic to beta-lactams, clindamycin has been excluded due to potential adverse effects and replaced with other antibiotics. It is important to note that the administration protocol remains a single dose given 30–60 minutes before the invasive procedure, primarily in the dental setting.

There is an emphasis on implementing general education measures for populations at high risk of endocarditis. This includes maintaining optimal oral health, proper skin hygiene, responsible use of antibiotics, and ensuring the patient is fully aware of the risk of endocarditis. It is crucial for the patient to recognize when antibiotic prophylaxis is necessary and to communicate it accordingly.

A Class I A recommendation for nasal screening for *Staphylococcus aureus* carriers prior to cardiac surgery or prosthetic implantation is retained. Additionally, the recommendation for perioperative antibiotic prophylaxis before any device implantation has been revised and elevated to Class I A. Significant new measures include the recommendation to apply skin antisepsis before device implantation and general aseptic measures when handling catheters in hemodynamic or electrophysiology labs. Directed antibiotic prophylaxis to cover common skin pathogens such as *Staphylococcus aureus*or *Enterococcus* is also proposed prior to transcatheter valve implantation, particularly transcatheter aortic valve implantation (TAVI).

Summary:
The key updates include general prevention measures for patients at moderate and high risk of IE, new indications for prophylaxis, and the modification and expansion of prophylactic antibiotic therapy.

2. **Diagnosis of Infective Endocarditis**

The microbiological diagnostic algorithm presented in these guidelines does not differ significantly from the previous 2015 guidelines. However, innovations are observed in imaging techniques. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) remain the fundamental tests for diagnosing IE.

The following updates are noteworthy:

- The recommendation for TEE when IE is suspected, even if TTE results are positive, has been elevated to Class I. Exceptions include cases with isolated right-sided native valve vegetations or involvement, provided TTE findings are of good quality and unequivocal.
- A new Class I recommendation has been introduced to perform TEE prior to transitioning from intravenous to oral antibiotic therapy—one of the most significant innovations in these guidelines.
- Echocardiography is now recommended not only in cases of *Staphylococcus aureus* bacteremia but also for *Enterococcus faecalis* and *Streptococcus* bacteremia.

Regarding advanced imaging techniques:

- Cardiac computed tomography (CT) and positron emission tomography/computed tomography (PET/CT) with 18F-fluorodeoxyglucose (18F-FDG) are recommended with a Class I designation for diagnosing IE in native valves, prosthetic valves, and paravalvular lesions.
- Techniques like technetium-99m-labeled white blood cell (99mTc-WBC) imaging are mentioned with lower levels of evidence and are primarily reserved for detecting complications (both cardiac and extracardiac) or identifying the source of bacteremia.

3. **Diagnostic Criteria**

The newly proposed diagnostic criteria in these guidelines do not significantly deviate from the modified Duke criteria previously outlined in the 2015 guidelines. The main addition is the inclusion of *Enterococcus faecalis* as a typical microorganism.

The true innovation lies in imaging techniques, although not in TTE or TEE, which remain the cornerstone tests for diagnosis. Instead, a multimodal imaging approach is promoted.

Key advancements include:

- PET/CT and SPECT no longer require waiting three months after prosthetic implantation to be considered a major criterion, as was stipulated in the 2015 guidelines. Current evidence supports their ability to differentiate between inflammation and infection during this early postoperative period. As a result, PET/SPECT can now be performed immediately when needed.
- Minor criteria remain largely unchanged, as does the classification of IE as definite, possible, or rejected.

New algorithms are presented to address suspected IE in native valves, prosthetic valves, and devices. In all these algorithms, Class I recommendations establish that the first-line diagnostic approach should consider clinical characteristics, blood cultures, TTE, and TEE.

For possible endocarditis, which may be the most relevant scenario:

- A Class I recommendation is made to repeat blood cultures if initial results are negative or inconclusive, repeat TTE/TEE within 5–7 days, and perform cardiac CT if there is suspicion of a lesion on a native valve.
- For prosthetic valves, it is recommended to perform cardiac CT or 18F-FDG PET/CT.
- Advanced imaging techniques for detecting minor criteria are reserved as a secondary option, with a Class IIa recommendation.

4. **Antibiotic Therapy**

No significant changes have been made to the therapeutic regimens established in previous guidelines, as no new evidence has emerged to support modifications. Most of the available evidence remains classified as Class I with B/C levels of evidence, maintaining stability in this area.

However, a pivotal modification in the therapeutic approach to IE arises from the POET study, published in January 2019. After overcoming the critical acute phase during the initial 10-day hospitalization with intravenous (IV) antibiotic therapy, transitioning to oral therapy in stable patients is now a possibility. This is translated into close outpatient follow-up, supported by a Class I recommendation for a prior TEE, once the critical hospital phase has been completed.

Criteria for Stability

Patients eligible for this transition must meet specific stability criteria, which include:

- Positive blood cultures for *Staphylococcus aureus*, *Streptococcus*, coagulase-negative staphylococci, or *Enterococcus faecalis*.
- Controlled infection, demonstrated by the absence of fever, normalization of C-reactive protein levels, and absence of leukocytosis.
- Completion of at least 10 days of IV antibiotic therapy or 7 days post-valve surgery.
- No new surgical indications following TEE.

This innovative approach with oral therapy is expected to reduce hospitalization duration, among other long-term benefits already demonstrated. The recommendation for this group of patients is classified as Class IIa A.

5. **Surgical Treatment**

The three basic pillars of surgical indication in the 2015 guidelines—heart failure, uncontrolled infection, and high embolic risk or established embolism—remain unchanged. Heart failure continues to be the primary surgical indication, with its classification, class, and level of evidence remaining unaltered, as is the case for uncontrolled infection.

Notable Updates in Embolism Prevention

- A new Class I recommendation introduces urgent surgery for patients with vegetations ≥10 mm and other surgical indications.

- A new Class IIb recommendation suggests urgent surgery for patients with aortic or mitral IE who have vegetations ≥10 mm, without severe valve dysfunction or clinical evidence of embolism, provided they are at low surgical risk.

Timing of Surgical Interventions

The guidelines define timelines for these surgical indications:

- **Emergent surgery**: Performed within 24 hours.
- **Urgent surgery**: Carried out within 3–5 days.
- **Non-urgent surgery**: No specific timeframe is provided but must be performed before discharge during hospitalization.

A Class I C recommendation has been added for early surgical treatment involving valve replacement and complete debridement in cases of early prosthetic valve endocarditis (within six months of valve surgery).

Stroke Management and Surgical Indications

In the diagnostic and management algorithm proposed for IE, the type of stroke must first be determined:

- For ischemic stroke, surgery should not be delayed, with the recommendation upgraded to Class I.
- For hemorrhagic stroke, waiting for one month is ideal (Class IIa). However, in patients with hemorrhagic stroke who also present clinical instability due to heart failure, uncontrolled infection, or persistent high embolic risk, urgent or emergent surgery is considered, weighing the likelihood of neurological damage. This is also classified as Class IIa.

New recommendations include the use of mechanical thrombectomy and the contraindication of fibrinolysis in cases of embolic stroke.

Summary:

The guidelines emphasize the necessity of early surgical intervention. Surgery should not be delayed after ischemic stroke, while hemorrhagic stroke patients may undergo surgery under specific conditions. Early surgical treatment is recommended for IE on prosthetic valves, and surgical flexibility has been expanded to enhance thromboembolic prevention.

6. **Device Implantation and Management**

A Class I recommendation is established for the immediate removal of infected cardiovascular implantable electronic devices (CIEDs) once empirical antibiotic therapy has been initiated. This measure aims to reduce the risk of systemic complications and ensure effective infection control.

Additionally, a Class IIa recommendation suggests extending antibiotic therapy for 4–6 weeks after device removal in cases of septic embolism or when the patient has a prosthetic valve.

New Recommendations

- A Class IIa recommendation supports the implantation of epicardial pacemakers in patients with complete heart block who exhibit certain high-risk characteristics, such as:
  - Presence of *Staphylococcus aureus*.
  - Aortic root abscess.
  - Tricuspid valve involvement.
  - Prior valve surgery.

7. **Musculoskeletal Complications**

New recommendations, absent in previous guidelines, focus on musculoskeletal complications, particularly spondylodiscitis. The guidelines establish a Class I recommendation for the use of magnetic resonance imaging (MRI) or PET/CT in cases of suspected spondylodiscitis or vertebral osteomyelitis associated with IE.

8. **Coronary Artery Assessment Before Cardiac Surgery**

For patients with hemodynamic stability and aortic valve IE requiring cardiac surgery and at high risk of coronary artery disease (CAD), the guidelines recommend:

- High-resolution coronary CT angiography (CTA) with a Class I B recommendation.
- In cases where IE does not affect the aortic valve, coronary angiography remains the standard, with a Class I C recommendation.

9. **Right-Sided Infective Endocarditis**

The surgical indication for right-sided IE has been reviewed, and its recommendation has been elevated to Class I compared to previous guidelines. Surgery is considered in the following scenarios:

- **Persistent vegetations >20 mm** with recurrent pulmonary embolism.
- **Right ventricular dysfunction** secondary to severe tricuspid regurgitation, unresponsive to diuretics.
- Simultaneous involvement of left-sided structures.

New Recommendations:

- A Class IIa recommendation advises tricuspid valve repair whenever possible.
- Preventive placement of a pacemaker lead during tricuspid valve procedures is also recommended (Class IIa).

10. **Patient-Centered Care**

The guidelines conclude with a representation of contemporary medicine's emphasis on individualized care. The patient plays an active role in decision-making regarding diagnostic tests and therapeutic options.

Preventive Measures:

Patients are encouraged to adopt general prevention measures, such as optimal oral health, early infection detection, and timely communication with healthcare providers about the need for antibiotic prophylaxis.

Final Highlights

The 2023 ESC guidelines will likely be remembered for two groundbreaking changes:

1. **Reintroduction of antibiotic prophylaxis** for invasive procedures beyond dental interventions, marking the first revision in nearly 15 years.
2. **Incorporation of oral antibiotic therapy**, a transformative approach to completing treatment for infective endocarditis.

REFERENCE:

Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, et al.; ESC Scientific Document Group. *2023 ESC Guidelines for the management of endocarditis.* Eur Heart J. 2023 Aug 25:ehad193. doi: 10.1093/eurheartj/ehad193.

Bunty Ramchandani

New Duke criteria for the diagnosis of infective endocarditis

Update of the diagnostic criteria for infective endocarditis by the International Society of Cardiovascular Infectious Diseases.

Since the establishment of the Duke criteria for diagnosing infective endocarditis (IE) in 1994, with subsequent updates in 2000, the microbiological, epidemiological, diagnostic, and therapeutic landscapes have evolved significantly. The Infective Endocarditis Diagnostic Criteria Working Group of the International Society of Cardiovascular Infectious Diseases (ISCVID) has released a consensus document introducing the new diagnostic criteria: the 2023 Duke-ISCVID criteria.

COMMENTARY:

As this publication only highlights modifications relative to the previously used modified Duke criteria, many of which remain current, we will provide a summary of all the criteria, both new and pre-existing, that are currently utilized to establish a diagnosis of infective endocarditis:

1. Pathological Criteria:

The classical criteria included:

- Demonstration of microorganism presence through culture and/or histological examination of a cardiac vegetation, or one that has embolized, as well as histological analysis of a cardiac abscess specimen.

- Lesions, vegetations, or abscesses confirmed by histological examination consistent with IE.

In the new Duke criteria definition, compatible histological findings can now be detected not only in cardiac tissue but also in explanted prosthetic valves and prosthetic rings, vascular conduits from the ascending aorta (involving the aortic valve), and the intravascular portion of implantable electronic cardiac devices. Moreover, new genetic, molecular, and staining techniques are incorporated beyond histological analysis for diagnosis. The independent or combined use of 16S/18S rRNA gene PCR and fluorescence in situ hybridization has allowed up to a 30% increase in etiological identification for IE.

Clinical Criteria:

Traditionally, clinical criteria have been divided into two categories: major and minor. This classification remains in place, with new modifications incorporated into various components:

2.1 Major Clinical Criteria

2.1.1 Microbiological Criteria:

The previously required temporal criteria for drawing blood cultures from separate venipunctures have been removed. Isolating the microorganism in at least two independently drawn blood cultures is sufficient to meet the major criterion for typical pathogens; however, at least three cultures are needed for atypical pathogens. The updated criteria no longer require specific intervals between blood cultures, instead

emphasizing the extraction of two independent samples if bacteremia is suspected. The list of typical IE agents has been expanded to include new species, such as Staphylococcus lugdunensis, Enterococcus faecalis, Streptococcus spp. (excluding S. pneumoniae and S. pyogenes), Granulicatella spp., Abiotrophia spp., and Gemella spp. Additionally, in prosthetic material samples, not from blood cultures, typical IE pathogens include coagulase-negative Staphylococcus, Corynebacterium striatum, Corynebacterium jeikeium, Serratia marcescens, Pseudomonas aeruginosa, Cutibacterium acnes, non-tuberculous Mycobacterium, and Candida spp.

Approximately 10% of patients with IE present with negative blood cultures. This may result from bacterial inhibition due to prior antibiotic treatment or a pathogen that cannot be isolated by traditional culture techniques. New criteria now consider positive PCR tests and other nucleic acid-based assays on blood samples for Coxiella burnetii, Bartonella spp., or Tropheryma whipplei as positive. For Coxiella burnetii, an IgG phase I antibody titer greater than 1:800 or detection in a single blood culture is sufficient. New indirect immunofluorescence criteria for detecting IgM and IgG antibodies against Bartonella henselae and Bartonella quintana with an IgG titer of 1:800 are also included.

2.1.2 Imaging Criteria:

Echocardiography remains the cornerstone of clinical diagnosis. Diagnostic criteria for IE will be established by identifying vegetations, perforations/ruptures of native or bioprosthetic leaflets, intracardiac/paravalvular abscesses, pseudoaneurysms, or intracardiac fistulas. Additionally, the presence of new regurgitation (native or prosthetic) is diagnostic, while worsening of a pre-existing regurgitation is insufficient in the absence of other findings. The presence of new paravalvular leakage within prosthetic valves is considered significant.

The new criteria introduce CT as a complementary imaging test due to its higher spatial resolution for detecting paravalvular lesions. It may supplement transesophageal echocardiography if doubts exist or serve as a substitute if contraindicated (e.g., in aortic endocarditis). The criteria for endocarditis findings are consistent with those described for echocardiography.

The PET-CT scan is also recognized as an imaging technique with high positive predictive value. The use of 18F-fluorodeoxyglucose (18-FDG) as a metabolic activity marker is accepted. Other techniques, such as Tc-99m-labeled leukocyte scintigraphy, commonly used in our setting, are not recognized. Intense, focal/multifocal, or heterogeneous uptake detected after 3 months from surgical implantation of intracardiac prosthetic material (valve, valvular conduit, and/or intracavitary electrodes) is classified as a major criterion. If the prosthetic implant is less than three months old, this finding is considered a minor criterion.

2.1.3 Surgical Criterion

A new surgical section has been added to the major clinical criteria. It is defined as intraoperative evidence of IE documented through direct inspection during surgery. This becomes a new major criterion without requiring prior microbiological or pathological confirmation. This criterion supports the management of cases requiring emergent intervention before culture/laboratory results or intraoperative pathological analysis are available, thereby allowing diagnosis and initiation/maintenance of antibiotic therapy.

2.2 Minor Clinical Criteria

In this heterogeneous section, many previous criteria are retained, some are modified, and others are added. They can be categorized as follows:

- Predisposition: The presence of prosthetic material for valve replacement or repair is retained, but intracavitary electrodes and prosthetic material for transcatheter valve repair or implantation are now included. A history of prior IE is also added. Criteria for congenital heart disease (any, not necessarily cyanotic), valvular insufficiency (more than mild), stenosis (any degree), hypertrophic obstructive cardiomyopathy, and intravenous drug use remain unchanged.

- Fever: The criterion for documented temperature >38ºC during the clinical course is retained.

- Vascular Phenomena: The criterion for evidence of septic arterial emboli causing pulmonary infarction, cerebral or splenic abscesses/infarcts (now included), mycotic aneurysms, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions, and septic purpura is retained.

- Immunological Phenomena: Criteria for the presence of positive rheumatoid factor, Osler's nodes, Roth spots, and immune-complex-mediated glomerulonephritis are retained.

- Incomplete Major Criteria: This category, where most changes have been made, includes clinical findings that are significant but insufficient to define a major criterion. Among these:

    - Positive blood cultures that do not meet the requirements for a major criterion (<2 cultures for typical organisms, <3 cultures for atypical organisms).

    - A new criterion is added for the presence of positive cultures, PCR, or other nucleic acid-based tests (e.g., AMPLICON, shotgun sequencing, in situ hybridization) for IE-causing organisms in cardiac tissue, prosthetic material, or emboli without prior clinical or microbiological criteria to support them. This criterion appears to cover intraoperative samples of incidental findings that allow re-evaluation of preoperative diagnosis.

    - The finding of new valvular regurgitation identified by auscultation is downgraded to a minor criterion if echocardiography is unavailable. Worsening or changes in a pre-existing murmur are insufficient. This criterion was previously considered major. It remains useful for diagnosis in settings with limited resources (developing countries) or without direct access to echocardiography (primary care, first-level hospitals).

    - Pathological 18-FDG uptake in PET-CT within the first three months after prosthetic implantation, as previously indicated.

With the criteria outlined above, IE diagnosis is established based on the number of criteria met, unchanged from the previous version:

- Definite endocarditis: 1 pathological criterion or 2 major clinical criteria or 1 major + 3 minor clinical criteria or 5 minor clinical criteria

- Possible endocarditis: 1 major clinical + 1 minor criterion or 3 minor clinical criteria

However, the new document updates two of the three rejection criteria for IE:

1. An alternative diagnosis exists for the signs or symptoms, requiring three conditions: bacteremia due to an atypical pathogen, rapid resolution of bacteremia, and absence of IE evidence on imaging.

2. A new criterion for absence of recurrent bacteremia despite antibiotic therapy for less than 4 days. This expands the classic criterion of no autopsy or pathological findings compatible with IE despite antibiotic therapy for less than 4 days.

3. Failure to meet the criteria for definite or possible IE mentioned above.

In summary, most of the included criteria adapt the diagnosis to current resources and practices, which is welcome. However, one main limitation of these new criteria is the requirement for three blood cultures to meet the microbiological criterion for atypical pathogens. In an emergency or inpatient setting, two blood cultures are the norm. This could be problematic for diagnosing such pathogens. Nonetheless, blood culture requirements are simplified compared to previous temporal criteria for venipuncture extractions, which were rarely adhered to.

In conclusion, the Duke criteria emerged three decades ago to standardize the diagnosis of a complex condition like IE. These types of updates are essential for integrating technological and therapeutic advances into clinical practice.

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Fowler VG, Durack DT, Selton-Suty C, Athan E, Bayer AS, Chamis AL, et al. The 2023 DukeISCVID Criteria for Infective Endocarditis: Updating the Modified Duke Criteria. Clin Infect Dis. 2023 May 4:ciad271. doi: 10.1093/cid/ciad271.

José Manuel Martínez Comendador

Cardiac invasive treatment in patients with advanced cancer: whom, when, and how?

Updated and comprehensive review from JACC addressing the relevance of various cardiac invasive procedures in patients with advanced cancer.

Definitive evidence exists that certain invasive cardiac procedures can reduce morbidity and mortality in patients with acute coronary syndrome (ACS), severe valvular disease, heart failure, and ventricular arrhythmias. However, it is important to note that the randomized clinical trials (RCTs) supporting these findings excluded individuals with advanced cancer. Simultaneously, the approach to cancer treatment has undergone a paradigm shift in recent years, significantly improving patient survival rates. Until recently, patients with advanced cancer (also referred to as metastatic) were excluded as candidates for any type of cardiac procedures due to the high risk of death from cancer before benefiting from an invasive cardiac intervention. Nonetheless, changes in survival expectations for many of these patients radically challenge this outdated approach.

This review study presents an updated summary of current evidence with the aim of guiding decision-making for metastatic cancer patients who are eligible for cancer-specific treatments and simultaneously present severe cardiovascular disease. It should be noted that the cardiac interventions recommended in this review to improve survival and/or quality of life carry a Class I recommendation and Level A evidence in patients without advanced cancer.

Primary Percutaneous Coronary Intervention in the Context of STEMI

The mortality rate following a STEMI treated with percutaneous coronary intervention (PCI) ranges from 3% to 6%. Primary PCI has shown a significant reduction in short-term mortality (within 4-6 weeks) compared to thrombolytic therapy (Odds Ratio [OR]: 0.7). Additionally, there has been a decrease in the incidence of reinfarction (OR: 0.35) and stroke (OR: 0.46), along with improvements in symptoms and patient quality of life.

On the other hand, the prevalence of coronary artery disease in patients with cancer is higher than in those without it, likely due to an increased inflammatory and prothrombotic state that makes atherosclerotic plaques more vulnerable. Furthermore, primary PCI in patients with STEMI and advanced cancer has shown a lower in-hospital mortality rate compared to those who do not receive percutaneous treatment. However, the evidence on this is limited and biased, as the option of PCI tends to be contraindicated in cancer patients in a preterminal stage.

Following primary PCI for STEMI to treat the culprit lesion, a second-stage PCI targeting non-culprit lesions to achieve complete revascularization has been associated with a reduction in cardiovascular mortality and myocardial infarctions. Additionally, improvements in angina and quality of life have been recorded for at least three years of follow-up. However, it is essential to note that RCTs investigating this complete revascularization strategy exclude patients whose life expectancy unrelated to cardiovascular issues is less than five years.

Therefore, given the immediate benefits of primary PCI, it is recommended in all cases of invasive cancer undergoing first- or second-line treatment, except in terminal cases with a very short life expectancy.

Routine Invasive Strategy in Non–ST-Segment Elevation Acute Coronary Syndrome (NSTEACS)

The comparison between routine invasive and selective invasive strategies in meta-analyses of RCTs involving NSTEACS patients has shown a reduction in the incidence of nonfatal complications. Over a follow-up period of 6 to 24 months, a significant decrease in mortality, acute myocardial infarction (MI), hospital readmissions, and angina was demonstrated, with ORs in all cases below 0.8. Additionally, various RCTs have shown similar results when comparing early catheterization (within the first 24 hours) with delayed catheterization (24-72 hours), suggesting a suitable timeframe to discuss the case in an oncology patient before making a definitive decision.

Although there are no specific RCTs for patients with both NSTEACS and cancer, exploring contemporary administrative records of patients with both conditions seems to indicate that outcomes when comparing medical and invasive treatments are similar to those observed in patients without cancer. However, conducting dedicated studies addressing this population faces the challenge of significant heterogeneity across different cancer types.

In terms of access, when performing PCI, the radial approach has proven more effective than the femoral approach, with a Hazard Ratio (HR) of 0.77 for mortality and 0.55 for major bleeding. Although these findings could be applied to patients with advanced cancer, who have a higher bleeding predisposition, caution is warranted when making such extrapolations.

Dual antiplatelet therapy (DAPT) is recommended for these patients for at least 12 months. However, in situations where dual antiplatelet therapy is contraindicated due to the oncological condition, the indication for routine cardiac catheterization becomes less clear and should be individualized, considering factors such as response to oncological treatment and expected life expectancy. Most studies on NSTEACS patients with cancer are based on single-center, retrospective, or administrative cohort studies. These limitations introduce biases that favor more favorable prognostic outcomes.

According to expert opinion, patients who may benefit less from a routine invasive strategy include those with thrombocytopenia or those whose cancer treatments increase the risk of this condition, as well as patients with a life expectancy of less than six months. Conversely, patients with persistent or recurrent ischemia, signs of hemodynamic instability, or an extensive area of myocardial ischemia are more likely to benefit from an invasive approach, especially if dealing with advanced cancer under first-line treatment.

Multivessel Coronary Disease or Left Main Coronary Artery Disease

Given the comparable outcomes in terms of mortality between surgical revascularization and PCI for left main coronary artery (LMCA) disease, percutaneous revascularization stands out as the preferred option in advanced cancer patients, provided it is technically and anatomically feasible.

In asymptomatic multivessel coronary artery disease in patients with metastatic cancer, optimal medical management is considered sufficient and appropriate. However, in symptomatic patients, coronary revascularization is recommended. In this context, the pros and cons of coronary surgery versus PCI must be weighed carefully. A recent analysis of 12 RCTs reported a low 30-day mortality rate for both procedures, below 1.4%. However, five-year survival was significantly higher with coronary surgery (9.2% vs. 11.2%), especially in diabetic patients (10.7% vs. 15.7%). Consequently, in patients with multivessel disease and advanced cancer, especially those with diabetes, coronary

surgery can be considered the first option, provided there is a reasonable life expectancy of at least five years (typically patients on first-line treatment). Ultimately, this determination should be based on a comprehensive assessment that considers the patient's morbidity, individual preferences, and the potential interruption of oncological treatment due to surgical intervention, along with other relevant variables.

Considerations on Dual Antiplatelet Therapy

After an ACS, DAPT should be maintained for at least 12 months, with the option to transition to P2Y12 monotherapy after completing 1-3 months of DAPT. For patients with chronic ischemic heart disease, DAPT may be switched to P2Y12 inhibitor monotherapy after one month of treatment if there is a high risk of bleeding.

The likelihood of hemorrhage following PCI is higher in cancer patients due to bleeding risks associated with the tumor itself and/or thrombocytopenia, which may arise due to bone marrow infiltration, autoimmune factors, or as a side effect of oncological treatment. In parallel, cancer may also be associated with a prothrombotic state, potentially increasing the risk of stent thrombosis after PCI in these patients. Therefore, the choice of antiplatelet therapy should be highly individualized.

Evidence related to antiplatelet therapy in the context of ACS in patients with thrombocytopenia is limited. A recent systematic analysis indicated that thrombocytopenia (defined as a platelet count <150,000/mm³) was linked to higher in-hospital mortality (Relative Risk [RR]: 2.6), bleeding, and long-term mortality. More recent reviews have also established a connection between thrombocytosis and an increase in cardiovascular events.

Experts suggest not excluding cancer patients from invasive treatment if thrombocytopenia is mild or moderate. According to the latest expert consensus recommendations, aspirin may be initiated if the platelet count exceeds 10,000/mm³, DAPT with clopidogrel if above 30,000/mm³, and DAPT with prasugrel or ticagrelor if above 50,000/mm³. However, these recommendations lack robust supporting evidence. The most widely accepted recommendation is likely to avoid PCI and antiplatelets in platelet counts below 50,000/mm³.

Severe Aortic Stenosis

Over a decade ago, the PARTNER clinical trial clearly established that, for patients with symptomatic aortic stenosis who are contraindicated for surgical aortic valve replacement due to high comorbidity levels (risk of mortality or severe irreversible complications >50%), transcatheter aortic valve implantation (TAVI) significantly reduces mortality (Hazard Ratio [HR]: 0.55) and the composite of death or hospitalization (HR: 0.46).

In cases of symptomatic severe aortic stenosis with a life expectancy of over 12 months, TAVI is considered to offer substantial benefits, regardless of whether patients are undergoing first- or second-line cancer treatments.

Implantable Cardioverter-Defibrillators (ICD) and Cardiac Resynchronization Therapy (CRT)

Ventricular dysfunction induced by oncological treatments for advanced cancer may present varying patterns of reversibility. In some cases, as with trastuzumab, it can be reversible, whereas with agents like anthracyclines, this dysfunction is irreversible.

In general, it is well-established that for cases of heart failure (HF) with reduced ejection fraction (EF), ICDs constitute an effective strategy for reducing the risk of sudden cardiac

death. The most robust clinical studies on ICDs, in both the primary and secondary prevention of sudden death, do not explicitly exclude cancer patients; rather, they tend to exclude those with a life expectancy of one or two years due to other comorbidities. Alongside these results, new therapeutic approaches for HF, such as sodium-glucose cotransporter-2 inhibitors and angiotensin receptor-neprilysin inhibitors, have shown efficacy. Therefore, in cases of advanced cancer, these new HF therapies should be exhaustively optimized before considering the implantation of these devices. Additionally, non-resynchronization implantable devices appear to provide little improvement in quality of life or HF symptoms. Although they may reduce mortality, they could also increase morbidity. Hence, careful deliberation is warranted before deciding on implantation.

For patients with severe HF, EF <35%, and QRS duration >120 milliseconds, CRT has demonstrated a reduction in mortality, HF-related hospital readmissions, and symptom improvement. In cases of advanced cancer, considering the implantation of these devices may be appropriate.

One crucial consideration is the potential impact of ionizing radiation used in radiotherapy for various cancer types, which can damage implantable devices. Approximately 6.6% of these devices exhibit malfunctions after radiotherapy. Additionally, therapy-induced thrombocytopenia and neutropenia increase the risks of bleeding and infection. Therefore, when making decisions about these therapies, it is essential to factor in the scheduling of oncological therapies, particularly radiotherapy and chemotherapy.

A Conceptual Framework for Invasive Cardiac Interventions in Patients with Advanced Cancer

Similar to the transformation of HIV infection into a chronic disease, advancements in treatments for various cancer types have significantly improved life expectancy for tumors that previously had poor prognoses, effectively converting them into chronic conditions. These achievements have been made possible through advances in immunotherapy and targeted molecular therapies. This paradigm shift requires a reassessment of how we approach cardiovascular conditions in cancer patients, which, in turn, demands a more accurate understanding of the prognosis of those with advanced cancer.

This study provides an updated and valuable table (Table 3) summarizing recent advances and prognoses for the most common types of cancer treatments. It offers relevant and essential information so that cardiologists can stay informed about the most significant innovations in the field. Table 2 provides specific recommendations for cardiac interventions in common cancer types, considering the treatment line and its progression. Some specific examples include: 1) In patients with small-cell lung cancer receiving first-line therapy with oncogenic mutations, an early invasive approach should be considered if contemplating TAVI or CRT; 2) For prostate cancer with hormone-sensitive disease, invasive approaches should be considered in cases of STEMI, NSTEACS, symptomatic severe aortic stenosis, and when ICD or CRT is indicated.

COMMENTARY:

Although current evidence on the benefits of invasive cardiac interventions in patients with advanced cancer is limited, this thorough review provides an updated perspective on available evidence and successfully achieves its goal by offering solid guidance to inform decision-making in this patient group.

Based on this article, some key considerations when making decisions for these patients include: 1) Evaluating the balance between the benefits of invasive cardiac intervention

and the risks of adverse cardiovascular events if not intervened; 2) Analyzing cancer prognosis and the need to continue treatment without interruptions; 3) Considering the impact of thrombocytopenia, whether actual or anticipated; 4) Clearly defining patient care goals, prioritizing improvements in quality and life expectancy.

To facilitate understanding, invasive cardiac interventions can be categorized into two groups based on their short- and long-term benefits. Interventions with notable short-term results include primary PCI in STEMI, routine invasive percutaneous strategy in NSTEACS, and TAVI in cases of symptomatic severe aortic stenosis. Meanwhile, interventions providing long-term benefits include CRT, primary prevention ICDs, and revascularization in patients with multivessel coronary artery disease. Based on this classification, a simplified approach can be established depending on the stage of advanced cancer: 1) For patients with metastatic cancer undergoing first-line treatment and a reasonable life expectancy, all the aforementioned invasive cardiac interventions could be performed; 2) In patients showing disease progression despite initial treatment, invasive cardiac interventions with short-term benefits are recommended. Among the options with long-term benefits, CRT or revascularization in cases of multivessel disease may be considered, depending on the situation. Primary prevention ICDs are not recommended; 3) For patients with disease progression during second-line treatment or in palliative situations, invasive treatments are generally not suggested, with exceptions potentially made for primary PCI or in select cases of NSTEACS.

As evident, in the final decision-making process, it is essential to consider the patient's fragility and the presence of multiple conditions, involving the patient and a multidisciplinary team consisting, at the very least, of a cardiologist, cardiac surgeon, and oncologist.

Although it is impossible to exhaustively address advances and prognoses for all advanced cancer types in this article, this review offers a practical and highly useful consideration by providing, for the first time, an updated overview of life expectancy for the most common cancers in light of the latest available treatments. This provides an essential guide for professionals making decisions on the suitability of invasive procedures for patients with advanced cancer. The increased survival of those facing advanced tumor diseases alongside severe cardiovascular conditions has prompted a crucial reassessment of indications for invasive procedures. As a result, there has been a progressive and consistent expansion in the indications for invasive procedures in patients with advanced cancer, a trend that will undoubtedly continue in the future.

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Elio Martín Gutiérrez

Treatment of Cardiac Sarcomas: Much to Learn

Update on classification, prognosis, therapeutic management, and surgical techniques for the resection of primary cardiac sarcomas from the Houston group.

The study under discussion today represents a valuable resource due to its thorough and educational approach to a complex topic such as the treatment of primary cardiac sarcomas. Authored by a multidisciplinary team that includes surgeons, cardiologists (Houston Methodist, Texas), and oncologists (Anderson Cancer Center, Houston, Texas), this work reflects extensive experience, far surpassing that available at any center in our country, and even the individual experience any of us could accumulate over our professional career.

Primary cardiac sarcomas are a diagnostic rarity, with an incidence of 1-3 cases per 100,000 people. Although they do not technically qualify as rare diseases, which are defined by a prevalence of fewer than 5 cases per 10,000 people, the low frequency of these tumors explains the lack of extensive knowledge in this field. This rarity is further compounded by the fact that the ratio of benign to malignant heart tumors is approximately two to one. However, primary cardiac sarcomas are particularly uncommon among malignant neoplasms, with heart involvement more commonly resulting from infiltration by neighboring organs (such as lung, breast, or lymphoma) or from metastatic disease (such as melanoma). Additionally, the metastatic spread to the heart follows a distinct pattern, with the pericardium and epicardium being the most commonly affected areas (adenocarcinomas and squamous cell carcinomas), followed by the myocardium (melanoma). Endocardial involvement is rare and is mainly observed in tumors with intravascular growth, such as renal cell carcinoma, hepatocellular carcinoma, and uterine neoplasia. Other aspects related to cardiac surgery in oncologic patients have been analyzed in previous blog entries.

The study, beyond the wealth of details derived from the extensive experience accumulated by this team, follows a simple design as a classic case series summarizing the institution's retrospective experience. They compare their results from 1998 to 2021 with those from a U.S. database, dividing their cases into two evolutionary periods (1998-2010, 2011-2021) to determine if there was any impact on outcomes with the accumulation of experience, modernization, and implementation of postoperative care and therapies. All procedures were performed by a single senior surgeon (Michael J. Reardon), and the series includes 122 cases (excluding metastatic tumors, benign tumors, and malignancies originating from other locations with cardiac involvement). Survival rates from the U.S. database at 1, 3, and 5 years were 40%, 15%, and 9%, respectively, while the Houston group’s experience showed improvement with rates of 88%, 43%, and 27%, respectively. No significant differences in survival were observed between the analyzed periods, suggesting the prognosis is more heavily influenced by the pathology than by potential technical or therapeutic advancements. It is also worth noting that the U.S. statistics span 43 years, and given such a wide time frame, a temporal analysis similar to that used for the Houston group's experience might also have been appropriate. Median survival in the U.S. database was 7 months, while in the Houston group, it was 467 days (15 months) from surgery and 871 days (28 months) from diagnosis.

The authors conclude that managing these complex patients requires centers with extensive experience and multidisciplinary teams. They observed no survival improvements over time, likely due to the systemic nature of the disease.

COMMENTARY:

The lessons gathered from this study are numerous. First, the authors characterize the profile of patients with primary malignant cardiac tumors. These patients have few relevant medical histories that might correlate with the origin of such neoplasms, are relatively young (average age 45 years), and have a slight male predominance (52%). Most are White (73%), although, as commonly observed in the American healthcare system, access to high-level and costly resources often correlates with coverage disparities. The most common location was the left atrium (40%), followed by the right atrium (32%). In fact, tumor location influences clinical presentation, with left-sided tumors typically manifesting symptoms earlier and thus being diagnosed sooner. Right-sided tumors, however, tend to exhibit greater intraluminal growth, leading to later diagnoses and higher degrees of extension to neighboring structures (superior vena cava 1-3%, right ventricle 6%) and presenting distant disease. Ventricular involvement is, fortunately, much less frequent (right 5%; left <2%), as is involvement of the great vessels (pulmonary artery <2%; no cases were reported in the aorta). However, as an extension from the atrial origin, pulmonary vein involvement is not uncommon, which has significant implications for surgical technique.

The authors highlight that many patients were referred from other institutions (54%) where the diagnosis of malignancy was made only after the excision of a tumor initially considered benign, with affected resection margins subsequently identified upon histopathological analysis. The presentation symptoms were varied, with dyspnea (59%), chest pain (29%), cough (12%), and syncope (10%) being the most common. Regarding disease extension, 31% of patients already had metastases at the time of intervention. Although this was not statistically significant, this percentage showed a notable decrease between the two analyzed periods of the Houston experience, from 39% between 1998-2010 to 25% between 2011-2021. Metastases primarily occurred through hematogenous spread, with lung (17%), bone (7%), liver (6%), and brain (3%) as the main sites. The predominant etiologies included angiosarcoma (39%), high-grade sarcoma (15%), anaplastic sarcoma (11%), leiomyosarcoma, and intimal sarcoma (7% each). Remarkably, rhabdomyosarcoma accounted for only 1.6% of the cases.

A significant volume of early reoperations was motivated by patients referred from other centers who had undergone incomplete surgery with histopathological diagnoses of malignancy and affected resection margins. This altered the management protocol considerably compared to patients without prior intervention. The authors describe the therapeutic course followed for a typical patient. First, imaging studies to determine lesion anatomy (cardiac MRI) and disease extension (CT/PET) are essential. The addition of a biopsy, particularly in right-sided tumors, helps exclude etiologies like lymphoma, which may benefit significantly from neoadjuvant treatment. For patients with distant disease, biopsy of the lesion and/or metastases enables the initiation of neoadjuvant treatments before surgery (4-6 cycles of doxorubicin/ifosfamide, taking into account the cardiotoxicity of the former chemotherapeutic agent). The authors emphasize assessing lung function, particularly if resectability involves lobectomy/pneumonectomy techniques when pulmonary veins are affected and/or metastases are present in that location. Coronary angiography was also a relevant study, especially in cases of right-sided involvement where the right coronary artery is often implicated. After multidisciplinary evaluation and shared decision-making with the patient, therapeutic indications for both medical and surgical treatment are made. Eighty-two percent of patients received a neoadjuvant chemotherapy cycle. After the surgical technique, which will be analyzed below, oncological care and treatment were continued.

Regarding the surgical technique, the group has published several studies and proposed various classifications. First, primary cardiac tumors are classified according to the 4th edition of the WHO classification as benign, malignant, and of uncertain behavior (e.g., benign tumors but potentially causing severe or fatal complications such as obstructive myxomas, highly mobile pedunculated tumors, embolizing tumors, etc.). Many classifications focus on histopathology, but the Houston group recommends classification according to the chamber of origin (right heart, left heart, pulmonary artery), due to the technical implications for resection. Briefly, right-sided tumors often involve the right atrioventricular groove and the right coronary artery, infiltrating the ventricle. Their resection may require reconstruction of the coronary artery with an interposition graft and repair/replacement of the tricuspid valve (<10% of the series). In left-sided cases, involvement is typically more restricted to the atrial level, with one of the main limitations for resectability being pulmonary vein involvement. Extension through some of these veins required associated lobectomy and pneumonectomy procedures (24%). The group has described a protocol in which they perform the cardiac intervention with cardiopulmonary bypass on the first day, followed by the thoracic intervention the next day, once organ damage has recovered, and coagulopathy has been reversed. The high complexity of some cases, with biatrial involvement, required autotransplantation techniques in 37% of cases. In-hospital mortality for patients undergoing autotransplantation was 19%, compared to 18% for the entire series. Mortality for cases requiring both autotransplantation and pneumonectomy reached 50%, with the authors noting a reduction in mortality with the two-stage strategy. Notably, likely due to the poor prognosis of these patients given the systemic nature of the disease, the Houston group does not consider alternatives like the total artificial heart (preferred over transplantation to avoid the need for immunosuppression) when resection of the disease is extremely complex or limited by irreparable cardiac defects. Likely, the institution's policy is reflected in the fact that the series presented consists only of selected cases with resectability options. The volume of patients rejected is not indicated, but the importance of neoadjuvant treatment response is suggested for considering candidates for surgery.

Finally, the authors analyze results based on resective success. They follow a classification of resection margin involvement, common to oncologic surgery and more familiar to other surgical specialties than to ours. R0 indicates the absence of disease at the margins, with adequate microscopic and macroscopic resection margins. R1 denotes microscopic involvement of the resection margin, or that some of the margins are insufficient microscopically to be considered free of disease. R2 is usually an intraoperative diagnosis where macroscopic involvement of the resection margins is evident. Despite good pathological outcomes (R0 47%, R1 39%, R2 5%), the authors conclude that survival was not affected by achieving better resection grades. This finding highlights the unique nature of these neoplasms, which, given their contact with the circulatory system, could be considered systemically disseminated from diagnosis, with the associated prognostic implications. In the case of other solid tumors, findings such as vascular infiltration or affected resection margins have clear prognostic implications. However, conceptually, the initial presentation of these neoplasms in such adverse circumstances almost inherently suggests that applying oncologic surgical principles from other specialties is not entirely relevant; instead, other concepts and classifications should be considered.

In conclusion, efforts to treat patients with primary cardiac tumors continue to yield poor outcomes. Median survival between 7 months (U.S. database) and 15 months (Houston group's experience) seems inadequate given the monumental diagnostic, surgical, and oncological efforts involved. However, beyond this discouraging paradigm, lie the expectations and decisions of the patient. Thus, without ever losing sight of them, the apparent futility compared to the excellent clinical outcomes achieved in other areas of

our specialty can become a benefit, particularly when considering that this devastating disease affects very young patients (35 to 56 years in the Houston series). Hopefully, future advancements in oncology therapy will improve survival outcomes for a disease almost systemic by definition, where resective efforts do not translate into a reduction in recurrence, which seems almost inevitable in the short to medium term.

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Miguel Ángel Parada Nogueiras

Oxygen delivery-guided perfusion for the prevention of acute kidney injury

Comparison between two perfusion strategies during cardiopulmonary bypass: one guided by an oxygen delivery index (DO2i >300 mL/min/m²) based on body surface area and another conventional strategy based solely on pump flow according to the patient's body surface area (2.6 L/min/m²).

Postoperative acute kidney injury (AKI) in cardiac surgery represents a severe complication associated with increased morbidity and mortality. Its development is mediated by reduced renal blood flow induced by a variety of factors, including endogenous and exogenous toxins, metabolic disturbances, ischemia-reperfusion injury, and the use of cardiopulmonary bypass (CPB) itself. Several authors have identified oxygen delivery (DO2) during CPB as a critical factor in AKI, estimating a critical threshold for DO2 between 225 and 300 mL/min/m².

This study is a prospective, randomized, blinded, single-center trial with a sample of 300 cardiac surgery patients. Patients with chronic renal failure, circulatory arrest, CPB temperature below 34ºC, or postoperative need for ECMO or intra-aortic balloon pump were excluded. The primary objective was to assess the incidence of postoperative AKI based on KDIGO criteria. Secondary objectives included red blood cell transfusion rates, mechanical ventilation duration, ICU and hospital length of stay, peak serum creatinine 48 hours post-surgery, and perioperative mortality.

The sample consisted of 127 patients in the DO2i-guided perfusion strategy group and 138 in the conventional strategy (CS) group. In the DO2i group, DO2 was adjusted by modifying pump flow, initially set at 2.6 L/min/m², and by red blood cell transfusion when hemoglobin levels dropped below 8.5 g/dL, a threshold deemed sufficient to maintain DO2 above the critical level. The CS group relied on a fixed pump flow of 2.6 L/min/m² based solely on the patient's body surface area (BSA). Red blood cell transfusion was performed when hemoglobin dropped below 7 g/dL. Both groups maintained normothermia (temperature >35ºC) and a mean arterial pressure (MAP) >60 mmHg.

Pre- and intraoperative variables were comparable between groups. However, the DO2i group exhibited a higher pump flow rate, with an average index of 2.82 L/min/m² compared to 2.63 L/min/m² in the CS group ($p < .001$). Using real-time gas monitoring (Terumo® CDI 500®) and data logging with the Livanova® Connect® system, it was observed that the area under the curve (AUC) for DO2i <300 mL/min/m², as well as for venous oxygen saturation (SvO2) <70 mmHg and MAP <60 mmHg, were consistently lower in the DO2i group ($p < .001$). This translated to significantly lower times with DO2i <300 mL/min/m² (DO2i 2.7 min vs. CS 20.3 min, $p < .001$), SvO2 <70 mmHg (DO2i 0 min vs. CS 0.7 min; $p < .001$), or MAP <60 mmHg (DO2i 19 min vs. CS 24.8 min; $p < .005$) in the DO2i group. Consequently, the AKI incidence in the DO2i group was 14.6% versus 30.4% in the CS group (RR = 0.48; $p = .002$). Significant differences were only observed for KDIGO stage 1 AKI (DO2i 12.4% vs. CS 25.4%, RR = 0.42; $p = .006$), with no differences in stages 2 and 3. No significant differences were found in red blood cell units transfused, ventilation time, ICU and hospital stays, peak serum creatinine at 48 hours post-surgery, or postoperative mortality.

A univariate logistic regression analysis showed that perioperative variables associated with AKI included time with DO2i <300 mL/min/m² ($p = .023$), age ($p = .013$), baseline glomerular filtration rate ($p = .001$), surgical technique ($p = .006$), and perfusion time ($p = .004$). In multivariate analysis, only perfusion time remained significantly associated ($p = .024$) with increased AKI incidence.

The main finding of this study suggests that in subgroup analysis, DO2i proved superior for protecting against postoperative AKI in patients aged 60 to 74 years, with a BSA <1.4 m², baseline glomerular filtration rate of 60-89 mL/min/1.73 m², nadir hematocrit <23%, and CPB duration <120 min.

COMMENTARY:

This single-center study, with a limited sample, analyzed small subgroups, thus limiting the validity of the conclusions. However, as a perfusionist, I believe it is crucial to have as much information as possible during CPB through continuous gas monitoring systems that measure gasometric values and oxygen consumption (VO2) as well as hemoglobin levels. The addition of the Livanova® Connect® system, which logs data in real-time and calculates DO2i by integrating perfusion variables such as pressures, flows, gas values, and medication administration, provides essential data to optimize patient conditions during cardiopulmonary bypass and allows real-world data for ongoing research aimed at improving perfusion and reducing its adverse effects.

According to the study's findings, it is evident that maintaining elevated hemoglobin levels in all patients or increasing perfusion flow above 3 L/min/m² to achieve acceptable DO2i values is not the solution, as both have demonstrated detrimental effects: higher transfusion rates increase morbidity and mortality in cardiac surgery, and higher pump flow leads to hemodilution, hemoglobinuria, which predisposes to AKI, and increased inflammatory response and coagulation issues. DO2i is particularly effective in patients with low BSA who are more sensitive to hemodilution, struggle to maintain adequate DO2, and in patients with nadir hematocrit <23%.

However, due to the detrimental nature of CPB, its duration remains the main factor associated with AKI in multivariate analysis. The role of DO2i is still unclear, and further research is needed to establish the optimal balance between pump flow and red blood cell transfusion. Future studies with real-time data systems like Livanova® Connect® will provide valuable insights for identifying patient characteristics that respond best to each strategy.

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Juan Blanco Morillo

Lights and shadows in the use of del nido cardioplegia in cardiac surgery

This literature review aims to address key questions regarding the use of Del Nido cardioplegic solution in cardiac surgery.

Del Nido cardioplegia (DNC), first introduced by Dr. Pedro Del Nido in 1994 at Boston Children's Hospital, was initially developed for pediatric cardiac protection but has been increasingly applied to adult patients over the last decade. DNC is a blood-based solution in a 1:4 ratio, with Plasmalyte A as its base, enriched with K+ and NaHCO3, along with Mg+2 and lidocaine as membrane stabilizers. This composition limits Na+ and Ca+2 entry into the myocyte after aortic unclamping, promoting energy repletion and the removal of anaerobic metabolites, thereby reducing ischemia-reperfusion injury.

In this article, Waterford et al. conduct a non-systematic literature review aimed at addressing frequently raised questions regarding DNC usage in adult patients. Their framework follows a question-and-answer format, summarized below:

What is the best clinical method for evaluating the quality of myocardial protection today?

The authors note that studies assessing DNC's protective effects focus on postoperative troponin measurements (at 2, 12, and 24 hours postoperatively), inotropic support requirements, and contractility as observed via transesophageal echocardiography (TEE). However, they suggest that prospective, randomized studies are needed to include CK-MB determinations and contractility measurements before and after surgery, using both TEE and magnetic resonance imaging (MRI).

When should the Del Nido dose be repeated, and what amount should be used for maintenance dosing?

The authors indicate that the standard dose is 1000 mL for 90 minutes of clamp time. In cases where surgeries may be prolonged, evidence suggests that a second dose of 500 mL is safe, particularly in low-risk patients. However, they warn of the risk of lidocaine cardiotoxicity from successive doses, recommending a switch to blood cardioplegia (e.g., Buckberg) in coordination with the perfusionist if additional doses are needed.

Is Del Nido suitable for all cases? Are there any specific considerations?

There appears to be insufficient evidence for its suitability in patients with low preoperative left ventricular ejection fraction, right ventricular dysfunction, or anticipated prolonged clamp times. In such cases, alternatives like HTK may be recommended if single or limited doses of cardioplegia are desired.

Should topical cooling be applied concurrently when using Del Nido?

The authors find no evidence on this aspect and suggest that, when changing cardioplegia solutions, it is reasonable to maintain the usual protocol regarding topical cooling.

Can Del Nido be administered retrogradely in patients with aortic insufficiency?

In these cases, a retrograde route combined with effective intermittent antegrade delivery appears to be a safe option. The authors also advise against continuous retrograde administration, even in a 4:1 format, to avoid lidocaine overdose.

COMMENTARY:

The authors' approach is of great interest; however, several methodological limitations must be considered. This is an expert review focused on 21 references, lacking major meta-analyses that might provide a broader perspective on DNC's value in various aspects.

Gambardella et al., in a meta-analysis involving 5516 patients, reported that DNC reduces clamp and cardiopulmonary bypass times, incidence of reperfusion fibrillation, and postoperative troponin peak compared to multidose cardioplegia and HTK. Similarly, a meta-analysis by Misra et al. confirms these observations, adding that compared to patients treated with blood cardioplegia (Buckberg), those treated with DNC received lower cardioplegia doses, exhibited better glycemic control, and required fewer blood product transfusions.

On the other hand, the experience of our center, with over 4000 patients treated with DNC, including cardiac transplants, aligns with findings by Sanetra et al. Their propensity-matched analysis demonstrated that DNC is an appropriate alternative to cold blood cardioplegia in patients with impaired contractility and complex surgeries, showing lower troponin release and improved postoperative left ventricular ejection fraction. Additionally, other studies have observed that, compared to HTK and blood cardioplegia, DNC is associated with reduced release of myocardial injury biomarkers and apoptosis in pediatric patients.

While further evidence on DNC's use in high-risk patients and prolonged surgeries requiring redosing is still necessary, it appears that this cardioprotective strategy may be optimal for a substantial range of procedures, provided meticulous administration ensures uniform distribution of the solution across the myocardium.

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Bunty Ramchandani

Postoperative bleeding? Don't waste time

A retrospective study from Johns Hopkins Hospital analyzing the impact of reintervention for bleeding on postoperative morbidity and mortality.

Surgical patients bleed; this is a reality every cardiac surgeon must confront. The importance of this has led to the rate of reinterventions for bleeding becoming a quality indicator. Yet, the rule has a workaround; sometimes quality can be maintained by avoiding reinterventions at the cost of multiple transfusions. The price paid includes hemolytic reactions and organ damage, such as renal or pulmonary injury secondary to transfusion. Consequently, there is an increase in mechanical ventilation duration, pneumonia incidence, sepsis, renal failure, and postoperative mortality.

When should we intervene? We might consult Kirklin et al., various articles, or even our colleagues; each will likely give different guidelines. Clinical variability reflects a lack of consensus, often seen when attempting to standardize complex processes. In today's article, Shou et al. aim to identify temporal criteria for indicating reexploration for bleeding.

This retrospective study from the Adult Cardiac Surgery Department at Johns Hopkins Hospital includes all consecutive surgeries from 2010 to 2020, excluding heart transplants, ventricular assist device implantations, and patients with open chest following the initial procedure. The primary aim was to identify the association between reexploration timing and postoperative outcomes. The secondary objective was to evaluate potential relationships between bleeding location and chest tube output. Five categories of bleeding were assessed: suture line, chest wall, mediastinum (perivascular fat or thymus), multiple locations, and "dry reexploration." Morbidity was analyzed as a composite variable for the following complications: stroke, renal failure, pneumonia, and/or surgical wound infection. Mortality was defined as death within the initial postoperative days.

A total of 10,070 patients were analyzed, of whom 251 (2.5%) required reexploration. Reintervention patients had significantly more comorbidities ($p < .05$), such as liver disease, dialysis-dependent renal failure, cerebrovascular disease, and endocarditis. This group also had more urgent surgeries ($p < .01$) and longer cardiopulmonary bypass times ($p < .05$). A third of these reexplorations were "dry" (n = 75), followed by suture line bleeding (n = 70; 28%). Chest tube output was higher when bleeding involved mediastinal structures, with a median output of 450 mL/h, while dry explorations had a much lower median output of 151 mL/h. Delayed reexploration significantly increased morbidity (0-4 hours 12.3% vs. 25-48 hours 37.5%; $p = .001$) and mortality (0-4 hours 3.1% vs. 25-48 hours 43.8%; $p = .001$).

The authors conclude that delayed reexploration for bleeding increased morbidity and mortality. They advocate for early intervention, preferably within the first 4 hours, and highlight biases resulting from using reexploration for bleeding as a quality criterion.

COMMENTARY:

Studies on postoperative bleeding are nothing new, nor is its association with increased morbidity and mortality. It remains unclear whether the risk factor is reintervention itself, blood product transfusion, or a combination of these two with other factors. Few studies have assessed the temporal association between reexploration and clinical outcomes, but all agree that reexploration is preferable when necessary within the first 12 hours.

Although we would like a specific timeframe or output level to indicate reexploration, we should avoid oversimplification. In similar studies, it's common to cite a postoperative bleeding rate exceeding 1000 mL in the immediate postoperative period as a reexploration criterion, though this remains an arbitrary and lenient threshold. Critical variables, such as active anticoagulation and/or antiplatelet medication, EuroSCORE, and other unweighted risk factors (like liver dysfunction), as well as the characteristics and complexity of the procedure itself (aortic surgery, reoperation) and individual patient conditions (preoperative anemia, female gender, low body surface area, endocarditis/sepsis), were not considered for assessing temporal associations. Additionally, limitations arise from the retrospective, single-center nature of this study. However, the 10-year evaluation period allows time for perioperative improvements, staff experience gains, and protocol changes (e.g., thromboelastography and guided transfusion), introducing new biases in interpreting the results.

In conclusion, in cases of postoperative bleeding, one should not waste time on decision-making. Reexploration should be individually decided based on the patient's clinical status, the complexity of the intervention, the team's experience, and hemostasis test results. Some bleeding cases may be managed conservatively. Accepting variability in specific clinical practice aspects is essential; therein lies the art of surgery.

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Bunty Ramchandani

Mediastinitis; the elephant in the room

Meta-analysis of 24 studies with a total of 407,829 patients to assess morbidity and mortality associated with mediastinitis.

Mediastinitis is a surgical site infection arising during an intervention. The term “surgeon” originates from the ancient Greek *kheiroynos*, meaning “one who works with hands.” Thus, a surgical site infection could be considered facilitated by the “hand” of the surgeon. Since the days when we were called barbers—neither doctors nor physicians—surgical wound infection has been our most despised companion. It is the elephant in the room that no one wants to address due to the stigmas it carries.

The impact of surgical wound infections was significant enough that even the WHO took action in 2016 to reduce them. In Europe, such infections triple healthcare costs, increase hospital stays by nearly a week, and incur an annual cost of 5-10 billion euros. The outlook for mediastinitis has not improved much over the last decade. With an incidence of <2%, it carries a mortality rate of almost 10%, quadruples hospital stays, and increases costs by nearly five times. In an era where antibiotic resistance is more common than the exception, the future for these infections remains uncertain without proactive measures.

In today’s study, Gaudino et al. conducted a meta-analysis on mortality associated with mediastinitis following cardiac surgery. The primary objective was to assess overall mortality, while secondary objectives included evaluating in-hospital mortality, follow-up mortality, major adverse cardiovascular events, myocardial infarction, and the need for repeat revascularization. They performed a systematic search for studies examining short- and medium-term outcomes, comparing patients who developed mediastinitis with those who did not. They identified 24 studies, encompassing 407,829 patients, of whom 6,437 (1.6%) developed mediastinitis. The average follow-up was 3.5 years. Patients with mediastinitis had double the risk of overall mortality, follow-up mortality, major cardiovascular events, and triple the risk of in-hospital mortality ($p < .001$). There were no statistically significant differences in myocardial infarction or repeat revascularization, likely due to limited studies for these comparisons. Mediastinitis was also associated with longer postoperative stays and higher incidences of stroke, myocardial infarction, respiratory failure, and renal failure. The authors concluded that mediastinitis increases both mortality and clinical complications in the short and medium term.

COMMENTARY:

Meta-analyses hold a privileged place in scientific literature, second only to randomized clinical trials. However, the quality of a meta-analysis is only as good as the studies it builds upon. Their role is to synthesize knowledge and present it in a structured way to answer a clinical question. Gaudino et al. raise a relevant and pertinent question: they want to determine the mortality associated with mediastinitis following cardiac surgery. However, their clinical question is somewhat ambitious and thus broad. They encompass a highly heterogeneous patient profile, with studies that only examine isolated coronary surgery patients, others with only transplant cases, and many others with mixed cases. Additionally, there is a bias in the literature search as conference presentations were excluded, and no mention was made of searching grey literature (e.g., doctoral theses). The studies evaluated span almost three decades, incurring further bias by comparing articles from 1992 with those from 2021. Sufficient time has passed to incorporate surgical advancements, postoperative care improvements, and even antibiotic treatments that complicate comparisons, given that mediastinitis is, by definition, a

multifactorial complication. Examining the consistency of results expressed in the forest plot reveals variability or heterogeneity. An I^2 statistic of 89% confirms heterogeneity and suggests interpreting the results with caution, as the validity of the model and the effect size are compromised.

Regardless of the study's precision in answering the clinical question, it is clear that mediastinitis is a complication to avoid. No single intervention can resolve the problem of surgical site infections. Embracing the philosophy of Dave Brailsford (the British cycling team coach) and implementing “the aggregation of marginal gains” is essential. Preoperative measures, such as using antiseptic soap showers the night before surgery, preparing the chest skin with chlorhexidine, avoiding shaving the surgical site by using disposable clippers, administering antibiotics within the hour before incision, limiting the use of bone wax, handling tissues gently, minimizing operating room traffic, securing proper wound closure with good hemostasis and stable osteosynthesis, are some of the measures that should be implemented. I emphasize the use of negative-pressure wound therapy in both infected wounds and healthy ones with risk factors for dehiscence. This technology has existed for over a decade but was mentioned in only two of the 24 studies included in this article. Although the results on the benefits of negative-pressure therapy are inconclusive, its use has been on the rise. We hope that soon, with more data, its use will be standardized for both treatment and prevention of surgical wound infections.

In conclusion, as surgeons, we cannot settle for anything less than perfect wounds. By incorporating a comprehensive package of measures to reduce surgical site infections, we should aim for a zero-mediastinitis policy. We must do everything possible to eliminate infections from our wounds.

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Carolina Mayor Deniz

4 A's Test: clarifying confusion over postoperative delirium in cardiac surgery

This single-center, prospective observational study assesses the diagnostic accuracy of the 4 A's Test for screening acute confusional syndrome in postoperative cardiac surgery patients, compared to a reference standard.

Acute confusional syndrome (ACS), or delirium, is a neuropsychiatric disorder of attention and awareness with an acute onset and fluctuating course. It occurs in at least 20% of patients during the postoperative period of cardiac surgery and is associated with increased morbidity and mortality rates. However, it remains underdiagnosed in over half of cases. The 4 A's Test, a recently introduced tool for ACS screening, comprises 4 items (alertness, Abbreviated Mental Test-4, attention, and acute change or fluctuating course) with a scoring range of 0-12 points; a score ≥4 suggests delirium. The test can be administered quickly (<2 minutes) by non-specialist personnel without prior training. However, no studies have yet established its diagnostic accuracy in cardiac surgery patients.

To address this, Chang et al. designed this single-center, prospective observational study in two phases, depending on whether the 4 A's Test was administered once daily by research assistants (Phase 1, double-blind) or three times daily by the nursing staff (Phase 2). They included a cohort of 316 patients from St. Boniface Hospital (Canada) in their first three postoperative days on the ward following ICU discharge. The outcomes were then compared with the Confusion Assessment Method (CAM), routinely conducted three times daily by nursing staff, and with the reference standard based on the DSM-5 criteria. The secondary objective was to assess its predictive value for adverse surgical events, including mortality, postoperative complications, and hospital stay. Finally, they conducted a survey to gather nurses' opinions on the 4 A's Test implementation.

In Phase 1, a total of 137 patients were included, 24.8% of whom presented with ACS. The 4 A's Test demonstrated an 85% sensitivity and 90% specificity, while the CAM showed a sensitivity of 23% and specificity of 100%. In Phase 2, nursing staff screened 179 patients, with an ACS prevalence of 13%. In this phase, the 4 A's Test yielded a sensitivity of 58% and a specificity of 94%. Regarding patient outcomes, those with a positive 4 A's Test had a hospital stay that was 2 days longer ($p = .003$), with no statistically significant differences in mortality or adverse events at 30 days. After implementing the 4 A's Test, 64% of nurses felt it improved their confidence in detecting ACS, and 76% would consider its routine use.

The study concludes that the 4 A's Test is an effective tool with moderate sensitivity and high specificity for detecting ACS in postoperative cardiac surgery patients in real-world clinical practice. It is recommended that its frequency be reduced to once daily to improve staff adherence and enhance early ACS detection.

COMMENTARY:

ACS is one of the most prevalent complications following cardiac surgery, with risk factors including extensive atherosclerotic disease, use of cardiopulmonary bypass for surgery, and the need for opioid analgesics. It is associated with a higher risk of mortality, hospital readmission, cognitive decline, and overall quality-of-life reduction. As ACS often has potentially treatable underlying causes (e.g., electrolyte imbalances, stroke, nosocomial infection, or adverse drug event), early diagnosis poses a challenge in the postoperative period of any cardiac surgery. Numerous screening tools have been developed for this purpose, some of which are validated in the ICU setting (e.g., CAM),

yet none have shown proven effectiveness once patients are transferred to general wards.

A good screening test should not only have high sensitivity and specificity but should also be rapid, easy to administer, and reproducible. However, this study demonstrated that the test's sensitivity was significantly reduced when administered by nursing staff, likely due to methodological inconsistencies and low adherence to test administration. Furthermore, ACS can manifest as hyperactive, hypoactive, or mixed forms, complicating initial detection by non-specialist staff in psychiatric diagnosis. One of the strengths of this study is its execution under real clinical conditions, with results reflecting the routine underestimation of neuropsychiatric evaluations and their complex prevalence. Notably, patients with prior neurocognitive deficits were not excluded, and the overall ACS prevalence aligns with other studies.

The authors themselves acknowledge several limitations, noting that in Phase 2, the results were not double-blinded since the same nurses conducted both tests. This study interestingly highlights that, when the 4 A's Test was administered three times daily, the quality of the assessments decreased, impacting sensitivity results. Additionally, due to ACS's fluctuating nature, it is possible that some phases of testing did not capture positive scores for ACS. Thus, given the workload burden on nursing staff, the authors recommend administering the test only once per day to optimize sensitivity and specificity and improve detection of a condition with potentially treatable causes.

While this study, due to its limited sample size and the inherent limitations of a single-center observational design, cannot provide sufficient validity to generalize its results to other centers, it lays the groundwork for future research to answer unresolved questions, such as whether early diagnosis improves patient outcomes, reducing morbidity and hospital stay.

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Bunty Ramchandani

Pump-head: cognitive impairment and cardiac surgery

This review article documents and analyzes the literature on the prevalence, pathogenic mechanisms, and potential treatment strategies for cognitive decline following cardiac surgery.

Neurological complications rank as the second cause of morbidity and mortality post-cardiac surgery, after heart failure. These complications can be classified into three categories: cerebrovascular complications, encephalopathy, and peripheral nervous system disorders. Encephalopathy includes conditions such as coma, delirium, seizures, and neuro-cognitive decline (NCD).

Today's article provides an updated review on the prevalence of NCD, its pathophysiological mechanisms, and potential treatment strategies. This topic is particularly relevant as the persistence of these neurological sequelae causes a significant impact on both the quantity and quality of life.

COMMENTARY:

NCD following cardiac surgery encompasses impairments in memory, executive, motor, and attentional functions, among others. Depending on the adopted definition and diagnostic measures used, this complication can be detected in 3% to 79% of patients in the immediate postoperative period. Given the highly variable nature of this complication, which has proven to be significantly prevalent in various studies, it is essential to explore the potential long-term implications on the quality of life for our patients.

One of the primary limitations in diagnosing NCD lies within its own definition. Broadly, it is the loss of neurocognitive function when comparing a patient's preoperative to postoperative state. But what specific metrics should be assessed to determine this decline? Should we evaluate discrete neurocognitive items or take a global approach? It is important to differentiate NCD from conditions like stroke, as it does not involve focal deficits. To ascertain this type of deficit, preoperative and postoperative assessments are fundamental. The timing of assessment is also critical; some studies consider the diagnosis of NCD beyond 30 days post-surgery to differentiate it from alterations characteristic of an acute postoperative phase. These deficits can be detected through a range of methods, from simple questionnaires or complex scoring systems to imaging tests like MRI. However, imaging lacks a clinico-radiologic correlation and thus does not contribute to diagnosis. In many cases, these deficits are not apparent to the patient or their treating physicians. Therefore, is it even worth detecting it? Despite the limitations of a homogeneous diagnostic definition, it is evident that a patient with NCD has an elevated risk of adverse events, including prolonged hospitalization, mortality, hospital costs, and reduced quality of life.

What Causes It?

The etiology of NCD is multifactorial, starting with microemboli of air, fat, or other particles entering the cerebral circulation. However, this factor alone does not appear decisive, given that valvular surgery has a sevenfold higher frequency of microemboli compared to coronary surgery, yet the incidence of NCD does not vary significantly between the two. Other potential causes range from cerebral ischemia due to low cardiac output, intraoperative malperfusion, and anemia. Additionally, there is increasing evidence linking inflammation to NCD. Inflammatory "triggers" are equally varied: pre-existing inflammation exacerbated by diabetes, whether due to poor control or long disease

duration, impacts neurological function during surgery. Moreover, cytokine release and complement activation secondary to surgical trauma, extracorporeal circulation, and ischemia-reperfusion injury may cross the blood-brain barrier both directly and indirectly, often via vagal nerve stimulation.

Who Is Affected?

The article highlights risk factors such as cardiovascular disease, advanced age, diabetes mellitus, depression, heart failure, prior stroke, carotid stenosis, and baseline cognitive impairment. Although up to 98% of patients recover by the third month post-surgery, in some, the effects persist up to six years after the intervention. It is likely that these individuals already had subclinical cognitive impairment or dementia, which worsened following surgery.

What Can Be Done?

The article suggests various recommendations: avoid prolonged intubation, use heparin-coated extracorporeal circuits, ensure adequate individualized cerebral blood flow, maintain strict glycemic control, rewarm slowly without reaching hyperthermia, manipulate the aorta carefully, minimize renal damage and anemia, and identify at-risk patients for early rehabilitation.

In Conclusion Today's article is an expert review on a topic that is seldom discussed in daily practice. It addresses an issue of significant relevance that warrants our attention, yet it is essential to maintain a clear focus. The lack of a consensus definition within the scientific community regarding NCD prevents uniform comparisons across studies, limiting our understanding of the magnitude of this problem. Meanwhile, it is important to remember that despite the risk factors predisposing our patients to NCD, cardiac interventions can provide them with years of high-quality life. Cardiac surgery is sometimes a “necessary evil” that has a positive impact on our patients' lives.

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Miguel González Barbeito

The implication of the anterior mitral leaflet size on septal myectomy outcomes: Does length matter?

This retrospective study investigates whether, in hypertrophic obstructive cardiomyopathy (HOCM), the anterior mitral leaflet (AML) length impacts the outcomes when an isolated septal myectomy is performed as a surgical intervention.

Surgery for hypertrophic cardiomyopathy (HCM) is complex. Typically, the foundation of this procedure is septal myectomy, with the primary goal of alleviating left ventricular outflow tract (LVOT) obstruction. Over time, the mitral valve apparatus has been recognized as a key factor in this pathology. First, from a functional standpoint, as systolic anterior motion (SAM) of the AML in systole plays a crucial role in LVOT obstruction. Second, anatomically, since various mitral abnormalities associated with HCM have been documented, among which is a longer leaflet size in both leaflets compared to controls without the condition.

These findings have led many surgical teams to integrate techniques to reduce AML size (e.g., plication, resection) alongside septal myectomy to achieve greater and more effective LVOT obstruction relief. Although these techniques have been successfully reported in current literature, fewer studies describe surgical outcomes after extensive isolated septal myectomy without concomitant mitral procedures. Moreover, only a limited number analyze the direct relationship between mitral leaflet length and surgical outcomes following an isolated septal myectomy.

The primary aim of this study was to determine whether AML length influences surgical outcomes following extensive isolated septal myectomy for LVOT obstruction in HCM. The primary outcome measure was the reduction in LVOT gradient after isolated septal myectomy, while secondary outcomes included reductions in mitral regurgitation (MR) and the incidence of postoperative SAM. Additional relevant variables, such as posterior leaflet length and coaptation height, were also analyzed. To this end, a comparison of pre-procedural mitral leaflet lengths was conducted between the series of HCM patients undergoing septal myectomy and a control cohort undergoing surgery for other pathologies. A total of 564 HCM patients were treated with isolated septal myectomy, without any pre-planned mitral procedure. These patients were compared to controls undergoing coronary artery bypass grafting (CABG, n=90) and aortic valve replacement (AVR, n=92). Among the patients treated with septal myectomy, 74.5% (n=420) underwent isolated septal myectomy, while the remainder had CABG or AVR as concomitant procedures. Furthermore, 6.4% (n=36) and 1.4% (n=8) underwent concurrent mitral valve repair or replacement, respectively, for intrinsic pathology, and were excluded from the analysis.

A cut-off point for excessive AML length was set at 30 mm, categorizing patients into those with AML ≥30 mm (n=264) and those with AML <30 mm (n=300). Significant differences in patient distribution were observed between groups, as well as in pre- and intraoperative characteristics that could potentially impact outcomes. Bivariate analysis revealed an association between AML length, posterior leaflet length, and coaptation height with the development of postoperative SAM and the degree of residual MR, which was not significant in the multivariable model. HCM patients had an average AML length 5 mm longer than the control cohort.

Preoperative LVOT gradients were not correlated with leaflet lengths (AML <30 mm: median 49 mmHg vs. AML ≥30 mm: 50.5 mmHg; $p = .76$). Similarly, gradient reduction after myectomy did not correlate with leaflet length; patients with AML <30 mm had a

median gradient reduction of 33 mmHg compared to 36.5 mmHg in patients with AML ≥30 mm (p = .36). The AML length was not associated with increased one-year mortality (p = .75). Differences between groups were observed only in the percentage of postoperative SAM: 65.5% in AML ≥30 mm vs. 47.6% in AML <30 mm.

COMMENTARY:

This article presents a high level of complexity with interesting findings. It is certainly a study open to multiple interpretations, from which we will highlight the most notable. Of particular interest is the single-center sample size of 564 HCM patients undergoing isolated septal myectomy within a three-year interval (2015-2018), which is a remarkable patient volume that is difficult to match. Thus, the techniques, experience, and resources used are likely challenging to replicate in other settings. Despite the debatable statistical methodology and interpretation, a series of this scale inevitably yields significant conclusions.

It is well-known that HCM patients have longer mitral leaflets. In this case, to validate this hypothesis, a comparative control cohort of patients operated for other pathologies at the same center was used. This cohort exhibited demographic differences in all variables except for BMI, making the groups difficult to compare. A propensity score analysis might have been more objective in assessing whether mitral leaflet length is associated with HCM, while recognizing the limitations of this method.

The HCM patient series was divided into two groups, with none undergoing mitral leaflet size reduction. Instead, only isolated septal myectomy was performed. Concomitant CABG or AVR procedures were deemed to have minimal impact on post-op LVOT hemodynamics concerning SAM, gradient variation, or residual MR (though in patients with AVR, this assumption might not hold, and they should perhaps have been excluded from the analysis). A 30 mm AML length threshold was used, a measure widely adopted in current literature to decide whether to include AML reduction techniques in surgery. Bivariate and multivariable analyses were conducted to define associations.

Although bivariate analysis suggested associations between mitral leaflet lengths or coaptation height, no associations were found in the multivariable analysis. While no significant association or differences in residual gradients between groups were observed, the proportion of residual SAM was higher in the AML ≥30 mm group. Hence, aside from the residual SAM percentage (not defined in detail or severity), no relationship between greater AML length and poorer surgical outcomes was found without applying techniques to the AML. These results must be interpreted cautiously, as patients with AML ≥30 mm had a higher body surface area, a greater proportion of males, and a younger age.

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Elio Martín Gutiérrez

Preoperative liver dysfunction: an overlooked comorbidity not accounted for in risk assessment scores

A meta-analysis reviewing studies on outcomes of cardiac surgery in patients with liver dysfunction, assessed through the Child-Pugh and MELD scoring systems.

Preoperative liver dysfunction presents a significant risk factor for severe morbidity and mortality in the postoperative period of cardiac surgery. However, neither commonly used surgical risk assessment tools nor most registries account for it, as these scores were initially developed at a time when patients with advanced liver disease were frequently excluded from surgical treatments. With an increasingly elderly and comorbid patient population, and the rise of less invasive therapeutic options, the need to reassess surgical risks remains essential to select appropriate candidates.

The primary assessment tools for liver dysfunction include the Child-Pugh and MELD scores. The Child-Pugh score evaluates three laboratory parameters (bilirubin, albumin, and prothrombin time/INR) and two clinical features (ascites and encephalopathy) to classify liver dysfunction into three categories: Class A (well-compensated liver disease, 5–6 points), Class B (significant functional impairment, 7–9 points), and Class C (decompensated liver disease, 10–15 points). This classification provides a prognostic indicator, with a 1-year survival rate of 100% (85% at 2 years) for Class A, 80% for Class B, and 45% for Class C. The MELD score, developed later to prioritize liver transplant candidates, assesses four laboratory parameters (creatinine, bilirubin, INR, and sodium, with the latter added to refine the model as the MELD-Na score) and the need for dialysis ≥2 times per week. This scoring system predicts a 3-month mortality risk of <2%, 6%, 20%, >50%, or >70% for scores of <9, 10–19, 20–29, 30–39, and ≥40 points, respectively.

This meta-analysis included 33 studies with a total of 48,891 patients, comparing perioperative mortality and morbidity (neurological events, prolonged mechanical ventilation, bleeding and/or transfusion requirements, and acute renal failure), as well as long-term mortality, between patients scoring above and below established cutoffs: 6 points for Child-Pugh (Class A vs. B/C) and 15 points for MELD. All adverse outcomes were significantly worse for groups scoring above the cutoff (perioperative mortality HR = 3.72, neurological events HR = 1.49, prolonged ventilation HR = 2.45, bleeding HR = 1.95, acute renal failure HR = 3.84, and long-term mortality HR = 1.29).

The authors concluded that staging via these risk scores is essential in assessing patients with advanced liver disease to ensure appropriate decision-making and assign the best therapeutic options available.

COMMENTARY:

This is the most comprehensive study to date on the impact of advanced liver disease in patients undergoing cardiac surgery. Both scores have proven useful in evaluating candidates for cardiac surgery, establishing cutoffs at ≤6 points for Child-Pugh and ≤15 points for MELD.

It is logical to associate higher cardiac surgery mortality with more severe liver dysfunction, given the increased rates of preoperative morbidity and the development of postoperative complications. In a subanalysis of one study included in the meta-analysis (Gopaldas et al.), the main detrimental effect of surgery was related to the use of cardiopulmonary bypass (CPB), which increased mortality by 4.6 times compared to surgeries without CPB. This factor could open the door to considering CPB-free

procedures as a preferable alternative for these patients, particularly in terms of myocardial revascularization and structural heart disease treatment (TAVI, mitral clip, percutaneous mitral prosthesis, tricuspid clip, etc.) or aortic pathologies (TEVAR). Nonetheless, this indication, based on sound clinical judgment, remains compassionate and outside clinical guidelines, as this patient profile has been systematically excluded from the evidence that currently guides these recommendations (except for the PARTNER I B study, which included patients with advanced liver disease as a reason for TAVI inoperability vs. medical treatment).

Finally, the prognostic value of liver dysfunction grading offered by these scales, beyond the mentioned cutoffs, should be considered. Scores above 9 points on the Child-Pugh scale or 20 points on the MELD scale may be deemed markers of futility, associated with nearly 50% annual mortality and thus offering no significant clinical benefit from correcting the underlying heart disease. Therefore, in the absence of liver dysfunction considerations within traditional risk scores, categorizing patients with specific scoring systems with prognostic implications becomes crucial for determining the best therapeutic management for patients with advanced liver disease.

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Bunty Ramchandani

Pulmonary vein stenosis in adults: rare, but it exists

Review of JACC on the study and management of acquired forms of pulmonary vein stenosis in adults.

Pulmonary vein stenosis (PVS) may have various etiologies, classifiable into three categories: congenital, acquired, or iatrogenic. Its manifestation is insidious, complicating and delaying diagnosis. A high index of suspicion is necessary, along with knowledge of targeted noninvasive studies for accurate diagnosis. Once diagnosed, techniques are used to determine its clinical relevance for the patient. Etiological treatment and transcatheter procedures, including balloon angioplasty and stent implantation, are cornerstones in managing this condition. There are no established guidelines regarding diagnosis, treatment, or follow-up management. Institutions rely on their experience, and today's review aims to highlight the latest trends in diagnosing and treating this rare pathology.

COMMENTARY:

PVS can result from extrinsic compression or luminal narrowing, though no universal definition of PVS exists. In adults, an average pulmonary vein diameter ranges from 10 to 15 mm; it must be reduced to 4-6 mm to cause symptoms. The 2017 atrial fibrillation consensus defined PVS severity as mild for caliber reductions <50%, moderate for 50-70%, and severe for >70%. In addition to stenosis degree, the number and location of affected veins are critical since involvement at the veno-atrial junction differs from bifurcations or intraparenchymal segments. There are three primary PVS patterns: focal "hourglass" constriction, tubular hypoplasia, and extensive bilateral extramural involvement.

Acquired PVS etiologies include mediastinal inflammatory diseases and iatrogenic injury from invasive procedures. Historically, PVS followed extrinsic compression by fibrosing mediastinitis, hypersensitivity to *Histoplasma capsulatum*, tuberculosis, or IgG4-related diseases. Other causes include malignancies or sarcoidosis with similar symptoms. Iatrogenic forms often result from pulmonary vein surgeries or atrial fibrillation (AF) ablation, now the leading PVS cause, with an incidence ranging from .3% to 4% depending on the series. Given nearly 10,000 AF ablations performed worldwide annually, hundreds of patients are at risk of developing this complication.

Symptoms are often insidious and nonspecific, commonly including dyspnea, pleuritis, chest pain post-exertion, fatigue, malaise, and hemoptysis. Misdiagnosis is frequent; one in three patients typically receives prior diagnoses of pneumonia, bronchitis, or malignancy. Early diagnosis impacts prognosis, especially if secondary to AF ablation, as stenoses can rapidly obstruct and cause pulmonary infarction.

Both noninvasive and invasive techniques are crucial for diagnosing and treating PVS. Among noninvasive methods:

- Contrast-enhanced computed tomography angiography (CTA) aids diagnosis and procedural planning, allowing dual-phase imaging to rule out left atrial appendage thrombus. CTA is valuable for pre- and postprocedural evaluation, though it may be less sensitive for subocclusive/occlusive PVS. Invasive procedures may be warranted even if CTA suggests occlusion.

- Magnetic resonance imaging (MRI), a non-ionizing modality, is ideal for renal insufficiency patients but limited by lower spatial resolution and signal loss with stents.

- Ventilation/perfusion tests using technetium-99 help assess physiological repercussions but need correlating anatomical imaging. Significant perfusion deficits appear in severe stenoses, but intermediate stages may go undetected.

- Transesophageal echocardiography (TEE) enables stenosis assessment in adults by measuring diameter reduction, peak diastolic velocity (>0.9-1.1 m/s) with Doppler, or turbulent flow. Visualization is challenging and lacks standardized criteria for PVS.

Invasive evaluation through cardiac catheterization assesses pulmonary venous hypertension across segments. The classic parameters include the diastolic gradient between the pulmonary artery wedge pressure or left atrium and the left ventricle. Cross-referencing with CTA allows precise segment evaluation and comparison to unaffected areas. Exercise testing can reveal true hemodynamic compromise in inconclusive segments.

Unlike congenital PVS, which is treated surgically, acquired cases are managed percutaneously through balloon angioplasty with or without stenting, though restenosis is common. Restenosis predictors include vessel thickness; veins <10 mm have a 70% restenosis rate versus 10% in veins >10 mm. Typically, stents are placed in vessels >10 mm, while angioplasty is used for those 7-8 mm, with possible stent placement later. No superiority between drug-eluting and bare-metal stents has been established, with both showing up to 30% restenosis.

Follow-up is individualized by stent size and stenosis complexity. Routine CTA is performed at 3 and 9 months, with double antiplatelet therapy for six months post-intervention, shifting to aspirin monotherapy if needed. Persistent symptoms after exhausting hemodynamic options may prompt surgical alternatives with uncertain outcomes.

In conclusion, today's JACC article highlights a rarely discussed condition, providing key insights but warranting full reading for comprehensive management, including handling complete occlusions and restenosis strategies. The article's contribution to general awareness is significant; it encourages clinicians to include PVS in differential diagnoses for respiratory symptoms in patients with an AF ablation history.

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