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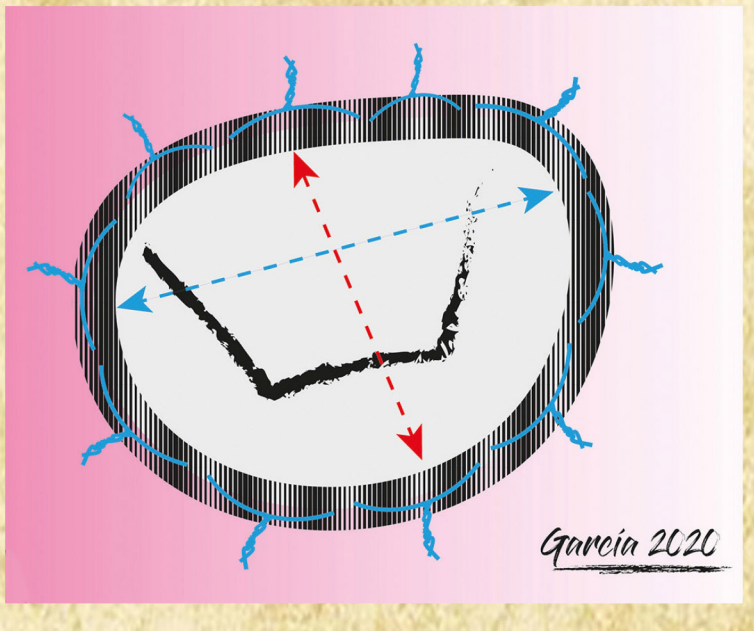

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Contenido

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Contenido

Contenido / Contents

Volume 9 • Issue 4 • October-December 2024

Editorials / *Editoriales*

Original articles / *Artículos originales*

Review article / *Artículo de revisión*

Case report / *Reporte de caso*

EDITORIAL
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A critical analysis of the RESHAPE-HF2 trial: biases and limitations that should be considered before incorporating it into next clinical guidelines

Análisis crítico del ensayo RESHAPE-HF2: sesgos y limitaciones que deben tenerse en cuenta antes de incorporarlo a las próximas guías clínicas

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Keywords: functional mitral regurgitation, guided directed medical therapy, mitral valve, transcatheter edge-to-edge repair.

Palabras clave: *insuficiencia mitral funcional, tratamiento médico dirigido, válvula mitral, reparación transcatéter borde-a-borde.*

The recently published Transcatheter Valve Repair in Heart Failure with Moderate to Severe Mitral Regurgitation (RESHAPE-HF2) trial[1] presents a randomized controlled comparison of guided directed medical therapy (GDMT) with and without transcatheter edge-to-edge repair (TEER) in patients with moderate to severe functional mitral regurgitation (FMR). A total of 505 patients were enrolled in a 1:1 ratio to receive either GDMT alone (n = 255) or GDMT plus TEER (n = 250). The trial featured a novel triple primary endpoint, comprising the combination of cardiovascular mortality and heart failure hospitalization (HFH), and HFH alone, both of them assessed at 24 months. Notably, a third primary endpoint was added once the trial was completed: The Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score at 12 months.

The most compelling results showed a significant reduction in HFH rate at 24 months, favoring TEER plus GDMT, with 26.9 events per 100 patient-years versus 46.6 events per 100 patient-years in the GDMT alone group (RR = 0.59; 95% CI, 0.42 to 0.82; p = 0.002). Additionally, TEER plus GDMT demonstrated a positive effect on the Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS) score, with a mean increase of 21.6 ± 26.9 points versus 8.0 ± 24.5 points in the control group (mean difference, 10.9 points; 95% CI, 6.8 to 15.0; p < 0.001).[1]

At first glance, the results of this trial seem to suggest a clear benefit of combining TEER with GDMT for the treatment of moderate to severe FMR. However, several concerns warrant careful consideration, tempering the initial enthusiasm for this therapeutic approach.

Firstly, notably a triple primary endpoint was used in this trial. Moreover, the primary endpoint was shifted once the trial was completed by adding HFH rate at 24 months, and the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score at 12 months.

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A dual concern arises in this context. On one hand, the modification of endpoints after a trial's initiation (and particularly after its completion) contravenes standard research protocols. On the other hand, the retroactive addition of the KCCQ-OS score at 12 months as a primary endpoint in a concluded trial raises significant ethical and methodological concerns. This circumstance prompts the question of whether this alteration was a deliberate attempt to secure a more readily achievable endpoint within an abbreviated follow-up interval, thereby avoiding potential declines in subjective clinical improvement as assessed by the KCCQ in patients with HF with reduced ejection fraction (HFrEF). Furthermore, the improvement in KCCQ-OS) score at 12 months in the device group is somewhat debatable due to its inherently subjective nature and the trial's non-double-blinded design, which may introduce bias because of the placebo effect in favor of TEER.

The second critical issue emerging from this trial pertains to the inclusion criterion of patients presenting with overt HF symptoms, despite being on GDMT, coupled with moderate to severe functional mitral regurgitation (FMR) (graded 3+ or 4+), as defined by the European Association of Echocardiography. It is essential to note that these echocardiographic recommendations primarily focus on criteria for the imaging assessment of prosthetic heart valves, as reported by the European Association of Cardiovascular Imaging. Specifically, moderate mitral regurgitation (MR) is characterized by the following quantitative parameters: effective regurgitant orifice area (EROA) = 20-39 mm^2, regurgitant volume (RVol) = 30-59 ml, and regurgitant fraction (RF) = 30-50%. In contrast, severe MR is defined by EROA $\geq$ 40 mm^2, RVol $\geq$ 60 ml, and RF > 50%.[2] These severity criteria for MR are also endorsed by the American Society of Echocardiography.[3]

The RESHAPE-HF2 trial revealed a mean EROA of 23 mm^2 (range, 19 mm^2 - 30 mm^2) and a RVol of 35.4 ml (range, 28.2 ml - 43.9 ml), indicating a predominantly moderate degree of FMR. Notably, a mere 14% of patients exhibited an EROA > 40 mm^2, whereas a substantial one-quarter of patients (23%) displayed an EROA < 20 mm^2, suggestive of mild FMR prior to the procedure. This disparity raises important questions regarding patient selection and the potential impact on trial outcomes.

The Mitral Valve Academic Research Consortium (MVARC) defines an "acceptable" outcome following TEER as a reduction in MR by at least two grades or a residual MR of $\leq$ 2+, tantamount to moderate MR. Under these circumstances, it is strikingly discordant that the definition of "acceptable MR" subsequent to TEER serves as the benchmark for the inclusion criteria in the RESHAPE-HF2 trial.

The third pivotal issue arising from this trial pertains to the GDMT employed in patients with HFrEF and FMR. According to the current guideline for HF management, in patients with HFrEF and New York Heart Association (NYHA) class II to III symptoms, the use of angiotensin receptor-neprilysin inhibitors (ARNi) is recommended to reduce morbidity and mortality (Class of Recommendation [COR] 1, Level of Evidence [LOE] A). Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) are reserved for cases where ARNi is not feasible. Furthermore, in patients with chronic symptomatic HFrEF (NYHA class II or III) who tolerate ACEI or ARB, replacement with ARNi is recommended to further reduce morbidity and mortality (COR 1, LOE B-R). In patients with symptomatic chronic HFrEF, sodium-glucose cotransporter 2 inhibitors (SGLT2i) are recommended to reduce HFH and cardiovascular mortality (COR 1, LOE A).[4]

A meta-analysis comprising 75 trials, which enrolled 95,444 patients with HFrEF, demonstrated that the maximum benefit was achieved with a quadruple combination therapy consisting of ARNi, beta-blockers (BB), mineralocorticoid receptor antagonists (MRA), SGLT2i, resulting in a significant reduction in all-cause mortality and the composite outcome of cardiovascular death or first HFH.[5] Furthermore, the combination of ARNi/BB/MRA was superior to ACEI/BB/MRA and ARB/BB/MRA in improving LV adverse remodeling and increasing LV ejection fraction in patients with HFrEF.[6] The use of SGLT2 inhibitors has been associated with significant improvements in patient-centered outcomes, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ).[7] Moreover, regarding the improvement in clinical status measured by KCCQ in the trial, it is noteworthy that a comprehensive meta-analysis of 17 studies, encompassing 23,523 patients, has consistently demonstrated that SGLT2 inhibitor therapy is associated with substantial enhancements in patient-centered outcomes, as quantified by the Kansas City Cardiomyopathy Questionnaire-overall summary score (KCCQ-OSS) (mean difference, 1.90 points; 95% CI, 1.41-2.39 points; $p < 0.001$).[8] Notably, the low usage rates of ARNi (11%) and SGLT2i (8.4%) in the control group at baseline in the RESHAPE-HF2 are striking. Moreover, there is no report available on GDMT across the entire follow-up period. Under these circumstances, it is impossible to establish any comparison between the two groups, where GDMT is a crucial element of utmost importance. Therefore, given the suboptimal quality of GDMT reported at least in baseline in this study, it is difficult to obtain results with sufficient reliability in terms of a comprehensive and up-to-date GDMT based on quadruple therapy (ARNi, SGLT2i, beta-blockers, and mineralocorticoid receptor antagonists).

Confronted with such profound uncertainty, the initial euphoria surrounding the RESHAPE-HF2 trial's outcomes

gives way to disillusionment, compelling us to pursue alternative solutions firmly rooted in pragmatic trials that rigorously uphold the foundational principles of exemplary clinical practice.

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EDITORIAL
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Mechanical circulatory support and coronary artery bypass grafting in ischemic cardiomyopathy. *Veritas Filia Temporis*

Soporte circulatorio mecánico y revascularización coronaria en cardiomiopatía isquémica. Veritas Filia Temporis

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Keywords: coronary artery bypass grafting, mechanical circulatory support, ischemic cardiomyopathy.

Palabras clave: *revascularización coronaria, soporte circulatorio mecánico, cardiomiopatía isquémica.*

Coronary artery bypass grafting (CABG) in patients with low ejection fraction carries a significant risk of perioperative mortality and morbidity related to the development of postcardiotomy shock. Preoperative optimization with pharmacological or mechanical support (MCS) is highly required. Multiple series and analysis found postoperative mortality rate between 6.5-7.5%.[1-3]

I read with interest the manuscript by Soomer et al,[4] in which they found a better survival with early vs delayed Impella implantation in patients underwent CABG with left ventricular failure. They analyzed 27 patients who underwent simultaneous Impella implantation during CABG surgery and 15 patients who underwent delayed Impella therapy. Survival after 30 days (75.6 vs 47.6%, p = 0.04) and 1 year (69.4 vs 29.8%, p = 0.03) was better in the cohort receiving simultaneous Impella implantation. The results are promising and attractive; however as always, the most sophisticated truth lies in the small details.

It is very important to understand the mixed and heterogeneous substrate of ischemic cardiomyopathy. There is usually a combined coexistence between normal, stunned, hibernating and scar myocardium in the same myocardial region. Often there is an element of overlapping between two or more of these states, in fact, all together could represent the same process in different phases.[5] This concept guide to interpret feasibility studies with judgment and extreme care.

The STICH trial was a randomized multicenter non-blinded controlled trial, that compared medical therapy versus CABG, in patients with coronary disease and left ventricular dysfunction.[6] Among the conclusions obtained in that study, the following stand out:

1. Patients assigned to CABG had fewer mortality rates and hospitalizations for cardiovascular disease (the difference was borderline, p = 0.05). However, there was no difference between medical therapy and surgery with respect to mortality from any cause.
2. CABG was related to an early risk of mortality. About age, the older, the greater the likelihood of postoperative mortality due to non-cardiovascular causes.

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3. There was no benefit of CABG in patients without left coronary artery disease and/or class III/IV angina.
4. The study was not blind, and the difference between the two groups, regarding the motility for any cause, may be due to a limited follow-up of the patients.

We need to keep in mind that viable myocardium does not equate to ischemic myocardium. According to the above, the results in this study were subjected to various analyzes of specific topics. STICH viability sub-study reported the effects of myocardial viability (evaluated by DES and SPECT) in 5.1 years of follow-up. Patients with viability (with or without CABG) were more likely to survive in the univariate analysis, however, this benefit was not demonstrated in the multivariate analysis.[7] It is mandatory to highlight important facts of this study: a) only half of the STICH study underwent viability studies; b) MRI or PET was not used; c) there is no interaction between the effect of CABG and the presence or absence of viability, the fact of having myocardial viability does not adequately identify which patients would benefit more from surgical revascularization. STICH sub-study ischemia specifically studied STICH patients with myocardial ischemia during stress testing. No benefit of CABG was demonstrated versus medical therapy, based only on the presence or absence of ischemia.[8] The 2021 American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) guideline for coronary revascularization assigned a class 1 recommendation, level of evidence B-R for CABG in patients with severe left ventricle (LV) dysfunction (ejection fraction < 35%).[9]

However, taking into account that the assessment of myocardial viability and ischemia, failed to guide with certainty and precision the indication of CABG in ischemic cardiomyopathy (results to be taken with caution), the analytical approach turned towards the evaluation of anatomical and hemodynamic variables. Panza et al. studied the following factors in the STICH population: extent of coronary heart disease (3 vessels), EF ≤ 27% and LVESV index ≥ 79 ml/m^2. Their conclusions guided them to recommend surgical revascularization in patients who had two or more previously referred criteria.[10] All on this in correlation to match regional viability with coronary revascularization targets (adequate size and acceptable run-off) and to achieve complete revascularization. Some authors recommended that patients with severe ischemic cardiomyopathy should undergo right heart catheterization to identify degree of cardiogenic shock [cardiac index (CI) < 2.2 l/min/m^2], the degree of LV decompensation [pulmonary capillary wedge pressure (PCWP) > 20 mmHg] and right ventricular (RV) dysfunction [pulmonary artery pulsatility index (PAPi) < 2]. CABG could be performed directly if there is not any of those parameters. If unresponsive to medical treatment alone, and persist with some degree of cardiogenic shock, they may be candidates to receive mechanical support either preoperatively or intraoperatively.[11] On the other hand, Singh et al. does not evaluate the response to medical treatment; they recommended direct pre op MCS (Impella, IABP or ECMO) on the patient with cardiogenic shock, and an strong consideration of preemptive Impella on the patient without cardiogenic shock with very low ejection fraction (25%).[12] As we can see, this decision represents a complex dilemma, very similar to the blindness on the ideal setting, strategy and timing for postcardiotomy extracorporeal support, venoarterial (VA) extracorporeal membrane oxygenation (ECMO) following cardiac surgery shows an overall survival between 25 to 42%.[13] Moreover, the reports focus on mechanical circulatory support on ischemic cardiomyopathy undergoing CABG, are limited to small case series. Sommer et al.[4] found a better survival after CABG with early Impella implantation, all the patients had ischemic cardiomyopathy and on post cardiotomy low cardiac output. A simplistic take on this finding is that we should be used more liberally, and prevent more mortality. However, usually the big answers are in the small details.

There is no information in this small sample about viability and ischemia evaluation, as well LV end systolic volume index and the preoperative hemodynamic parameters (CI, PCWP, Papi). Without this, it is very difficult to conclude the real impact of the MCS timing. Not all the patients with ischemic cardiomyopathy are necessarily extreme high risk. I think a preoperative evaluation that combine the anatomic, functional and hemodynamic areas, will lead to a more precise indication of the MCS on this complex population, resulting in more favorable survival. The debate is ongoing, the published small cohorts showed a modest favorable results with prophylactic MCS.[14,15] The rationale behind preemptive LV unloading is to mitigate the effects of the cardiopulmonary bypass while waiting for the ventricle to recover, thereby maintaining end-organ perfusion and avoiding high doses of vasopressors. I agree with that statement, However, the risk-to-benefit ratio is unclear at this point. MCS can also result in serious complications. A careful judgment of the indications for MCS has the potential to improve the safety of CABG for high-risk patients but requires well-designed, long term and prospective studies to evaluate its impact on patient outcomes. *Temporis filia veritas* (truth as a daughter of time), an ancient proverb expressing the notion that the truth often reveals itself only after the passage of time.

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ORIGINAL ARTICLE

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Thoracic aortic aneurysm surgery in a third level single center. Five years experience

Cirugía del aneurisma de aorta torácica en un centro hospitalario de tercer nivel. Experiencia de cinco años

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ABSTRACT

Introduction: aortic aneurysms and acute aortic syndrome are the two most frequent entities within the thoracic aortic pathology that require surgical intervention. The indication for aneurysm is elective, while acute aortic syndrome is an emergency. **Objective:** to describe the current state of surgical treatment of patients with aortic aneurysm in a third level single center from January 2016 to December 2020. **Material and methods:** this is a descriptive cross-sectional study to identify demographic characteristics, risk factors, clinical presentation, imaging, perioperative variables, morbidity and mortality. **Results:** eighty patients were included, 39 with the diagnosis of thoracic aortic aneurysm and 41 with the diagnosis of thoracic acute aortic syndrome. Within the group of aneurysms, 34 (87%) were men and 5 (13%) women. The predominant symptom was dyspnea. Severe acute aortic regurgitation was present in 70% of cases, and bicuspid aortic valve present in 23%. The most frequent location was at the level of the root and ascending aorta in 51% of patients. The most frequently performed surgical procedure was the composite graft implantation with the Bentall technique. Early mortality was 15% and morbidity of 45%. **Conclusions:** aortic aneurysm is an entity that must be treated in third level units. A multidisciplinary team trained in thoracic aortic surgery is required to reduce morbidity and mortality and achieve international standards in terms of results.

Keywords: aortic surgery, bentall procedure, thoracic aortic aneurysm.

RESUMEN

Introducción: *los aneurismas de la aorta y síndrome aórtico agudo constituyen las dos entidades más frecuentes dentro de la patología de aorta torácica que requieren de una intervención quirúrgica. La indicación del aneurisma es electiva, mientras que el síndrome aórtico agudo es una urgencia.* ***Objetivo:*** *describir el estado actual del tratamiento quirúrgico de los pacientes con aneurisma de aorta torácica en un centro hospitalario de tercer nivel, de enero de 2016 a diciembre de 2020.* ***Material y métodos:*** *se trata de un estudio descriptivo para identificar las características demográficas, factores de riesgo, presentación clínica, de imagen, variables perioperatorias, morbilidad y mortalidad.* ***Resultados:*** *se identificaron 80 pacientes, 39 con diagnóstico de aneurisma de aorta torácica y 41 con síndrome aórtico agudo torácico. Dentro de los aneurismas, 34 (87%) fueron hombres y 5 (13%) mujeres. El síntoma predominante fue la disnea. La insuficiencia aórtica aguda severa estuvo presente en 70% de los casos, y válvula aórtica bivalva se identificó en 23%. La localización más frecuente fue a nivel de la raíz y aorta ascendente en 51% de los pacientes. El procedimiento quirúrgico más frecuentemente realizado fue el implante de tubo valvulado con técnica de Bentall. La mortalidad temprana fue de 15%, y la morbilidad de 45%.* ***Conclusiones:*** *el aneurisma aórtico es una entidad que debe ser atendida en unidades de tercer nivel. Se requiere de un equipo multidisciplinario capacitado en cirugía de aorta torácica para disminuir la morbimortalidad y alcanzar los estándares internacionales en cuanto a resultados.*

Palabras clave: *cirugía aórtica, procedimiento de Bentall, aneurisma de aorta torácica.*

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Pathology of the aorta includes different diseases such as aortic aneurysms, acute aortic syndrome, congenital anomalies and traumatic pathology.[1] The most serious complication is aortic dissection or rupture. Ruptures are usually fatal; symptoms include severe chest pain with low blood pressure or signs of shock. Patients with aortic dissection experience severe chest pain that is acute in onset and described as a tearing sensation.[2]

In 1968 Bentall and Bono described a technique to replace the ascending aorta and the aortic valve with a tubular graft containing a valve prosthesis with reimplantation of the coronary arteries, this technique being the technique of choice today.[3] In 1993 Sarsam and Yacoub described aortic root remodeling with aortic valve preservation.[4]

The aorta is an artery that arises from the left ventricle until its division at the level of the lower edge of the fourth lumbar vertebra, it is divided by the diaphragm into the thoracic and abdominal aorta. The thoracic aorta consists of four main segments: aortic root, ascending aorta, aortic arch, and descending aorta. The ascending aorta has an average length of 5 to 7 cm. Classically, its initial part is considered the aortic root, which is histologically different.[5] The aortic root represents a fibrous and complex structure, which by definition extends from the aortic annulus to the sinotubular junction, it is a short segment of around 2-3 cm in length, which consists of three components: the cusps, the sinuses of Valsalva and the intercalated triangles, in other literature the ostia of the coronary arteries are also included.[6,7] The aortic arch is the continuation of the ascending aorta, a structure outside the pericardium, below the lower half of the sternal manubrium, with a normal curvature to the left until the fourth thoracic vertebra to continue as the component descending thoracic aorta.

The normal diameter of the aorta depends on the age, sex and height of the individual. An aneurysm is an increase in diameter 1.5 times normal. In addition to its conduit function, it participates in the control of systemic vascular resistance and heart rate, as well as Windkessel (second pump) function. It has a diameter that does not exceed 40 mm in healthy adults (upper limit is 40 mm in men and 34 mm in women).[8]

The most common location for thoracic aortic aneurysms is in the aortic root and ascending aorta, they can also occur in the descending thoracic aorta and less frequently in the aortic arch. 70% involve the aortic root and/or ascending aorta, 40% affect the descending thoracic aorta, 10% affect the aortic arch, and 10% affect the thoracoabdominal aorta. The most common cause of thoracic aortic aneurysms is a cystic degenerative process of the media, where the elastic fibers of the wall degenerate, weakening it, causing aneurysmal dilation. This phenomenon occurs around 60-70 years of age. Smoking and systemic high blood pressure are also associated with aneurysm formation. In young patients it may have a genetic origin. These include connective tissue disorders such as Marfan, Loeys-Dietz and Ehlers-Danlos syndrome, or familial thoracic aortic aneurysm syndrome.[2,9]

The average growth rate of an aneurysm is 0.1 cm per year. Diameter is the main predictor of aortic rupture or dissection. Follow-up imaging studies are usually performed every six months and then annually. The annual risk of rupture or dissection of thoracic aortic aneurysms is approximately 2% for those with a diameter < 5 cm, 3% for 5-5.9 cm, and 7% for those > 6 cm. The growth rate is significantly higher for ascending aortic aneurysms. The definitive diagnosis requires an angiotomography or magnetic resonance angiography with the use of intravenous contrast material, an imaging technique that allows 3D reconstructions, obtaining an accurate diagnosis and thus a surgical/endovascular plan. Once a thoracic aortic aneurysm is detected, it requires abdominal imaging.[10]

Thoracic aortic aneurysm is an entity that is usually diagnosed incidentally, with complications occurring in many cases as the first manifestation, bringing with it a high fatality rate. In high-risk individuals who have conditions such as Marfan syndrome, other collagenopathies, bicuspid aortic valve, intracranial aneurysms, aortic arch anomalies, renal cyst, abdominal aneurysm, temporal arteritis and a positive family history for aortic aneurysms, the use of tomography is indicated.[11,12]

The guidelines of the American College of Cardiology, American Heart Association, Society of Thoracic Surgery & American Association for Thoracic Surgery recommends repair of all symptomatic aneurysms. On the contrary, in asymptomatic patients, elective surgery is recommended for aneurysms with a diameter > 5.5 cm. The risk of rupture is higher with lower diameters in patients with certain genetic disorders. Surgical intervention is recommended when it reaches 4.5 cm in diameter for patients with Marfan syndrome and 4.0 cm for Loeys-Dietz syndrome. For patients with a bicuspid aortic valve, surgery is recommended for aortic diameters > 5.5 cm, but intervention at 5 cm may be recommended in patients with a family history of dissection or who grew rapidly. In aneurysms of the descending aorta, the threshold for intervention is about 6 cm. For any patient with a growth rate greater than 0.5 cm per year, intervention is recommended since there is an increased risk of rupture.[8,11,12]

The French surgeon Ambroise Paré first described the rupture of a thoracic aortic aneurysm. He said that aneurysms that occur within internal parts are incurable. Concept that has changed for seven decades.[13] In a review of the literature from 1946 to 2017, 20 studies were included with 8,800 patients with a diagnosis of ascending aortic aneurysm, with a mean age of 57 years, the mean diameter of the aneurysm during the

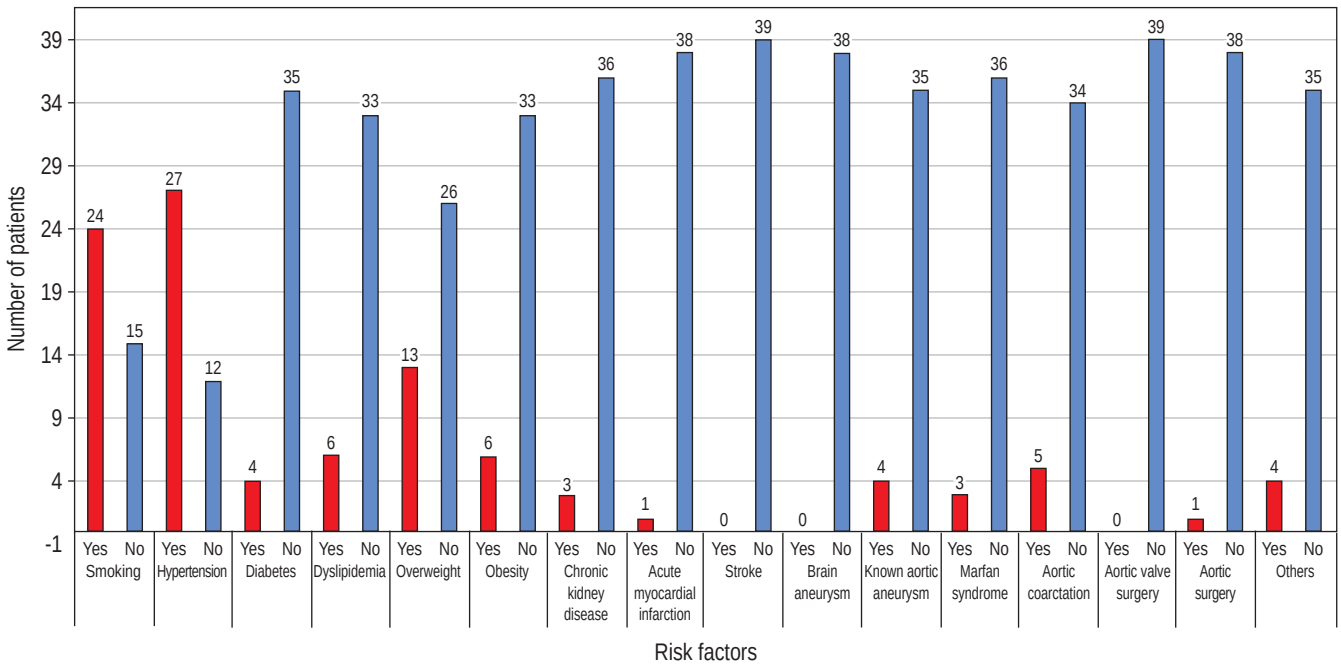

Figure 1: Risk factors in patients undergoing surgery for thoracic aortic aneurysm.

registry was 42 mm, with an elective surgery rate of 13.8% during a mean follow-up of 4.2 years.[14]

Replacement of the dilated segment with a valved tube used to be the standard treatment for patients with aortic root/ascending aorta aneurysm. However, in the last three decades, procedures have been developed whereby the aneurysm is replaced with a Dacron graft preserving the aortic valve, with good results in experienced centers.

The standard treatment has been replaced with a composite graft (the most commonly used conduit is a Dacron graft containing a mechanical valve). An alternative is valve-sparing surgery.[15] Aortic valve-sparing surgery includes reimplantation of the aortic valve performed with a tubular graft or with a custom graft to recreate the coronary sinuses. While aortic remodeling is performed with a Dacron tube adapted to recreate the coronary sinuses, suturing the tube to the sinuses and aortic ring. Both procedures have been shown to be effective, as long as there is adequate patient selection and the center has surgical experience.[16] Price et al. included 165 patients with Marfan syndrome and aortic root aneurysm 98 underwent aortic valve-preserving surgery (69 reimplantations and 29 remodeling) and 67 underwent the Bentall procedure. There were no in-hospital deaths, 10-year survival was 90.5% in the Bentall procedure and 96.3% in valve-sparing surgery.[17] In a retrospective study, Zhang et al. included 135 patients with Marfan syndrome; they were divided into four groups: David, Bentall surgery, proximal and distal arch surgery with endovascular prosthesis. After 15 years there were no deaths in the David Procedure group, while the 15-year survival rate for patients in the Bentall group was 73 + 13.5% and 71 + 13.9% for patients in the Bentall group and arch surgery. Therefore, it was determined that it had more benefits and a higher long-term survival rate.[18] Aortic root replacement surgery with David valve preservation was studied from 1993 to 2009 by Escobar et al, in 233 patients (40% of them with Marfan syndrome). Survival at 5 and 10 years was 98 and 93% respectively. Free of reoperation in 92% at 10 years (three reoperations were aortic valve replacement due to structural deterioration). The absence of structural deterioration of the valve at 10 years was 96%.[19] At our institution, Ramírez et al. reported from 1999 to 2003, 39 patients with thoracic aortic aneurysm undergoing surgical treatment. Of the 39 patients who underwent surgery, 16 (41%) had a secondary aortic aneurysm with dissection and 23 (59%) had aneurysm only. Of the 16 with dissection, 15 (87.5%) had type A dissection and two (12.5%) had type B dissection. 12 patients had Marfan syndrome. In 35 patients (88.7%) the aneurysm was located in the ascending aorta, 1 in the aortic arch and 3 (7.77%) in the descending aorta. With an early overall mortality of 7% and a postoperative morbidity of 68.9%.[20] In the world, aortic pathology is relatively common, occupying an important place in morbidity and mortality in the United States, Japan and Asian countries. Its care requires human, economic and infrastructure resources. In Mexico there are no adequate statistics, since it is an underdiagnosed pathology as it is a silent disease in many cases, only until the different complications already known are established.[21]

MATERIAL AND METHODS

A descriptive study was carried out which studied the demographic characteristics, risk factors, clinical presentation, findings in non-invasive imaging studies, mortality and morbidity of patients with a diagnosis of thoracic aortic aneurysm who required surgical treatment in our institution. Data collection was carried out retrospectively directly from the clinical records.

RESULTS

In the study period, from January 2016 to December 2020 at our institution, 80 patients were identified, 39 with the diagnosis of thoracic aortic aneurysm and 41 with the diagnosis of acute aortic syndrome (39 with dissection, 1 hematoma and 1 perforating ulcer). Within the aneurysm group, 34 (87%) were men and 5 (13%) women. The minimum age found was 21 years, maximum 85 years, median 54, and average 53 years.

Regarding the risk factors found in this series, the most relevant were high blood pressure and smoking; however, diabetes, overweight, obesity, stroke, known aortic aneurysm, Marfan syndrome and aortic coarctation were also present, but frequently lower than the first two *(Figure 1)*.

In the clinical presentation of patients with aneurysm, the most frequent symptoms were dyspnea and chest pain. *(Table 1)*. The dimensions and frequency measurements of the aortic annulus, root, sinotubular junction, and ascending aorta are represented in *Table 2*. The involvement of the aortic valve was present in the thoracic aortic aneurysm, finding in our series the predominance of lesions due to severe aortic insufficiency (74%), as well as bicuspid aortic valve (23%) *(Table 3)*. According to the location of the aneurysm, the most frequent presentation is in both the root and ascending (51%) *(Figure 2)*. The score most used to calculate surgical risk in our unit is the EuroScore II, in this series a minimum of 0.5, maximum of 19.6, median of 2.68, mode 1.27, mean 3.78 and SD 3.86 were calculated.

In relation to the most frequent location of the thoracic aortic aneurysm, the most frequently performed surgical procedure is the implantation of a composite graft with the Bentall technique in all cases. Additionally, two patients underwent myocardial revascularization surgery and four underwent packing. None underwent any surgical intervention in a second surgical stage during hospitalization, regardless of the unpacking procedure *(Figure 3)*. The most used type of cardioplegia was intracellular Bretschneider in 92% of cases, the degree of moderate hypothermia in 82% of cases and the most frequent rhythm after aortic unclamping was ventricular fibrillation with 51% *(Table 4)*. Regarding the operative variables of cardiopulmonary bypass, aortic clamping, bleeding, transfusion of blood products and cell recovery, they are reported in *Table 5*. A total of six deaths were identified (early mortality of 15.3%), two were intraoperative deaths and four were postoperative deaths. Five in the composite graft group (mortality 19.2% in the group), one of a composite graft with debranching, no deaths were identified in the root-preserving aortic valve surgery group or in the supracoronary graft. In this series, 16 patients presented some postsurgical complication (morbidity of 45.6%). The most frequent complications were related to bleeding greater than usual and its reintervention, as well as

Table 1: Symptoms in thoracic aortic aneurysm.

Symptoms	Number of patients	%
Asymptomatic	4	10
Chest pain	17	44
Abdominal pain	1	3
Low back pain	1	3
Dyspnoea	27	69
Nausea/Vomiting	0	0
Cough	3	8
Syncope	2	5
Dysphonia	0	0
Dizziness/Vertigo	3	8
Dysphagia	0	0
Shock state	0	0
Others	0	0

Table 2: Measurements of the aortic annulus and ascending aorta in patients with thoracic aortic aneurysm.

	N	Minimum	Maximum	Median	Mode	Mean	SD
Aortic ring	39	17	38	25	26	25.59	4.27
Aortic root	39	20	81	49	43	52.13	14.11
STJ	35	29	85	45	48	48.74	14.88
Ascending aorta	38	27	83	52	70	53.92	15.68

SD = standard deviation. STJ = sinotubular junction.

Table 3: Aortic valve disease in thoracic aortic aneurysm.

		Number of patients	%
Aortic stenosis	No stenosis	30	77
	Mild	1	3
	Moderate	1	3
	Severe	7	18
Aortic insufficiency	Without insufficiency	1	3
	Mild	6	15
	Moderate	2	5
	Severe	30	77
Bivalve aorta	Yes	9	23
	No	29	74

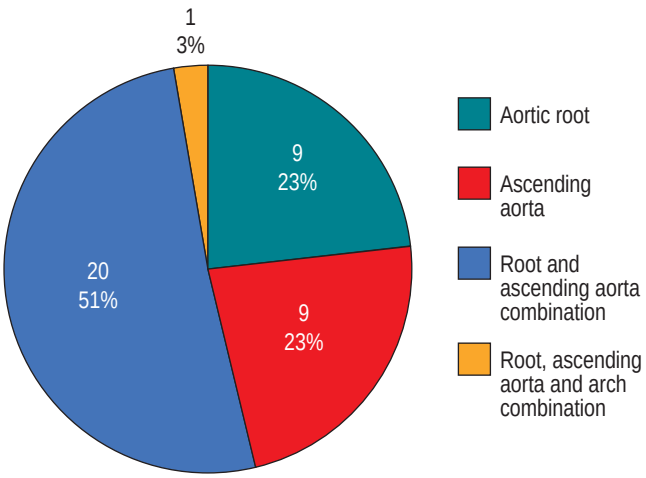

Figure 2: Location of thoracic aortic aneurysm

pneumonia *(Figure 4)*. Regarding the days of hospital stay in surgery for thoracic aortic aneurysm, we have found an average of 16.15 ± 8.8 days *(Table 6)*.

DISCUSSION

Thoracic aortic aneurysm and acute thoracic aortic syndrome are two different entities of the thoracic aorta, both in clinical presentation and the state with which they enter the operating room. The surgical indication for aneurysm is elective, while acute aortic syndrome is an emergency. Both entities share the same surgical techniques for their resolution.

Ascending aortic aneurysms are generally an asymptomatic entity with catastrophic complications of rupture and dissection. Aortic diameter is currently the main variable for the risk of dissection and rupture. The diameter in a healthy adult does not exceed 40 mm (upper limit of 40 mm in men and 34 mm in women).[2,8]

In our group of only thoracic aortic aneurysms, we found asymptomatic 10% of cases, while the predominant symptom was dyspnea (69%), followed by chest pain (44%). In our center, the population studied with thoracic aortic aneurysm has a mean age of 53.41 ± 16.3 years, similar to that reported

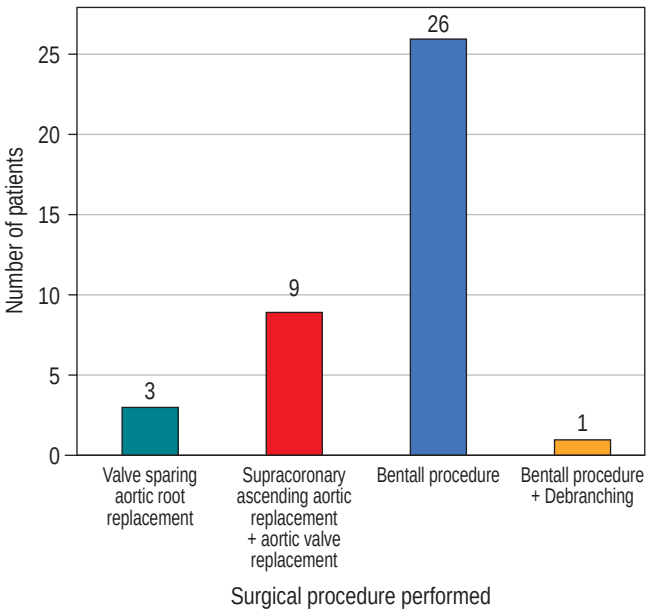

Figure 3: Type of surgical intervention in thoracic aortic aneurysm.

Table 4: Operative variables of cardioplegia, hypothermia and rhythm in patients undergoing surgery for thoracic aortic aneurysm.

		Number of patients	%
Type of Cardioplegia	Bretschneider	36	92
	St Thomas	3	8
	Of the nest	0	0
	Hematic	0	0
	Other	0	0
Degree of hypothermia	Mild	4	11
	Moderate	32	82
	Deep	3	7
Rhythm after aortic clamping	Sinus rythm	13	33
	AV block	4	10
	Atrial fibrillation	20	51
	Ventricular tachycardia	2	5
	Atrial fibrillation	0	0
	Other	0	0

Table 5: Operative variables of cardiopulmonary bypass (CBP), aortic clamping and use of blood products in patients undergoing surgery for thoracic aortic aneurysm.

	CBP (min)	Aortic clamping (min)	Bleeding (ml)	RBCC transfusion	FFP transfusion	PP transfusion	Cryoprecipitates transfusion	Autologous blood from Cell Saver (ml)
N Valid	39	39	38	39	39	39	39	39
N Lost	0	0	1	0	0	0	0	0
Minimum	83	58	210	0	0	0	0	0
Maximum	358	258	1,790	6	7	2	10	2,900
Mean	172.41	129.87	631.87	1.67	2.31	0.92	0.28	693.18
Median	148.00	122.00	537.50	1.00	2.00	1.00	0.00	613.00
SD	67.39	45.59	364.43	1.59	1.77	0.62	1.60	628.13

FFP = fresh frozen plasma. PP = plateletpheresis. RBCC = red blood cells concentrate. SD = standard deviation.

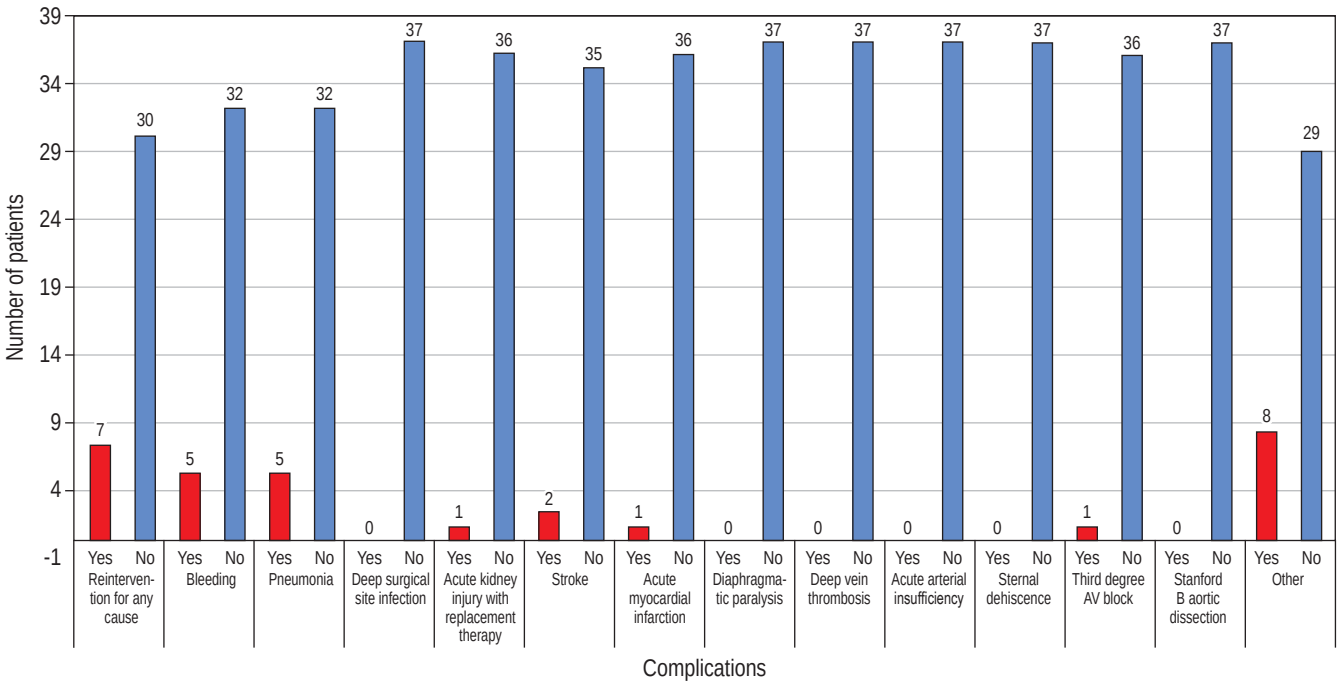

Figure 4: Complications in surgery for thoracic aortic aneurysm.

by Guo et al. in one review of 8,800 patients (mean age 57.75 ± 9.4 years) [14]. In our hospital, two decades ago, Ramírez et al. reported a younger age at presentation, with a mean of 47 years (range 2-78 years).[20]

The frequency of presentation with respect to sex was higher in men with 87% vs. women in 13%, a higher proportion than reported by Guo et al. (75.65% men),[14] being similar to what was reported by Ramírez et al. (82.05% men and 17.94% women).[20]

In our series of aortic aneurysms, we found a median diameter of the ascending aorta of 52 mm and a mean of 53.92 ± 15.68 mm. The mean size reported by Guo et al. at the time of registration was 42.6 mm (range 35.5-56 mm).[14] Ramírez et al. report a diameter of 6.5 to 15 cm (mean, 8 cm).[20] We observed a smaller aortic diameter at the time of the intervention after two decades in our institution.

The risk factors for thoracic aortic aneurysm described in the literature and found in our unit are systemic arterial hypertension (69%) and smoking (62%). Other factors such as overweight/obesity (19 cases), dyslipidemia (six cases), Marfan syndrome (three cases), aortic coarctation (five cases) and chronic kidney disease (three cases) are present, but

with better frequency. Although Marfan syndrome is highly associated with aneurysm and aortic dissection, in our unit, taking both entities into account, we have nine cases reported. Ramírez et al. reported that 41% (16 cases) had high blood pressure, 53% (21 cases) had smoking, and 30% (12 cases) had Marfan syndrome.[20]

In our series of ascending aortic aneurysms, we found greater aortic annuloectasia with a median diameter of the aortic annulus of 25 mm and mean of 25.59 ± 4.27 mm associated with severe insufficiency in 77% of patients and bicuspid aortic valve in 23%.

According to previously reported in the literature, thoracic aortic aneurysms are more frequent at the level of the aortic root and ascending aorta.[2] In our series, we found that 51% involve both the ascending aorta and the aortic root, followed by involvement of only the aortic root in 23% and isolated ascending aorta in 23%. Ramírez et al. report the ascending aorta as the most frequent site of aneurysm location in 88.7%.[20]

In our unit, the most used surgical technique for thoracic aortic aneurysm is the Bentall procedure compared to what happens worldwide where aortic root replacement surgery with preservation of the aortic valve is performed more frequently even in patients with Marfan syndrome with a 10-year survival of 90.5% for Bentall and 96.3 % for aortic valve-sparing surgery.[17]

The most commonly used type of cardioplegia in our unit is Bretschneider's intracellular cardioplegia. The cardioplegia used in large series is not specified. Also the most frequent exit rhythm is ventricular fibrillation in 51% of cases and the most used type of hypothermia is moderate hypothermia in 82% of cases.

Circulatory arrest with and without cerebral perfusion has been used in this type of procedure. However, in our unit, it was only reported on one occasion without determining whether or not cerebral perfusion existed and the duration thereof.

Table 6: Days of hospital stay in patients undergoing surgery for thoracic aortic aneurysm.

	Days of cardiac surgery ICU stay	Days of hospital stay	Total days of stay
Minimum	3	2	7
Maximum	27	36	44
Median	5	8	15
Mode	4	6	15
Mean	7.33	9.09	16.15
SD	5.38	6.67	8.8

ICU = Intensive Care Unit. SD = standard deviation.

In our series, a morbidity of 45.6% was identified, the most frequent being bleeding, as well as pneumonia. Ramírez et al. reported a morbidity of 72.9%, the main one also being bleeding greater than usual.[20]

In the thoracic aortic aneurysm group, we have a median stay in cardiac surgery intensive care unit of five days and an average of 7.3 ± 5.38 days, a median stay in hospital of 8 days and a mean of 9.09 ± 6.67 days, a median total stay of 15 days and a half days 16.5 ± 8.8 days. Ramírez et al. report an average stay in cardiac surgery intensive care unit of 6.7 days (range of 2 - 46 days) and an average hospital stay of 14.4 days (range of 6-64 days).[20]

We can conclude that aortic aneurysm is a disease of the aorta that, although rare, has high clinical relevance due to its high morbidity and mortality and should be treated in a tertiary care unit. A multidisciplinary team trained in thoracic aortic surgery is required to reduce morbidity and mortality and achieve international standards in terms of results. This will allow standardization of the surgical technique, perfusion management, myocardial protection methods, and perioperative management for greater experience of the surgical, anesthetic and medical team.

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ORIGINAL ARTICLE

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Experience in ascending aorta surgery in a Tertiary Level Hospital

Experiencia en cirugía de aorta ascendente en un Centro Hospitalario de Tercer Nivel

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ABSTRACT

Introduction: ascending aorta surgery has a mortality rate of 8.1%, whose main indications are aortic dissection, dilation and rupture with mortalities between 94-100%. **Objective:** to describe a case series of ascending aorta surgery. **Material and methods:** patients admitted between 2020-2024 were studied, identifying sociodemographic data, comorbidities, procedures, and findings. **Results:** of 12 patients, 66.6% were male, the predominant ages were between 20 and 40 years (58%), with New York Heart Association functional class II (66.6%) and left ventricle ejection fraction between 40 and 60% (66.6%). The congenital pathologies found were: Marfan (25%), patent ductus arteriosus (8.3%) and coarctation of the aorta (8.3%). The main findings were: aortic root dilation (66.6%), Stanford A aortic dissection 33.3%, and endocarditis (25%) with perforation of an abscessed non-coronary sinus aneurysm (16.6%). The Bentall procedure was the most frequently performed surgical intervention, accounting for 75% of cases, and was associated with a mortality rate of 16.6%. **Conclusions:** surgery of the ascending aorta is reproducible and safe. Studies with larger samples are required in order to obtain stronger conclusions.

Keywords: aortic aneurysm, aortic dissection, ascending aorta surgery, sinus of Valsalva perforation.

RESUMEN

Introducción: *la cirugía de aorta ascendente tiene una mortalidad de 8.1%, cuyas principales indicaciones son disección, dilatación y rotura aórtica con mortalidades entre 94-100%.* ***Objetivo:*** *describir una serie de casos de cirugía de aorta ascendente.* ***Material y métodos:*** *se estudiaron pacientes ingresados entre 2020-2024 identificando datos sociodemográficos, comorbilidades, procedimientos y hallazgos.* ***Resultados:*** *de 12 pacientes, 66.6% fueron masculinos, las edades predominantes fueron entre los 20 y 40 años (58%), con clase funcional II de la New York Heart Association (66.6%) y fracción de eyección del ventrículo izquierdo entre 40 y 60% (66.6%). Las patologías congénitas encontradas fueron: Marfan (25%), persistencia del conducto arterioso (8.3%) y coartación aórtica (8.3%). Los principales hallazgos fueron: dilatación de raíz aórtica (66.6%), disección aórtica Stanford A 33.3% y endocarditis (25%) con perforación de aneurisma de seno no coronariano abscedado (16.6%). El procedimiento de Bentall fue la cirugía más realizada (75%) con una mortalidad de 16.6%.* ***Conclusión:*** *la cirugía de la aorta ascendente es reproducible y segura. Se requieren estudios con muestras mayores para obtener conclusiones más robustas.*

Palabras clave: *aneurisma aórtico, disección aórtica, cirugía de aorta ascendente, perforación de seno de Valsalva.*

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Ascending aorta surgery is a complex procedure due to its relationship with anatomical structures such as the aortic leaflets, coronary ostia, coronary arteries and because it is one of the areas of greatest pressure in the circulatory system. The main indications for these procedures are dissection, dilation, aneurysm, intramural hematoma, penetrating atherosclerotic ulcer, blunt trauma, which are associated with a mortality rate between 94-100%.[1,2]

Aortic dissection consists of the rupture of the intimate layer with separation of it and the middle layer, forming a false lumen that causes aortic regurgitation and haemodynamic compromise. The most frequent are Stanford A or DeBakey type I (50%), type II (35%), type III (15%). Aneurysm is defined as the dilation of the aortic root greater than 5.25 cm, in Marfan Syndrome with a diameter less than or equal to 5 cm. Patients with root diameters greater than 4.5 cm have an 89-fold increased risk of type A dissection, aneurysm, sudden death.[3,4]

The characteristics associated with increased risk of aortic dissection in patients with no identified genetic causes are family history of dissection with aortic diameter < 5 cm, sudden unexplained death in < 50 years, rapid aortic growth > 0.5 cm in 1 year and 0.3 cm in 2 consecutive years, and coarctation of the aorta. Patients with Marfan syndrome are associated with an increased risk of aortic complications when they have a family history of dissection, rapid aortic growth > 0.3 cm per year, diffuse dilation of the root and ascending aorta, and marked tortuosity of vertebral arteries.[5,6]

The main objectives of ascending aorta surgery are to restore the flow in the true lumen, eliminate tears or ruptures, reestablish anatomy and valve competence, in order to treat and avoid life-threatening complications, such as rupture, shock, poor visceral perfusion, persistence of false lumen in 60%, and early mortality in 20-30%. The need for reoperation after surgery at 10-year ranges around 5%, significantly impacting quality of life and complications in the short and medium term, making it the treatment of choice. The main complications to be assessed are the formation of a pseudoaneurysm between the aortic wall and the vascular graft, the presence of significant aortic regurgitation, and the persistence of dissection of the descending aorta.[4,7,8]

The Bentall operation is one of the most well-known ascending aorta procedures. It consists of aortic root replacement with a Dacron tube including a prosthetic valve inside, and the reinsertion of the coronary ostia. It has a reoperation rate of 1.01%, with an in-hospital mortality related to the procedure of 5.6%, the main causes being low cardiac output in 29.4% and hemorrhage in 8.5%. The most common complication at 10 years of follow-up is valve dysfunction (26.6%), due to degeneration or obstruction by pannus or thrombus and, to a lesser extent, graft infection or pseudoaneurysm.[9,10]

MATERIAL AND METHODS

In this case series study, information was collected prospectively from primary sources of patients who underwent ascending aorta surgery at our institution from March 2020 to February 2024. All patients with an indication for ascending aorta surgery were included, representing a total of 12 patients. Patients' ages were between 23 and 67 years, 8 of whom were male and 4 female. Sociodemographic data were taken into account as variables: age, sex, functional class, comorbidities, type of dissection, type of surgery, risk and mortality. Clinical and sociodemographic characteristics of the cases are shown in *Table 1*. The collected information was entered into a database, a collection form was used as a data collection instrument. In relation to ethical aspects, the patients authorized the use of their information for the present study.

RESULTS

Sociodemographic analysis revealed that the majority of ascending aorta surgeries were performed on individuals between 20 and 40 years old (58.3%). Males predominated,

Table 1: Clinical and sociodemographic data of patients with ascending aorta surgery in a tertiary level hospital. N = 12.

Variables	n (%)
Age	
20-30	4 (33.3)
31-40	3 (25.0)
41-50	2 (16.6)
51-60	1 (8.3)
> 60	2 (16.6)
Sex	
Male	8 (66.6)
Female	4 (33.3)
Risk factors	
Hypertension	4 (33.3)
Smoking	3 (25.0)
Dyslipidemia	2 (16.6)
None	3 (25.0)
NYHA functional class	
I	1 (8.3)
II	8 (66.6)
III	3 (25.0)
LVEF	
31-40	1 (8.3)
41-50	3 (25.0)
51-60	5 (41.6)
> 60	3 (25.0)

LVEF = Left Ventricular Ejection Fraction. NYHA = New York Heart Association.

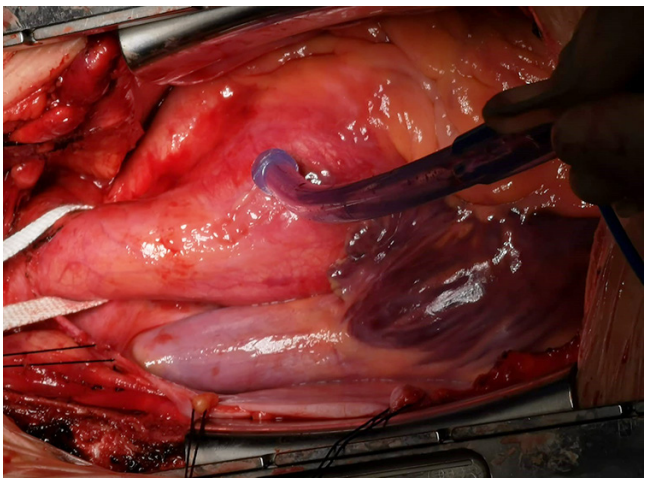

Figure 1: A 23-year-old male with ascending aorta aneurysm, with a 60 mm root, severe aortic regurgitation, Marfan, Pectus excavatum.

accounting for 66.6% of cases (8/12). The most common risk factors present were hypertension (33.3%, 4 cases), smoking (25%, 3 cases), and dyslipidemia (16.6%, 2 cases). The functional class of most patients was NYHA II in 8 cases (66.6%), and NYHA III in 3 cases (25%). Regarding left ventricular ejection fraction (LVEF), 5 patients (41.6%) had an LVEF between 51-60%, 3 patients (25%) had an LVEF between 41-50%, and only 1 case (8.3%) had an LVEF below 31% *(Table 1)*.

The most frequently found congenital pathologies were Marfan syndrome *(Figure 1)* with 3 cases (25%) and then patent ductus arteriosus, coarctation of the aorta, ventricular septal defect and bivalve aorta, all of them with 1 case (8.3%) each, adding up to a total of 7 cases (58.3%) with congenital pathologies present in patients with ascending aorta surgery.

Of the intraoperative findings, 10 cases (83.3%) had moderate to severe secondary aortic regurgitation. Regarding aortic dilation, 8 cases (66.5%) presented it, of which the majority 5 cases (41.6%) were dilated between 50 mm and 60 mm, 2 cases (16.6%) were dilated between 61mm -70 mm and 1 case (8.3%) presented dilation > 71 mm. The most common aortic dissection was the Stanford A type in 4 patients (33.3%), the rest had no dissection. Endocarditis was observed in 3 patients (25%), out of these 2 cases (16.6%) presented perforation of an abscessed non-coronary sinus aneurysm. Postoperative hemorrhage occurred in 3 cases (25%).

Regarding the procedures performed, 9 cases (75%) underwent Bentall procedure *(Figure 2)* and 3 cases (25%) underwent ascending aortic replacement without valve replacement or coronary ostia reinsertion. Of the total number of patients, 3 cases (25%) were reoperated, of which 2 (16.6%) were due to postoperative chest bleeding, and 1 (8.3%) due to retained hemothorax. Among the total number of cases, simultaneous procedures were performed in 4 instances (33.3%). These included supra-aortic vessel grafting in 1 case (8.3%) *(Figure 3)*, coronary revascularization in 1 case (8.3%), mitral valve replacement in 1 case (8.3%), and Ravitch surgery for pectus excavatum using the stratos system in 1 case (8.3%).

The mortality rate in this case series was 16.6% (2 patients), with the primary causes of death being hemorrhage in 1 case (8.3%) and friable tissues in 1 case (8.3%).

DISCUSSION

Aortic root replacement offers numerous technical options, thanks to decades of research and development yielding

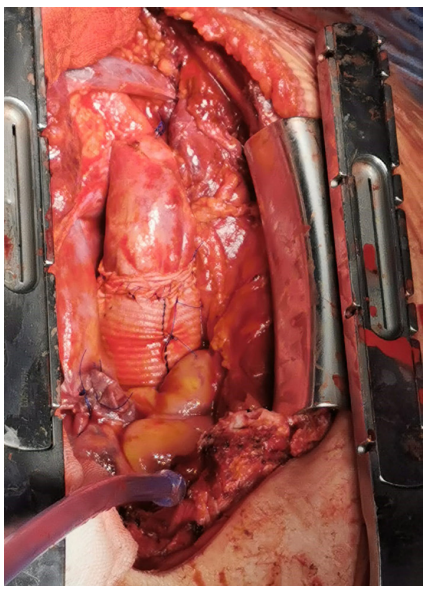

Figure 2:

A 23-year-old male with Bentall De-Bono surgery, with a 31 mm mechanical valved tube.

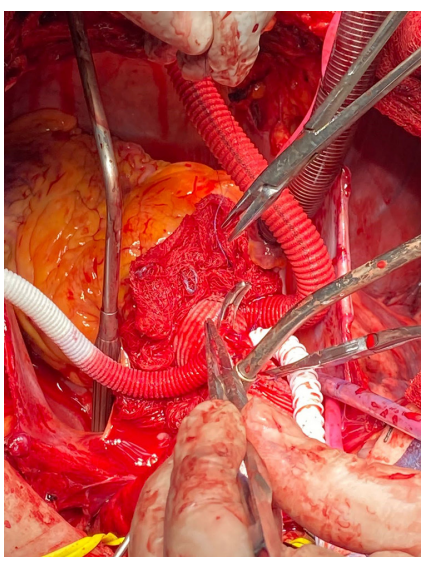

Figure 3:

A 74-year-old male with aortic valve endocarditis, with abscess in the non-coronary sinus and left coronary sinus, friable aorta, Bentall plus supra-aortic vessel grafting was performed.

favorable outcomes. These options address the individual patient needs, considering anatomical characteristics and risk factors to manage aortic pathology, prevent recurrence, valve dysfunction, progressive dilation, and dissection. Our 4-year experience with 12 consecutive patients undergoing ascending aorta surgery showed satisfactory surgical outcomes, with an early mortality rate of 16.6%, lower than previously reported at our hospital.[11]

Our findings align with current literature, indicating a twofold increase in males, predominantly in productive ages (average 30 years). Hypertension was the prevailing risk factor, increasing absolute tension on the arterial wall, leading to intima deterioration and middle layer weakening, creating conditions for progressive dilation or rupture. Smoking, a risk factor for hemostasis and atherosclerosis, exposes patients to toxicants, promoting cell proliferation, lipid accumulation, and atheromatous plaque formation. Dyslipidemia, particularly elevated low-density lipoprotein cholesterol and triglycerides, correlates with aortic dilation.

Marfan syndrome was the predominant congenital pathology, affecting 60-80% of adults, with aortic pathology being the most prognostically significant. The typical involvement is dilation of the root, starting in the sinuses of Valsalva, with histological findings showing middle layer degeneration, elastic lamina loss, and proteoglycan disorganization, leading to elastic fiber destruction, dilation, thinning, and aortic stiffness. Other connective tissue disorders, such as bicuspid aortic valve and coarctation of the aorta, are often associated with dissection.

Regarding intraoperative findings, aortic valve regurgitation in the presence of aortic root dilation (40-60%) is quite frequent, as in our results. According to literature, it is characterized by a regurgitating flow from the aorta to the left ventricle, giving way to an overload of diastolic volume, increased stroke ejection volume and elevated intra-aortic systolic pressures with probable dilation. Therefore, surgical intervention is justified with the aim of preventing acute aortic dissection.[12]

Aortic dilatation is more frequent in patients in the sixth decade of life who have a history of hypertension, smoking; however, patients with connective tissue or bicuspid aortic valve diseases present dilatation at younger ages. In most of the published series, aneurysms of the ascending aorta are the most frequent, their main etiology is arteriosclerosis and degenerative aorta. Histologically, they present degenerative changes of the elastic fibers and collagen of the middle layer of the wall, constituting an entity called cystic necrosis of the media, the surgical decision should be based on symptoms, comorbidities, imaging tests and risk-benefit.[13]

According to the literature, Stanford A type aortic dissection is the most common, accounting for approximately 70% of cases. In our study, however, it occurred in only 33.3% of patients. This type of dissection involves the proximal arch, extending to the left subclavian artery, and is influenced by anatomical and hemodynamic factors.

A common underlying factor in aortic dissections is the deterioration of the mechanical properties of the aortic wall, resulting from alterations in the middle layer. Frequently, this is accompanied by changes in the elastic component, including fragmentation of elastic fibers, similar to those seen in Marfan syndrome. Haemodynamically, most of them present hypertension with left ventricular hypertrophy. Death can occur within minutes to hours due to rupture or dissection of the pericardial sac, or dissection of the coronary arteries resulting in infarction, the Stanford A type invariably must be operated on.[14]

The evidence in the current clinical guidelines recommends evaluating urgent surgery when there is endocarditis in the presence of acute aortic dissection, Class of Recommendation I, Level of Evidence B.[1,15] Endocarditis is a complex disease with high morbidity and mortality; it leads to heart failure, perivalvular extension, embolic events; in contrast, its association with aortic dissection is not very frequent. In two case report studies, each one shows a patient with perivalvular abscess, severe aortic root dilation (52 mm), dilatation of the ascending aorta with root dissection,[15,16] similar to the cases presented in our study, in which we also report two cases that presented perforation of an abscessed non-coronary sinus.

The most performed operation was the Bentall-De Bono procedure, which has demonstrated its effectiveness for decades, and now remains as the "gold standard" for type A aortic dissection because it is safe and feasible (Evidence IB). Since in dissection the aortic leaflets remain intact, some literature considers the use of techniques that preserve the native leaflets such as the Yacoub technique; however, the lack of stabilization of the annulus can lead to recurrent aortic regurgitation, and due to the long anastomotic line, it increases the risk of bleeding, limiting the experience to perform this operation, especially in tissue dissection. David's modified technique shows advantages by not requiring long-term anticoagulation with complete restoration of the aortic root, which is why it is especially recommended in young patients.[17] In our study, the main complications were haemorrhage that required chest-packing in 25% of the cases, which were accompanied by endocarditis with friable tissues. Both of them were the most frequent causes of mortality.

The International Registry of Aortic Diseases (IRAD) reported 682 surgical cases across 18 centers, with only 5.8% of patients undergoing replacement surgery. Similarly, the German Registry of Acute Aortic Dissection Type A (GERAADA), which compiled data from 56 centers, found that merely 8.2% of patients received aortic replacement surgery. This low percentage is attributed to the technical complexity of these procedures, which involve prolonged surgical times,

extensive tissue dissection, and pose a significant challenge even for experienced surgeons, particularly during the acute phase of this pathology.[17]

CONCLUSIONS

The findings in our study allow us to suggest that the benefits of ascending aorta surgery are evident, being a reliable procedure in expert hands. A wide variety of techniques can be performed depending on the type of pathology and the factors related to each patient. We emphasize that it is necessary to carry out studies with larger samples for future generations of surgeons.

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ORIGINAL ARTICLE

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Minimally invasive surgery for correction of septal defects in pediatric patients

Cirugía de mínima invasión para corrección de defectos septales en pacientes pediátricos

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ABSTRACT

Objective: our aim was to investigate the safety, feasibility, and early outcomes of our initial experience in repairing atrial and ventricular septal defects using a right minithoracotomy. **Material and methods:** we conducted an observational retrospective study at a single center. The study included a total of 13 consecutive pediatric patients who underwent congenital cardiac surgery using this surgical technique from 2022 to 2023. **Results:** a total of 13 minimally invasive surgeries were performed to close septal defects, involving seven females and six males, aged between 2 and 11 years, with weights ranging from 11 to 40 kg. Cardiopulmonary bypass times ranged from 13 to 61 minutes (average 38.5 minutes), and aortic clamping times ranged from 12 to 37 minutes (average 30.5 minutes). The average ICU stay was 2.7 days (range 1 to 5 days), and the average postoperative hospital stay was 6.1 days (range 4 to 8 days). There were no postoperative deaths. Postoperative complications included one case of thoracic exploration for bleeding and one case of diaphragmatic paralysis. **Conclusions:** right lateral thoracotomy in cardiac surgery is a viable approach for correcting some well-selected intracardiac defects. It is a reproducible and safe technique. The small skin incision provides superior aesthetic results without increasing morbidity or mortality rates, offering psychological and social satisfaction to patients.

RESUMEN

Objetivo: *nuestro objetivo fue investigar la seguridad, viabilidad y resultados tempranos de nuestra primera experiencia en la reparación de defectos septales auriculares y ventriculares, mediante una minitoracotomía derecha.* ***Material y métodos:*** *realizamos un estudio observacional retrospectivo en un único centro. El estudio incluyó un total de 13 pacientes pediátricos consecutivos que se sometieron a cirugía cardíaca congénita utilizando esta técnica quirúrgica en un periodo de tiempo de 2022 hasta 2023.* ***Resultados:*** *se realizaron un total de 13 procedimientos de cirugía mínimamente invasiva para el cierre de defectos septales, involucrando a siete mujeres y seis hombres, con edades y peso entre los 2 y 11 años y 11 y 40 kg, respectivamente. Los tiempos de circulación extracorpórea variaron desde 13 hasta 61 minutos (promedio 38.5 minutos), los tiempos de pinzamiento aórtico fueron de 12 hasta 37 minutos (promedio 30.5 minutos). La estancia media en la unidad de cuidados intensivos (UCI) fue de 2.7 días (rango, 1-5 días) y la estancia hospitalaria media postoperatoria fue de 6.1 días (rango 4-8 días). No hubo muertes postoperatorias. Las complicaciones postoperatorias incluyeron: un caso de exploración torácica por sangrado y un caso de parálisis diafragmática.* ***Conclusiones:*** *la toracotomía lateral derecha en cirugía cardíaca es un abordaje viable para la corrección de algunos defectos intracardiacos bien seleccionados. Siendo una técnica reproducible y segura. La pequeña incisión en la piel proporciona resultados estéticos superiores sin aumentar las tasas*

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Keywords: atrial septal defect, congenital heart disease, minimally invasive cardiac surgery, thoracotomy, ventricular septal defect.

de morbilidad o mortalidad, ofreciendo satisfacción psicológica y social a los pacientes.

Palabras clave: *comunicación interauricular, cardiopatía congénita, cirugía cardíaca mínimamente invasiva, toracotomía, comunicación interventricular.*

Surgical repair in cardiovascular surgery traditionally involved a midline sternotomy due to procedure complexity and improved surgical field exposure. However, over the last two decades, this approach has evolved to include minimally invasive techniques, offering aesthetic benefits. One drawback of these methods is the visible scar on the chest, which can be psychologically burdensome for children.[1,2] Minimally invasive cardiac surgery (MICS) can utilize various approaches, including midline ministernotomy, right anterior minithoracotomy, and right lateral or subaxillary thoracotomy.[3,4] Among the benefits observed are improved aesthetics, shorter ICU and hospital stays, reduced blood product usage, decreased trauma, less surgical pain, and faster recovery.[5,6] A right anterior minithoracotomy yields favorable cosmetic results and avoids sternum division, reducing the risk of deformities like scoliosis compared to ministernotomy.[4] At our center, we initially performed repairs for atrial septal defects in patients weighing less than 20 kg. As experience grew, we expanded to include a wider range of pathologies and became more flexible with patient weights, gradually minimizing incisions.[5]

MATERIAL AND METHODS

We conducted a single-center, observational, retrospective study. The study included a total of 13 patients diagnosed with congenital heart disease with pulmonary overcirculation from February 2022 to February 2023, eligible for total correction, diagnosed via echocardiography. Patients with diagnoses of secundum atrial septal defect (ASD), primum ASD, ventricular septal defect (VSD), and partial anomalous pulmonary venous connection (PAPVC) were included. Exclusions were patients with patent ductus arteriosus (PDA), weight greater than 40 kg, and those who had undergone previous surgery. The procedures were performed by two surgeons. Demographic and clinical data are summarized in *Table 1*. We analyzed intraoperative and postoperative outcomes, including cardiopulmonary bypass time and aortic cross-clamp time, postoperative complications, mechanical ventilation duration, Intensive Care Unit (ICU) stay, and in-hospital stay *(Table 2)*.

Surgical technique

With general anesthesia and invasive monitoring, the patient is placed in a left lateral decubitus position at a 45° angle, and the right arm is fixed over the head. A line is traced from the xiphoid appendix to the scapular angle, subsequently identifying the anterior and mid-axillary lines. An incision is made at the convergence of these lines *(Figure 1)*, typically encountering only the serratus anterior and intercostal muscles. The incision is no more than 5 cm. Access is gained at the 4th intercostal space, using two thoracic spreaders *(Figure 2)*. Subsequently, a 1 to 2 cm pericardiotomy is performed above the phrenic nerve. Anterior and posterior traction stitches are placed on the pericardium, the thymus is displaced (usually preserved), and cannulation is performed-aortic and bicaval with angled cannulas. Occasionally, a second incision less than 1 cm below is made for inferior vena cava cannula placement, later used for pleuromediastinal drainage. Antegrade cold cardioplegia is administered, aortic clamping is performed, and correction of the heart defect is carried out conventionally. After completing the repair, deaeration

Table 1: Demographic data.

Age (years) [range]	6.1 [2-11]
Weight (kg) [range]	21 [11-40]
Sex, n (%)	
Males	6 (47)
Females	7 (53)
Diagnosis	ASD (9)
	ASD + PS
	ASD VS + device
	Embolism
	VSD
	TAPVC

ASD = atrial septal defect. PS = pulmonary stenosis. VS = vein stenosis. VSD = ventricular septal defect. TAPVC = total anomalous pulmonary vein connection.

Table 2: Results.

CPB time (min) [range]	38.5 [13-61]
Cross-clamp (min) [range]	30.5 [12-37]
Extubation in OR, n (%)	11 (84)
Lactate (max) [range]	4.2 [1.6-9.6]
ICU stay (days) [range]	2.7 [1-5]
Hospital stay [range]	6.1 [4-8]
Complications	1 Diaphragmatic paralysis
	1 Contralateral hemothorax

CPB = cardiopulmonary bypass. ICU = intensive care unit. OR = operating room.

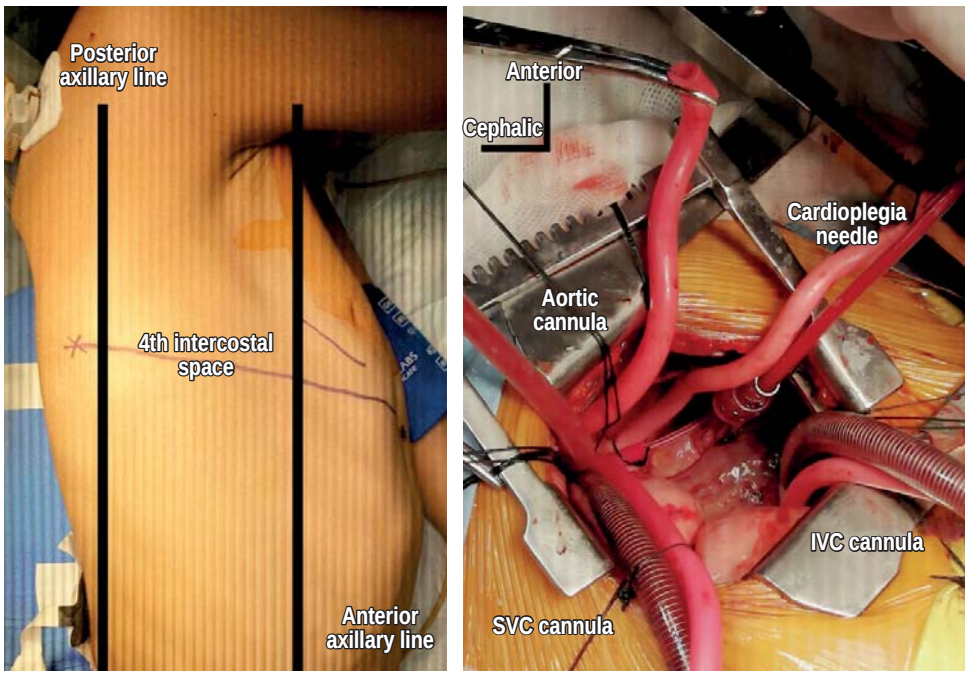

Figure 1:

Patients were positioned with the right side elevated 75 degrees, aligning the incision along the anterior axillary line, posterior axillary line, and the 4th intercostal space. We utilized conventional cardiac surgical instruments.
IVC = inferior vena cava.
SVC = superior vena cava.

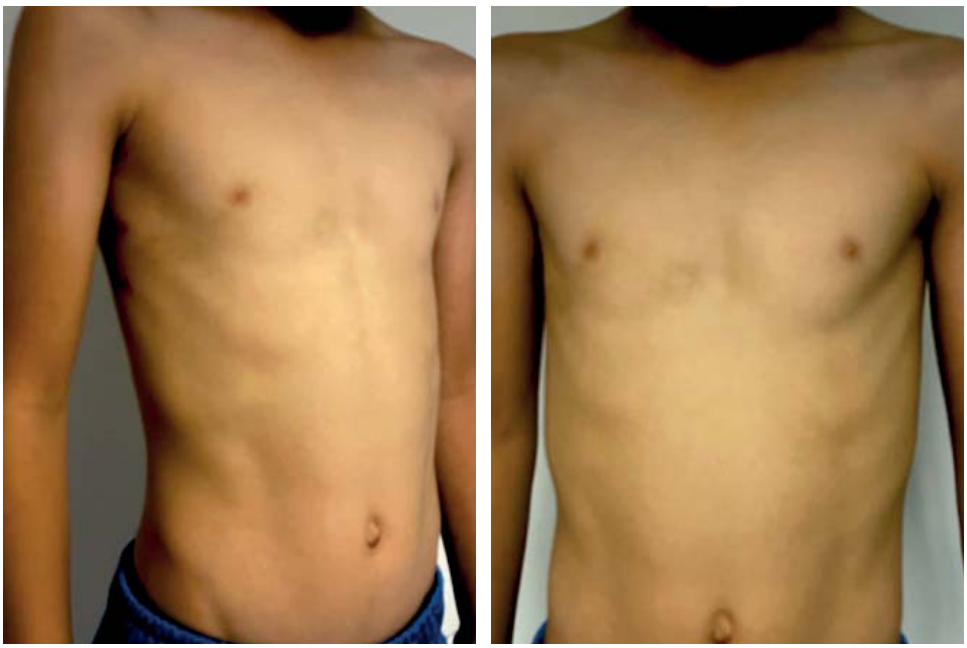

Figure 2:

The excellent cosmetic result of the right subaxillary thoracotomy.

is achieved through continuous suction via the cardioplegia, and the patient is routinely weaned off extracorporeal circulation. A postoperative echocardiogram is conducted for cardiac evaluation. The pericardium is partially closed, a pleuromediastinal chest drain tube is placed, temporary epicardial pacemaker leads are positioned, and the chest wall is closed in the usual manner.

RESULTS

A total of 13 minimally invasive surgical procedures for septal defect closure were performed using the previously described technique. The procedures involved seven girls and six boys, aged between 2 and 11 years, with weights ranging from 11 to 40 kg. The congenital heart defects repaired

included atrial septal defects such as superior vena cava, inferior vena cava, ostium secundum, fenestrated defects, and perimembranous ventricular septal defects. The perioperative data for atrial septal defects showed that 8 were corrected with primary closures and 4 with double velour patches. Cardiopulmonary bypass times ranged from a minimum of 13 minutes to a maximum of 61 minutes (average 38.5 minutes), while aortic cross-clamp times ranged from 12 minutes to 37 minutes (average 30.5 minutes). No significant residual defects were reported in the postoperative echocardiograms. There were no intraoperative deaths. Ten patients were successfully extubated in the operating room, although two required reintubation after arriving in the Intensive Care Unit (ICU) due to increased respiratory rate and elevated serum lactate levels. Mechanical ventilation time did not exceed 24 hours in any case. The average ICU stay was 2.7 days (range 1 to 5 days), and the average hospital stay post-surgery was 6.1 days (range 4 to 8 days). There were no postoperative deaths. Postoperative complications included one case of thoracic exploration for bleeding and one case of diaphragmatic paralysis. No associated thoracic deformities were reported.

DISCUSSION

In recent decades, significant advances have been made in MICS. Despite these advancements, the acceptance and practical implementation of MICS remain limited in developing countries due to various challenges.[7,8]

Surgical correction of atrial and ventricular defects has traditionally shown excellent results with routine median sternotomy.[8] With improvements in cardiac surgery safety, there has been a growing emphasis on reducing procedural trauma and enhancing cosmetic outcomes, particularly for children, adolescents, and young women.[6] Right lateral thoracotomy presents a viable alternative to median sternotomy, offering advantages such as reduced surgical trauma, faster recovery, and improved aesthetic results, especially for women.[8,9] This technique has been increasingly adopted for simple coronary disease repairs and has gained growing popularity.[6,10]

The successful establishment of cardiopulmonary bypass is essential for performing MICS. The arterial cannulation site is typically deep, and aortic cannulation often presents the greatest challenge. Some studies have reported using forceps to grasp the tip of the curved arterial cannula, which can facilitate this process.[11] In certain cases, the inferior vena cava cannula was placed through the sixth intercostal space, and this site was subsequently used for chest tube placement at the end of the surgery. A literature review found few comparisons of minimally invasive techniques for congenital heart defects, with no significant differences in operative time, duration of cardiopulmonary bypass, or blood transfusion volume, suggesting that different incisions did not complicate the procedure.[12]

In our series, we have not yet compared traditional median sternotomy with MICS to identify significant differences in intraoperative or postoperative outcomes. Nevertheless, our results indicate a reduction in the length of stay in the cardiovascular intensive care unit and overall hospital stay.

Yu Qing et al. reported in their study involving 665 patients that there were no significant differences in success rates (OR: 0.23; 95% CI 0.05-1.07) or rates of severe complications (OR: 1.46; 95% CI 0.41-5.22) between the MICS and sternotomy groups. MICS demonstrated an advantage in cosmetic outcomes, with a significant reduction in incision length by 8.97 cm. Further follow-up is needed to assess the psychological impact of the incision on our patient group.[13]

Unlike other emerging technologies, the right lateral thoracotomy approach does not require specialized instruments, and most of the procedure resembles conventional cardiac surgery. This means there is no significant increase in hospital costs, resulting in shorter hospital stays.[14,15] At our center, we successfully adapted conventional surgical instruments for MICS, which reduced costs related to hospital stay.

The success of all procedures is highlighted, with no conversions to full sternotomy and no recorded perioperative adverse events. The absence of deaths, low cardiac output syndrome, arrhythmias, reoperations for residual defects, complete atrioventricular block, or cerebrovascular events during postoperative follow-up underscores the safety and efficacy of this approach.[13,15] An et al. reported one early hospital death (2.1%) following total correction in a 4-month-old child. The patient died from low cardiac output syndrome and multiorgan failure on the seventh postoperative day.[16] In our study, the average ICU stay was 2.7 days (ranging from 1 to 5 days), and the average post-surgery hospital stay was 6.1 days (ranging from 4 to 8 days). There were no postoperative deaths. Postoperative complications included one case of chest exploration for bleeding, one case of diaphragmatic paralysis, and two cases of sternal costal dislocation.

This study has the following limitations: first, it is a retrospective study rather than a randomized controlled trial, which introduces some selection bias in the patient groups, though the results remain clinically relevant. Second, the study was conducted at a single center with a small sample size, so results may vary in other cardiac units. Additionally, long-term follow-up results need to be summarized in more detail.

CONCLUSIONS

We can conclude that MICS approach for atrial and some ventricular defects can be a reproducible surgical alternative that does not require changes to the infrastructure used in traditional approaches. However, further comparative studies

are needed to determine if there are significant differences compared to traditional methods. Nevertheless, some studies suggest that the smaller skin incision provides superior aesthetic results without increasing morbidity or mortality rates, offering psychological and social satisfaction to patients.

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REVIEW ARTICLE

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Transcatheter edge-to-edge mitral valve repair: a surrogate technique that imperfectly mimics. The cold hard truth from data-driven observations

Reparación de la válvula mitral borde a borde con catéter: una técnica sustitutiva que imita de forma imperfecta. La cruda y fría verdad a partir de observaciones basadas en datos

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ABSTRACT

The transcatheter edge-to-edge mitral valve repair procedure has gained prominence as a pioneering technology in structural interventional cardiology to treat degenerative mitral valve regurgitation in recent years. This innovative approach is rooted in the surgical technique of mitral valve repair, yet distinctively devoid of an annuloplasty ring, a *sine qua non* condition for surgical mitral valve repair. Therefore, the transcatheter edge-to-edge mitral valve repair shows uncertain long-term efficacy in treating mitral regurgitation. Hence, it is crucial to carefully consider the potential long-term consequences of an imperfect technique, encompassing patient survival, quality of life, and unplanned rehospitalizations for heart failure rates, as well as the likelihood of mitral regurgitation recurrence. From a theoretical perspective, integrating transcatheter edge-to-edge mitral valve repair with annuloplasty ring implantation, both percutaneous techniques, could potentially address the issue of long-term durability. Owing to the intricate nature of functional mitral regurgitation, this article will exclusively focus on degenerative mitral regurgitation.

Keywords: annuloplasty, degenerative mitral regurgitation, mitral valve repair, prosthetic annuloplasty ring, transcatheter edge-to-edge mitral valve repair.

RESUMEN

En los últimos años, el procedimiento de reparación de la válvula mitral de borde a borde mediante catéter ha ganado popularidad como una tecnología pionera en cardiología intervencionista estructural. Este enfoque innovador tiene sus raíces en la técnica quirúrgica de reparación de la válvula mitral, pero carece de un anillo de anuloplastia, una condición sine qua non para la reparación quirúrgica de la válvula mitral. Por lo tanto, la reparación de la válvula mitral de borde a borde mediante catéter muestra una eficacia incierta a largo plazo en el tratamiento de la insuficiencia mitral. De tal manera que es crucial considerar cuidadosamente las posibles consecuencias a largo plazo de una técnica imperfecta, que abarcan la supervivencia del paciente, la calidad de vida y las rehospitalizaciones no planificadas por tasas de insuficiencia cardíaca, así como la probabilidad de recurrencia de la insuficiencia mitral. Desde una perspectiva teórica, la integración de la reparación transcatéter borde a borde con la implantación percutánea de un anillo de anuloplastia podrían mitigar potencialmente el problema de la durabilidad a largo plazo. Debido a la complejidad del tema de la insuficiencia mitral funcional, este artículo se enfocará exclusivamente en la insuficiencia mitral degenerativa.

Palabras clave: *anuloplastia, insuficiencia mitral degenerativa, reparación valvular mitral, anillo protésico de anuloplastia, reparación valvular mitral transcatéter borde a borde.*

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Mitral valve (MV) repair is the technique of first choice for treating cases of degenerative mitral regurgitation (MR).[1,2] The mitral annuloplasty ring, first described by Carpentier, remains the cornerstone of this surgical technique.[3,4] This article explores the fundamentals of the surgical technique that led to the development of transcatheter edge-to-edge mitral valve repair (TEER). We also discuss the main difference between the two techniques, the omission of an annuloplasty ring in TEER, and assess the impact of this ringless approach on patient survival, quality of life, heart failure-related rehospitalization, and failure rates after procedure. Theoretically, a combined approach using both percutaneous TEER and annuloplasty ring implantation may offer a viable solution to the problem of long-term durability.

Mitral valve repair: annuloplasty ring, the essential sine qua non

A constant imperative in surgical MV repair, regardless of the underlying pathology, is the use of an annuloplasty ring, a cornerstone concept introduced by Carpentier[3-8] in the seminal French Correction[7] *(Figure 1)*. The annuloplasty ring fulfills several key functions; namely, reshapes the MV native annulus, preserving the optimal 3:4 diameter ratio between anteroposterior and transverse dimensions, fixes the annular size in systole promoting optimal leaflet coaptation and maximizing the coaptation surface area, and prevents progressive annular dilation, ensuring long-term stability[7,8] *(Figure 2)*.

TEER is based on the Alfieri technique

The edge-to-edge technique for repairing MR was first performed by Alfieri on April 25, 1991.[9] However, two crucial facts must be emphasized regarding this surgical technique. Firstly, despite the good results reported with this procedure, it has never been the preferred treatment for surgical MV repair. Secondly, edge-to-edge MV repair should not be the exception to the rule regarding the use of an annuloplasty ring as an integral part of this procedure.[9] In fact, the absence of an annuloplasty ring is the strongest predictor of failure after surgical MV repair.[10-14] Therefore, the complete edge-to-edge technique comprises two essential elements: the stitch that joins both MV leaflets, and the prosthetic annuloplasty ring that reinforces the repair.[15]

TEER as a ringless intervention

A pivotal distinction between surgical edge-to-edge repair and TEER is the absence of a prosthetic annuloplasty ring in the latter *(Figure 3)*. De Bonis et al. have investigated the importance of the annuloplasty ring in surgical edge-to-edge MV repair.[16-19] They found that this absence can compromise TEER outcomes, particularly in the long term.[18] Theoretically, the principles guiding MV repair remain unchanged, regardless of the approach employed; they universally apply to both surgical and percutaneous repairs. Therefore, the lack of annuloplasty ring in TEER renders this percutaneous technique only partially effective, resulting in a significant risk of MR recurrence over time.

Recurrent MR post-procedure as metric to evaluate TEER efficacy

Bearing in mind that the necessity for reoperation is subject to variability in physician clinical judgment and decision-making, as well as patient autonomy and individual preferences, recurrent MR ≥ 3+ after the procedure is the most objective and reliable metric for evaluating the efficacy of MV repair. The presence of recurrent or residual MR2+ after procedure and its inherent consequences on the patient's final outcome remains a topic of intense debate. Although it is not a definitive indicator for re-intervention, there are multiple reasons to suggest that MR2+ is a key predictor for the subsequent development of MR ≥ 3+, which may have a negative impact on the final outcome.[20-23] In turn, the incidence of recurrent MR ≥ 3+ is the most reliable indicator of the procedure's long-term effectiveness, particularly at 5 years of follow-up. Unfortunately, the vast majority of reports do not provide data on the specific incidence of MR 2+ post-procedure.

The EVEREST II trial reported a notable 50% incidence of MR ≥ 2+ at 5-year follow-up.[24] Öztürk et al. observed a significantly higher incidence in a series of 256 patients undergoing TEER, with 92.9% experiencing MR ≥ 2+ at 5 years post-procedure (MR2+: 87.5%, MR3+: 7.2%).[25]

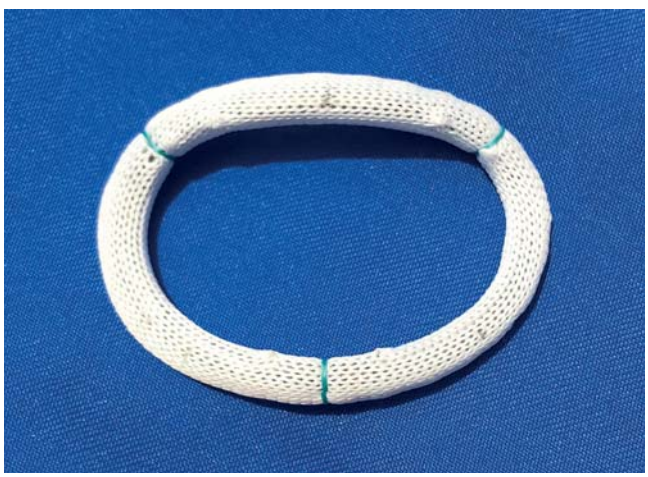

Figure 1: Annuloplasty ring commonly used in surgical mitral valve repair.

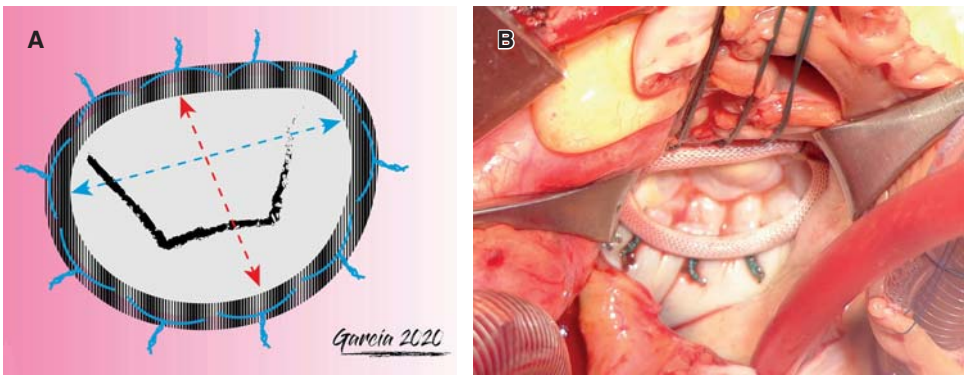

Figure 2:

A) Artistic illustration of the mitral annuloplasty ring. The blue and red arrows indicate the reshaping of the native mitral annulus by the prosthetic ring in the transverse and anteroposterior diameters (3:4 diameter ratio), respectively. **B)** Mitral valve repair using a prosthetic annuloplasty ring as a key component of the surgical approach.

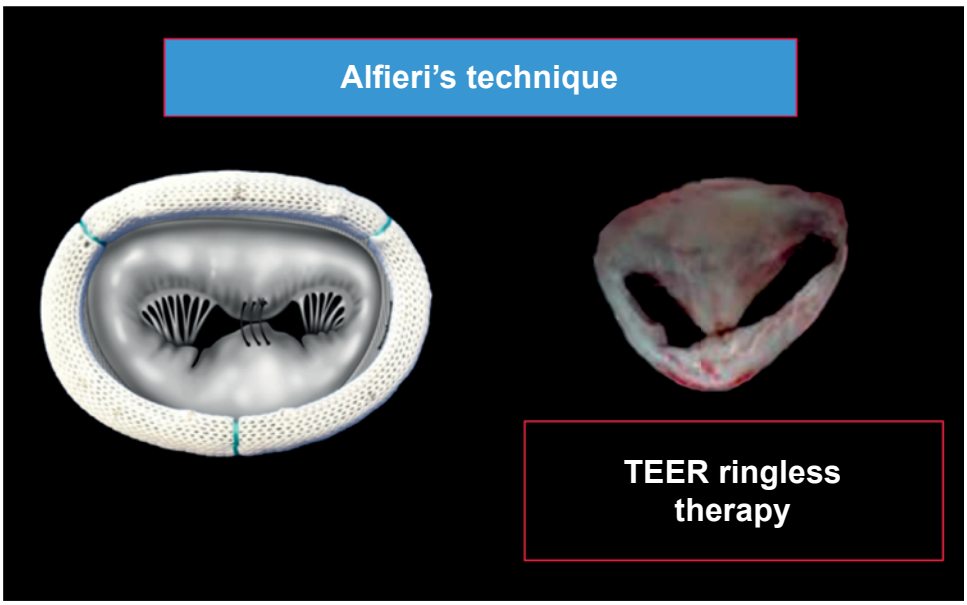

Figure 3:

Schematic illustration emphasizing the omission of an annuloplasty ring in transcatheter edge to edge repair, a key distinction between Alfieri's original edge-to-edge technique (left) and the percutaneous transcatheter edge-to-edge repair (right).
TEER = transcatheter edge to edge repair.

However, there is a scarcity of studies reporting the presence of recurrent MR ≥ 3+ after TEER at 5 years of follow-up. Feldman et al. documented **19%** of recurrent MR ≥ 3+ at 5 years of follow-up in the EVEREST II.[24] The GRASP-IT registry reported a notable **22.4%** incidence of MR ≥ 3+ at 5-year follow-up after TEER.[26] Similarly, Kar et al. observed recurrent MR ≥ 3+ in **25%** of patients at 5-years of follow-up in the EVEREST II High Risk Study.[27] The MitraSwiss registry, which included 1, 212 patients undergoing TEER, reported a higher incidence of **31.8%** with recurrent MR ≥ 3+ at 5-years.[28] The COAPT trial found a significantly lower rate of MR ≥ 3+ of 5.3% at 5-year follow-up.[29] In contrast to the aforementioned findings, the STS/ACC/TVT registry revealed a surprisingly high incidence of MR ≥ 3+ in 8.7% of 33,878 patients who underwent TEER, within just one month of follow-up.[30] This is particularly significant, as this registry reflects real-world outcomes.

To sum up, the presence of recurrent MR ≥ 3+ after TEER at 5-years of follow-up ranges between 5.3 and 31.8% (median: 22.4%, mean: 20.7 ± 9.8%) *(Table 1)*.

Adverse clinical outcomes associated with residual or recurrent MR ≥ 2+ post-TEER

TEER outcomes are compromised when residual or recurrent mitral regurgitation (MR) ≥ 2+ is present after procedure. Research by Reichart et al. revealed that patients with minimal residual MR (≤ 1+) fare better than those with moderate to severe MR (2+ or ≥ 3+) at discharge and one-year follow-up (p = 0.029).[31] Similarly, Buzzatti et al. discovered that MR 2+ post-TEER is a key driver of adverse outcomes, including increased MR ≥ 3+, poorer survival rates, and reduced quality of life, compared to patients with MR ≤ 1+ (HR: 6.71; 95% CI, 3.48-12.90, p < 0.001).[20] The GRASP-IT Registry highlights recurrent or residual MR ≥

2+ as the strongest predictor of all-cause mortality (HR: 2.17, 95% CI, 1.42-3.31, p < 0.001) and the composite endpoint of all-cause death and unplanned heart failure rehospitalization (HR: 2.20, 95% CI, 1.52-3.19, p < 0.001) at five-year follow-up.[26] Furthermore, Buzzatti et al. found residual MR 2+ after TEER to be the most critical predictor of all-cause mortality in both univariate (HR: 2.71; 95% CI, 1.73-4.25; p < 0.001) and multivariate (HR: 4.18; 95% CI, 1.87-9.37; p < 0.001) analyses at five-year follow-up.[21] According to an analysis from the The Italian Society of Interventional Cardiology (GIse) Registry of Transcatheter Treatment of Mitral Valve RegurgitaTiOn (GIOTTO) Registry, Adamo et al. found that patients with residual MR ≤ 1+ after TEER had significantly lower rates of all-cause and cardiac mortality (25.7 vs 40%, p < 0.001 and 16.3 vs 24.8%, p = 0.003, respectively) and heart failure hospitalizations (24 vs 30%; p = 0.035) compared to those with residual MR 2+ at 2-year follow-up.[32] An additional analysis of the same GIOTTO registry by Bedogni et al. revealed that residual MR ≤ 1+ was independently associated with a reduced risk of 1-year mortality in both multivariate (HR 0.62; 95% CI, 0.46-0.84, p = 0.002) and univariate analysis (HR 0.52, 95% CI, 0.40-0.67, p ≤ 0.001). Furthermore, at the 2-year follow-up, Kaplan-Meier estimates showed a significant correlation between all-cause mortality and the severity of residual MR. In fact, residual MR2+ was associated to 2-year all-cause mortality (HR 1.33, 95% CI, 1.02-1.73, p = 0.032).[33] De Felice et al. reported strong and independent association was found between the combination of a mean gradient > 4 mmHg after TEER and residual MR ≥ 2+ and an increased risk of adverse events (HR 1.98; 95% CI, 1.10-3.58)[34] *(Table 2)*.

Table 1: Recurrent mitral regurgitation ≥ 3+ after transcatheter edge to edge repair.

Study/Author	Year	Recurrent MR ≥ 3+ (%)	Follow-up (years)
EVEREST II[24]	2015	19.0	5
Kar[27]	2019	25.0	5
GRASP-IT[26]	2019	22.4	5
MitraSwiss[28]	2020	31.8	5
Oztürk[25]	2021	7.2	5
COAPT[29]	2023	5.3	5

Upon removing the COAPT trial data, which solely represent functional mitral regurgitation, the following results were obtained at five years of follow-up: median: 22.4%, mean: 21 ± 3%.
MR = mitral regurgitation.

Mean gradient after TEER

The application of one or multiple clips to both MV leaflets during TEER predictably reduces the MV area *(Figure 4)*. In fact, Alfieri recommends maintaining a minimum MV area of 2.5 cm² after surgical edge-to-edge repair.[9] According to the 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease, a MV area of ≤ 1.5 cm² is considered severe and typically correlates with a trans-mitral mean gradient of > 5 mmHg at a normal heart rate.[1] The Mitral Valve Repair Clinical Outcomes Committee (MVARC) defines post-procedural mitral valve stenosis as a mean gradient > 5 mmHg.[35] Post-TEER mitral valve stenosis is associated with significantly worse long-term clinical outcomes and increased mortality risk.[36] A study of 216 patients undergoing TEER for mitral regurgitation found that a post-TEER transvalvular gradient of > 4.4 mmHg (echo) or > 5.0 mmHg (invasive) predicted adverse outcomes during follow-up in both univariate (HR 2.1, 95% CI 1.3-2.4, p = 0.003) and multivariate analysis (HR 2.3, 95% CI 1.4-3.8, p = 0.002).[36] Moreover, patients with two or more clips exhibited a significantly higher mitral valve mean gradient and increased incidence of mitral valve stenosis post-procedure.[36] The STS/ACC TVT Registry reported that 26.3% of patients had a mean gradient > 5 mmHg after TEER at only one month of follow-up.[30] Additionally, the threshold for intervention in mitral valve stenosis is a MV area of ≤ 1.5 cm².[1] Of particular significance is the fact that the combination of residual MR ≥ 2+ and mean gradient > 5 mmHg was consistently linked to the worst outcomes.[36,37]

In summary, it is advisable to achieve a mean gradient ≤ 5 mmHg and residual MR ≤1+ as optimal outcomes after

Table 2: Residual or recurrent mitral regurgitation 2+ as predictor for development of mitral regurgitation MR ≥ 3+ after transcatheter edge to edge repair in degenerative mitral regurgitation.

Author	Year	Predictor	Hazard Ratio	95% CI	p
Buzzatti[20]	2016	MR 2+	6.71	3.48-12.9	< 0.001
Buzzatti[21]	2019	MR 2+	7.15	2.72-18.75	< 0.001
Sugiura[22]	2022	MR 2+	2.56	1.12-5.87	0.03
Kubo[24]	2023	MR 2+	1.59	1.30-1.95	< 0.001

CI = confidence interval. MR = mitral regurgitation.

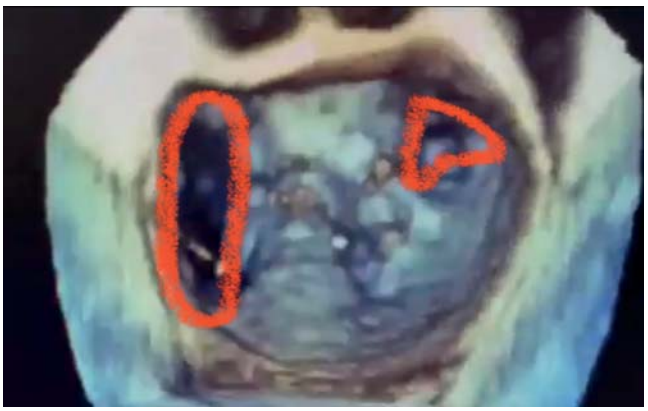

Figure 4: Mitral stenosis after placement of several clips. The red color indicates the perimeter of the functional mitral valve area after transcatheter edge to edge repair.

TEER. Of note, official statistics on the rate of reoperation for mitral stenosis subsequent to TEER are currently unavailable.

Reinterventions for failed TEER

First and foremost, it is crucial to note that, for a myriad of reasons, not all cases presenting structural failure in TEER undergo surgery. In a study published by El Shaer et al., only 31% of patients who experienced recurrent MR ≥ 3+ after TEER underwent subsequent mitral valve surgery. Furthermore, operative mortality was 4.5%. Reoperation was associated with significantly lower all-cause death (HR 0.33 [95% CI, 0.12-0.92], p = 0.001) compared with medial therapy alone.[38] In a cohort of 43 patients who underwent reoperation for failed TEER, Sugiura et al. found that reintervention was associated with significantly lower one-year mortality rates compared to medical therapy alone (10.5 vs 37.6%, p = 0.01). Additionally, reintervention conferred improved survival (HR 0.26, 95% CI 0.08-0.79, p = 0.02) and reduced the risk of the composite endpoint of mortality and heart failure rehospitalization (HR 0.34, 95% CI 0.15-0.78; p = 0.01) at one-year follow-up.[39] A data analysis conducted by Kaneko et al. on 11,396 patients who underwent TEER revealed that approximately 1 in 20 patients (4.8%) underwent repeat intervention due to TEER failure, with a mean time interval of 4.5 months between the original procedure and reoperation. Furthermore, notable rates of operative mortality (8.6%), 30-day hospital readmission (20.9%), and overall 30-day morbidity (48.2%) were observed in this patient cohort.[40] The data has been emerged piecemeal. The CUTTING-EDGE study conducted an in-depth analysis of 332 surgical cases involving MV surgery following failed TEER. The results showed a notable operative mortality rate of 16.6%, with a 1-year mortality rate of 31.1%. Additionally, the observed-to-expected mortality ratio was 3.6, indicating a higher-than-expected mortality risk. Moreover, MV replacement was deemed necessary in an overwhelming 92.5% of cases.[41,42] A retrospective study of the Society of Thoracic Surgeons database revealed outcomes for 524 patients undergoing MV surgery due to failed TEER. The analysis showed an operative mortality rate of 10.2%, with an observed-to-expected mortality ratio of 1.2, indicating a higher-than-expected mortality risk. Notably, MV replacement was necessary in 95% of patients.[43]

In summary, considering that TEER failure frequently necessitates high-risk MV replacement, the use of this ringless therapy should be call to caution, especially in patients with degenerative pathology who otherwise may have been suitable for a definitive surgical repair with a high success rate (≥ 90%), in contrast to the significantly lower success rate (6.8%) following failed TEER.[44]

Percutaneous direct annuloplasty ring complementing TEER

The similarity between percutaneous direct annuloplasty rings and surgical annuloplasty suggests that this technique may be beneficial in treating MR. It is essential to note that current studies on TEER do not include systematic use of a mitral annuloplasty ring. There are currently three percutaneous mitral annuloplasty systems available: a) Cardioband Mitral Valve Reconstruction System (Edwards Lifesciences, Irvine, California), a direct annuloplasty device that represents a partial band; b) Millipede IRIS device (Boston Scientific, Maple Grove, Minnesota), a semi-rigid, complete mitral annuloplasty ring; and c) AMEND system (Valcare, Herzliya Pituach, Herzliya, Israel), a rigid, complete mitral annuloplasty ring.[45] A comparative study between Cardioband and TEER, showed that patients with Cardioband had lower mortality and rehospitalization rates for heart failure within the first 12 months. Additionally, patients with Cardioband presented better New York Heart Association functional class, fewer hospital readmissions, and lower mortality compared to those who underwent TEER.[46] In 2018, Rogers et al. reported the outcomes in seven patients implanted with the Millipede IRIS™ with no device related death, stroke, or myocardial infarction, and ≤1+ MR at 30 days in all patients.[47] Recently, on January 27, 2021, Valcare Medical announced the first successful transseptal implantation of the AMEND™ Annuloplasty Ring for Mitral Valve Repair in a human patient.[48] None of them have been yet approved by FDA. Although promising, clinical experience with these types of devices is still in its initial stages.

Nonetheless, a remarkable fact is that the possibility of percutaneously implanting prosthetic rings is indeed a reality. Although we are still in the process of generating sufficient

data to acquire robust experience with the use of these types of rings, this development opens up the prospect of combining both therapies, TEER and percutaneous annuloplasty, akin to surgical approaches, in order to achieve optimal long-term outcomes.

TEER adherence to current clinical guidelines is not a minor issue

Despite its drawbacks and limitations, TEER has shown a steady trend of increasing adoption in recent years, driven by its less invasive approach. According to Young et al., among Medicare beneficiaries, the national trends of TEER versus surgical MV repair revealed a significant shift, with the annualized ratio of TEER to surgical repair increasing substantially from 0.05 to 1.32 between 2012 and 2019.[49] Shah et al. reported that US Medicare data from 2012 to 2019 shows a marked shift in MV therapy trends, with a 313% increase in TEER cases (1,552 per year, $p < 0.001$) and a 31.4% decrease in surgical MV repair procedures (1,446 per year, $p = 0.004$) from 2015 to 2020.[50] The STS/ACC TVT Registry revealed a total of 37,475 patients underwent mitral transcatheter procedures, including 33,878 TEER procedures, between 2014 and March 31, 2020. TEER procedure volumes have demonstrated a remarkable growth, increasing from 1,152 annual procedures in 2014 to 10,460 in 2019. This translates to a 908% increase, or a 9-fold rise in TEER utilization.[30] Kumar et al. reported that between 2015 and 2019, a total of 27,034 TEER procedures were performed on Medicare patients in the US. The national incidence rate rose from 6.2 per 100,000 patients in 2015 to 23.8 per 100,000 patients in 2019, representing a 283% increase over the study period ($p < 0.001$).[51] Chikwe et al. observed that among 53,117 Medicare beneficiaries with degenerative MR in the US from 2012 to 2019, there was a remarkable 23-fold increase in TEER procedure volume.[52]

The exponential growth in TEER adoption in the US over recent years is evident. Nevertheless, assuming the number of patients requiring MV intervention has remained relatively stable in the last years, and considering clinical guidelines clearly indicate that TEER may benefit a highly select group of patients with high-risk operative mortality,[1] a crucial question arises: what factors are contributing to this dramatic expansion in TEER adoption? Significant concerns have been raised about the degree of adherence to clinical guideline recommendations in the use of TEER. The multifaceted situation underlying the potential overutilization of TEER is influenced by various factors, including the Heart Team's practical application of the high-risk concept, advanced age as a decisive factor, the methodology employed to assess frailty, and incomplete information provided to the patient, which collectively may skew the decision-making process in favor of TEER.

Expanding TEER indications: a point of contention yet

Currently, two major randomized controlled trials are enrolling patients with degenerative (primary) MR, throughout the whole spectrum of operative risk (low-, intermediate-, or high- risk) comparing TEER with surgical MV repair. with special emphasis in intermediate and low-risk patients. The MitraClip REPAIR MR Study (NCT04198870) is actively recruiting patients aged ≥ 75 years or those < 75 years with STS-PROM score ≥ 2, anticipating a total enrollment of approximately 500 participants. In the percutaneous or surgical repair in mitral prolapse and regurgitation for ≥ 60 year-olds (PRIMARY) (NCT05051033), patients aged ≥ 60 years, spanning the entire surgical risk continuum (low, intermediate, and high risk), will be enrolled (n = 450 estimated) and randomized in a 1:1 ratio to undergo either TEER or surgical MV repair.

Notwithstanding the anticipated results of both trials, a fundamental truth remains, one that supersedes statistical evaluations, and potential biases. Failing to anticipate the long-term impact of a treatment can result in devastating effects. Expanding the indications for TEER without fully understanding its limitations may lead to catastrophic consequences, especially in young and intermediate- and low-risk patients. Therefore, we must exercise caution and carefully weigh the potential risks and benefits before proceeding.[53] Between reality and the abyss, an uncertain future awaits.

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CASE REPORT

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Pericardial histoplasmosis

Histoplasmosis pericárdica

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ABSTRACT

In Mexico, histoplasmosis is the systemic mycosis with the highest prevalence, both in its endemic and epidemic forms. We show here the case of a 65-year-old male patient who presented dyspnea as the main symptom. In the imaging radiological study, an image compatible with pericardial tumor was observed. Surgical resection was performed, with pericardial histoplasmosis as histopathological result. Specific treatment was administered and at 6-months of follow-up, the patient remains free from systemic complications.

Keywords: antifungal therapy, histoplasmosis, pericarditis, pericardium.

RESUMEN

En México, la histoplasmosis es la micosis sistémica de más alta prevalencia tanto en su forma endémica como epidémica. Mostramos aquí el caso de un paciente masculino de 65 años de edad, quien como sintomatología principal presentaba disnea; en el estudio radiológico, se observó una imagen compatible con tumor pericárdico. Se realizó procedimiento quirúrgico para resección del mismo, encontrando como resultado histopatológico histoplasmosis pericárdica. Se administró tratamiento específico. Después de seis meses de seguimiento, el paciente se encuentra sin complicaciones sistémicas.

Palabras clave: *terapia antifúngica, histoplasmosis, pericarditis, pericardio.*

Histoplasmosis is a disease caused by a fungus called *Histoplasma capsulatum*, which can lead to various health issues such as pulmonary, gastrointestinal, hepatic, splenic, and lymphatic diseases, and in some rare cases, chronic pericarditis.[1] This fungus is typically found in the soil of subtropical and temperate regions and is usually contracted through the inhalation of mycelia. Once inside the body, the fungus transforms into a yeast form to avoid triggering an immune response. In regions where histoplasmosis is common, more than half of the population may be carriers of the fungus, but only a small percentage develop symptoms. Symptoms of the disease include fever, chills, headache, muscle pain, loss of appetite, chest pain, respiratory issues, and in severe cases, death.[2]

Diagnosis of histoplasmosis involves various methods such as cultures, fungal stains, antigen detection, and serologic tests for antibodies. Cultures, particularly from different bodily fluids and tissues, are crucial for definitive diagnosis, although they may take several weeks to yield results.[3] Treatment for acute infections typically involves the use of itraconazole, while constrictive pericarditis, which is an inflammatory response to the fungus, is mainly managed with anti-inflammatory medications as antifungal therapy may not significantly impact the disease's progression. In

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cases of localized histoplasmosis, treatment is recommended for patients with moderate to severe symptoms that do not improve with observation. Itraconazole is commonly prescribed for a period of three months in such cases, as patients usually respond well to anti-inflammatory therapy, and the use of antifungal medication may not drastically alter the clinical outcome.[4]

CASE DESCRIPTION

Male, 65 years old, without chronic-degenerative history, with a history of intestinal metaplasia and atrial fibrillation with a moderate ventricular response. During cardiology follow-up, he reported moderate dyspnea, leading to an magnetic resonance imaging (MRI) and a transthoracic echocardiogram.

The MRI showed an intrapericardial lesion measuring 58.1 by 6.7 mm with irregular margins, heterogeneous in all sequences, predominantly hypointense. There was no contrast enhancement observed, and it showed compression of the right ventricle, restricting diastolic filling and limiting contractility *(Figure 1)*.

The transthoracic echocardiogram demonstrated significant left atrial dilation, normal valves, with a systolic displacement of the tricuspid annular plane of 5, a left ventricular ejection fraction of 55%, a pulmonary artery systolic pressure of 46 mmHg, a right ventricle of normal diameter, with a fractional area change of 35%. A mass dependent on the pericardium causing extrinsic compression of the right heart chambers was evident.

The patient was discussed in an internal committee at our hospital and accepted for pericardial tumor resection. A

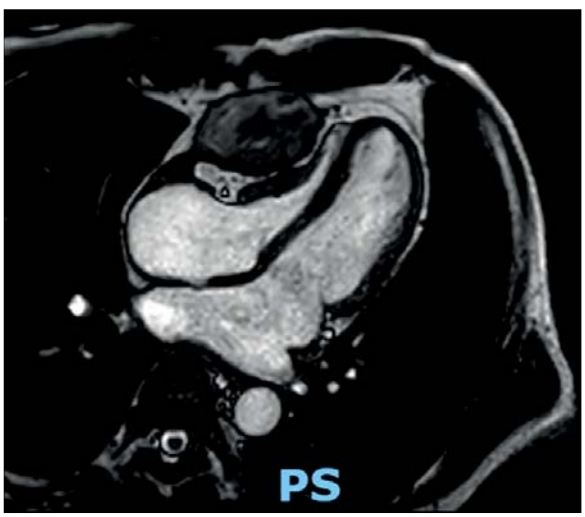

Figure 1: The magnetic resonance imaging showing a intrapericardiac lesion of 58.1 mm by 6.7 mm with irregular margins, heterogeneous in all the sequences, predominantly hypointense.

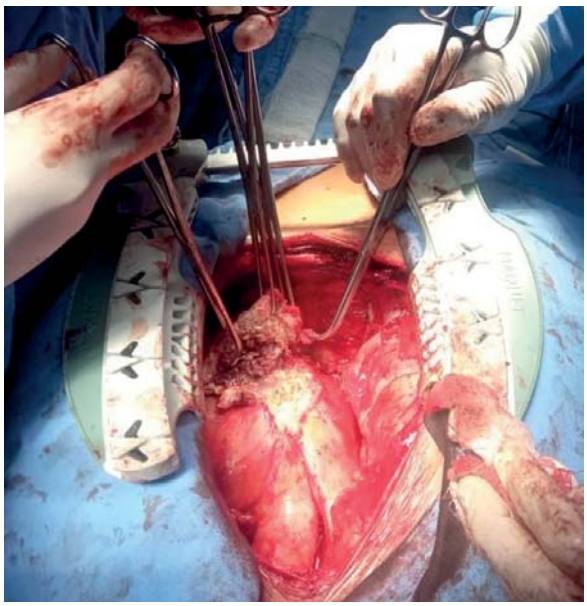

Figure 2: Surgical resection.

surgical procedure was scheduled with a median sternotomy approach, performing an interphrenic pericardiectomy without cardiopulmonary bypass. Findings included a thickened pericardium of 2 cm with severe calcification infiltrating the anterior wall of the right ventricle, pulmonary hilum, right atrium, and both venae cavae *(Figure 2)*. There was a chronic-appearing hematoma of approximately 20 cc on the anterior wall of the right ventricle *(Figure 3)*. There were no complications during the intervention, and the patient evolved favorably during his stay in intensive care.

The pericardium was resected, and part of the tumor was sent to pathology, which reported multifocal calcified granulomatous chronic pericarditis secondary to microconidia of *Histoplasma spp.* In the tissue sent to pathology after mass resection, not only inflammatory tissue but also microorganisms reaching the pericardium were found, which led to initiating antifungal treatment.[5]

The patient was treated with itraconazole without complications. Complementary studies for human immunodeficiency virus, hepatitis B, and C were negative. The patient was discharged to continue outpatient treatment.

In this patient without associated symptoms, the decision to perform surgery was based on the finding of constrictive pericarditis found in the MRI and the alteration of the functional class. The image of the unidentified mass on the anterior wall of the right ventricle, along with the calcified pericardium, reduced right ventricular filling, consistent with the diagnosis.

Two months later, an MRI revealed surgical changes associated with a remnant lesion that restricted the right

ventricle with preserved ejection (49%) *(Figure 4)*. Three months later, a follow-up echocardiogram showed a hypoechoic image dependent on the parietal pericardium compromising right ventricular filling, with decreased systolic function with a fractional area change of 52%. It also reported a thickened and calcified pericardium on the lateral and diaphragmatic walls of 13 mm.

In the MRI and echocardiogram during follow-up, there were no signs of disease progression. The finding of external compression of the right ventricle persists, consistent with the partial pericardial resection due to infiltration into the anterior ventricular wall, without impact on its systolic function, without deterioration in functional class according to the NYHA.

For now, the decision is to continue close follow-up, as, despite the persistence of external compression of the right ventricle seen in imaging studies, the patient remains clinically asymptomatic without signs of pulmonary congestion or lower limb edema.

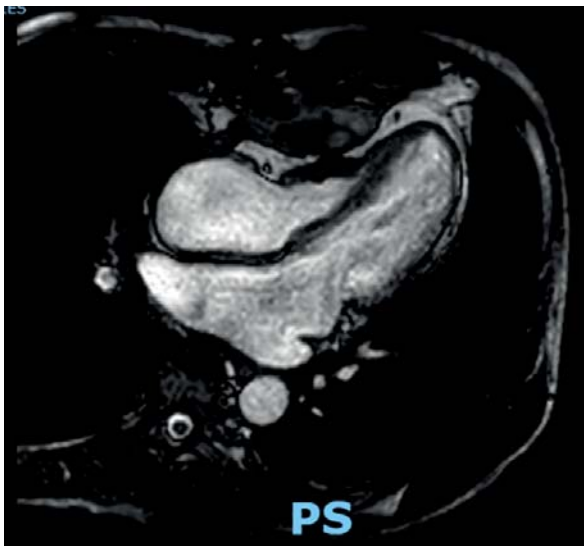

Figure 4: Surgical changes in the anterior mediastinum associated with a remnant of a known pericardial mass, 40 by 18 mm (previous 58 by 37 mm), with a restrictive effect on the right ventricle, with respected right ventricular ejection fraction of 49% (previous 43%).

COMMENT

Histoplasmosis is an endemic disease in many regions of the United States of America. In Mexico, systemic mycoses are not mandatory reportable diseases, so their incidence is unknown. However, Ashraf et al. report that between 112 and 325 cases are reported annually. In the last century, the infection mainly affected miners in the central states of the Mexican Republic, with a history of malnutrition, alcoholism, and association with tuberculosis.[6] Since the 1980's, many cases of histoplasmosis have been reported in patients with acquired immunodeficiency syndrome and associated with other immunosuppressive factors such as autoimmune diseases, prolonged use of high-potency steroids, use of next-generation immunosuppressants known as "biologicals", transplants, etc. Our patient has a history of gastrointestinal metaplasia.

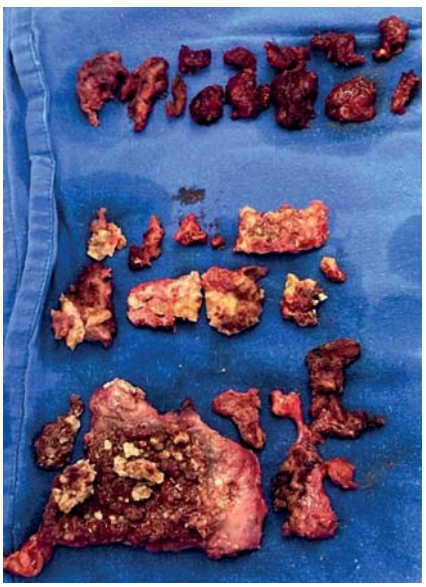

Figure 3:

Pericardium resected.

According to data collected by the Mycology Laboratory of the National Autonomous University of Mexico (UNAM), in Mexico, the systemic form of the disease is the most prevalent presentation.[7] In Mexico, it is the most prevalent systemic mycosis, both in its endemic and epidemic forms.[8] However, there are no cases in Mexico of histoplasmosis causing pericardial pathology, as in the case we present.[9] It is of utmost importance that physicians recognize the clinical syndromes and utilize epidemiological clues to diagnose pericarditis secondary to histoplasmosis, as the latter is a rare entity. However, we are in a region of Mexico where, as previously reported in the literature, histoplasmosis is endemic. Therefore, greater attention should be paid to its diagnosis.

CONCLUSIONS

In recent years, the diverse manifestations of histoplasmosis have been increasingly highlighted. Although heart involvement is rarely reported, *Histoplasma capsulatum* can invade the endocardium, myocardium, or pericardium, as we reviewed. Histoplasma can also cause constrictive pericarditis. We chose to describe our case for two reasons: first, to report a relatively rare manifestation of histoplasmosis, and second,

to show the importance of considering this fungus in every instance of pericardial disease.

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