



ARGENTINE JOURNAL OF

CARDIOVASCULAR SURGERY

OFFICIAL JOURNAL OF THE ARGENTINE COLLEGE OF CARDIOVASCULAR SURGEONS

Indexed in Latindex and LILACS.
Listed in ICMJE

ISSN 1667-5738 - Online version: ISSN 2796-9908



VOLUME XXII - ISSUE 2

Online version:
www.raccv.com.ar

May - June - July - August 2024

Endovascular aortic repair - thoracoabdominal

Zenith® t-Branch® THORACOABDOMINAL ENDOVASCULAR GRAFT



Active fixation

Our anchoring bars are the industry standard for design and migration resistance.



Radial force

Self-expanding z-stents provide radial force, added stability, and optimal graft-to-vessel apposition.



Columnar strength

The long main-body design features a time-tested balance of length, stability, and flexibility.

Zenith t-Branch
Thoracoabdominal
Endovascular Graft

Zenith Universal Distal Body
Endovascular Graft

Zenith Spiral-Z
AAA Iliac Leg Grafts





EDITOR COMMITTEE

Chief Editor

FERRARI AYARRAGARAY, JAVIER
Ciudad Autónoma de Buenos Aires

General Editor

DOMENECH, ALBERTO
Ciudad Autónoma de Buenos Aires

Editorial Secretary

RODRÍGUEZ PLANES, GERARDO
Ciudad Autónoma de Buenos Aires

Emeritus Editors

BORRACCI, RAÚL^(†)
TRAININI, JORGE CARLOS

Deputy Editors

ADULT CARDIAC
ARGÜELLO, MARIO
Santa Fe (ARG)
BASTIANELLI, GUSTAVO
Ciudad Autónoma de Buenos Aires (ARG)
DEL PERCIO, HERNÁN
Buenos Aires (ARG)
FARRANDO, MARTÍN

Ciudad de Mendoza, Mendoza (ARG)

GIRELA, GERMÁN
Neuquén, Río Negro (ARG)
KOTOWICZ, VADIM
Ciudad Autónoma de Buenos Aires (ARG)

International

BALAGUER, JORGE (EE. UU.)
BROZZI, NICOLÁS (EE. UU.)
CASTILLO, JAVIER (EE. UU.)
GARCÍA, OVIDIO A. (MEX)
MALDONADO, JAVIER (COLOMBIA)
NAFEH ABI-REZK, MANUEL (CUBA)
POMAR, JOSÉ LUIS (ESPAÑA)

CONGENITAL HEART

BARRETTA, JORGE
Ciudad Autónoma de Buenos Aires (ARG)
GARCÍA DELUCIS, PABLO
Ciudad Autónoma de Buenos Aires (ARG)
KREUTZER, CHRISTIAN
Buenos Aires (ARG)

International

NEIROTTI, RODOLFO (EE. UU.)

PHLEBOLIMPHOLOGY

AMORE, MIGUEL
Buenos Aires (ARG)
PAPENDIECK, CRISTÓBAL
Buenos Aires (ARG)
VELLETAZ, RUBEL
Buenos Aires (ARG)
ULLOA, JORGE (COLOMBIA)

VASCULAR & ENDOVASCULAR

DISEASE
CEREZO, MARCELO
La Plata, Buenos Aires (ARG)
LAMELZA, VÍCTOR
Ciudad Autónoma de Buenos Aires (ARG)
LUCAS, FERNANDO
Ciudad Autónoma de Buenos Aires (ARG)
PAOLINI, JUAN
Ciudad Autónoma de Buenos Aires (ARG)
PATARO, MARCELO
Ciudad Autónoma de Buenos Aires (ARG)
PEIRANO, MIGUEL
Buenos Aires (ARG)
TURCO, EMILIO
Buenos Aires (ARG)

International

BJORCK, MARTIN (SUIZA)
BRADBURY, ANDREW (UK)
CRIADO, FRANK (EE. UU.)
DIAMANT, MARCELO (URUGUAY)
MILLS, JOSEPH (EE. UU.)
NAVARRO, TULLIO (BRASIL)
QUIROGA, ELENA (EE. UU.)
SHAW, PALMA (EE. UU.)

EDUCATION

NIGRO, JUAN
Ciudad Autónoma de Buenos Aires (ARG)
PAOLINI, JUAN
Ciudad Autónoma de Buenos Aires (ARG)

ETHICS

BATELLINI, ROBERTO
Buenos Aires (ARG)
BRACCO, DANIEL
Ciudad Autónoma de Buenos Aires (ARG)
TURCO, EMILIO
Buenos Aires (ARG)

2024 BOARD OF DIRECTORS

President:	DR. GUILLERMO GARELLI
Vicepresident:	DR. HERNÁN DEL PERCIO
General Secretary:	DR. MIGUEL AMORE
Treasurer:	DR. ALEXIS ESPÓSITO

Editing Coordination:

MARISOL REY

Design and layout:

TATIANA MAINIKE

Translation:

HYGEA EDICIONES

Editor: ARGENTINE COLLEGE OF CARDIOVASCULAR SURGEONS

Catamarca 536, Ciudad Autónoma de Buenos Aires
Tel. (0054 11) 4931-5066 - Tel./Fax: (0054 11) 4931-2560
www.raccv.com.ar / revista@caccv.org.ar

Argentine Journal of Cardiovascular Surgery - ISSN 1667-5738 - Online version: ISSN 2796-9908

VOLUME XXII - ISSUE 2 - MAY - JUNE - JULY - AUGUST 2024

The *Argentine Journal of Cardiovascular Surgery* is the official journal of the Argentine College of Cardiovascular Surgeons. The first issue was published back in 2003. Our goal is to disclose and present updated information through studies conducted and manuscripts written by specialists across the world on different surgical techniques, and historic articles on significant physicians and surgeons. Also, pivotal moments in the history of our country and the rest of the world both on our medical specialty and other specialties like Cardiovascular Surgery, Endovascular Surgery, Cardiac Surgery, Circulatory Support, Phlebology, Lymphology, up to the latest tendencies by incorporating technological innovations like stem cell therapies and others. This journal is focused on surgical issues and is published on a four-month basis.

The content of the articles published is the sole responsibility of their authors, and the Editorial Board does not necessarily share their opinion. The Editorial Board shall not be liable or scientifically or legally responsible for the products or services disclosed or for the claims filed by those responsible of these products or services.

Supplementary information available online: www.raccv.com.ar - E-mail: revista@caccv.org.ar

Argentine College of Cardiovascular Surgeons. Catamarca 536, Ciudad Autónoma de Buenos Aires. Tel. (0054 11) 4931-5066

Tel./Fax: (0054 11) 4931-2560



The articles published in this magazine are under the Creative Commons license Attribution-NonCommercial-Share-Alike 2.5 Argentina

SUMMARY

- 37** **REVIEW ARTICLE**
TREATMENT OF SEVERE AORTIC STENOSIS IN PATIENTS WITH LOW SURGICAL RISK
Rafael Sádaba, Valentina Mescola
- 45** **SCIENTIFIC LETTER**
MASSIVE LATE ENDOLEAK TYPE IA, ASSOCIATED WITH SHOCK AND ACUTE ANEMIA: CONSERVATIVE SURGICAL TREATMENT
Juan Marín, Daniel Gutiérrez, Claudia Marín
- 48** **SCIENTIFIC LETTER**
DEFERRED CLOSURE IN THE SUCCESSFUL TREATMENT OF POST-INFARCTION VENTRICULAR SEPTAL RUPTURE
Jesús Saucedo-Castillo, Diana L. Labastida-Ramírez, Rutilio D. Jiménez-Espinoza, Ana Hernández-Pérez
- 53** **SCIENTIFIC LETTER**
ASCENDING AORTIC ANEURYSM, EXPERIENCE IN A PUBLIC HOSPITAL IN THE PROVINCE OF BUENOS AIRES
Gisele Mendoza, Carlos Salomon, Pablo Arenaza, José Acosta, Miguel Aranibar, Luis Soto, Carlos Soria, Nicolás Patrizi, Gabriel Basso

TREATMENT OF SEVERE AORTIC STENOSIS IN PATIENTS WITH LOW SURGICAL RISK

ABSTRACT

Following the first implantation of a percutaneous valve in 2002, two of the leading manufacturers of biological valve prostheses developed percutaneous aortic platforms, which have promoted transcatheter aortic valve implantation (TAVI) as an alternative to surgical aortic valve replacement (SAVR). In the last decade, both companies have funded six randomized studies grouping patients according to surgical risk and comparing the results between the two therapies. None of these studies has demonstrated the superiority of one technique over the other in terms of 5-year mortality. In general, patients who received percutaneous valves suffered a higher incidence of the need for pacemaker implantation, perivalvular leaks, and vascular complications, while surgical patients suffered more bleeding and atrial fibrillation. Following these results, the use of TAVI in young and low-risk patients has exponentially increased.

Keywords: *percutaneous valves, transcatheter aortic valve implantation, surgical aortic valve replacement.*

Authors:

Rafael Sádaba¹ and Valentina Mescola²

¹*Service of Cardiac Surgery, Hospital Universitario de Navarra, Pamplona, Spain.*

²*Service of Cardiac Surgery, Hospital Germans Trias i Pujol, Badalona, Spain.*

Corresponding author:

Rafael Sádaba

ir.sadaba.sagredo@navarra.es

INTRODUCTION

On April 16, 2022, Dr. Alain Cribier¹ implanted the first percutaneous valve in the aortic position as a last therapeutic resort for a 57-year-old man with severe calcific aortic stenosis (AS). Several teams of cardiovascular surgery professionals had rejected aortic valve replacement because of his hemodynamic instability and significant comorbidities. A marked clinical improvement was observed in the first 48 hours after implantation, with reduced signs of congestive heart failure. During the subsequent 4 months, several non-cardiac complications appeared: a) an episode of pulmonary embolism on day 3, which required intravenous fibrinolysis; b) an episode of septicemia on day 10 with septic shock; and c) a progressive worsening of the previous ischemia of the right lower limb, which required supracondylar amputation 10 weeks after implantation of the percutaneous prosthesis. The patient's clinical condition progressively deteriorated, leading to death 17 weeks after prosthesis implantation².

Following this episode, two leading manufacturers of biological valve prostheses, Edwards Lifesciences (Irvine, California, United States of America [USA]) and Medtronic Inc (Minneapolis, Minnesota, USA), each developed a percutaneous aortic stent platform, the Sapiens™, and the CoreValve™. These prostheses have spearheaded the establishment of transcatheter aortic valve implantation (TAVI) as an alternative to surgical aortic valve replacement (AVR).

In this regard, over the past two decades, the industry, supported by many interventional cardiologists, has tried to establish percutaneous treatment of aortic stenosis as the first choice in patients with severe aortic stenosis. To prove that percutaneous implantation of aortic prostheses is comparable to conventional surgery, both companies designed randomized studies in which they grouped patients according to surgical risk and compared the outcomes of patients who received percutaneous treatment and those who received surgical treatment.

TRIALS IN HIGH-RISK PATIENTS

The PARTNER 1A (Edwards Lifesciences Sapiens valve) and US Corevalve (Medtronic Inc. CoreValve) trials in high-risk surgical patients demonstrated promising results in the percutaneous prosthesis-treated groups.

In PARTNER 1A (mean age 84 years, mean Society of Thoracic Surgeons ([STS] score 11.7%), transcatheter and surgical procedures had similar

survival and significant complication rates in the first year (except major bleeding, which was more frequent in patients treated with RQVA, and vascular complications, which were more frequent in the TAVI group)³. At 5 years, although survival in the surgical treatment group was higher than in the TAVI group, this difference was insignificant⁴.

In the CoreValve US (mean age 83 years and STS score of 7.4%), the implantation of a self-expandable transcatheter aortic valve prosthesis was associated with a higher 1-year survival rate than that of RQVA⁵. At 5 years, the difference in survival rate had disappeared, and there were no significant differences in other variables, except major vascular complications or the need for permanent pacemaker implantation, which were higher in the TAVI group⁶.

In summary, these two randomized trials in patients at high surgical risk showed no significant differences in survival or complications, except vascular complications or the need for pacemaker implantation at 5 years with the self-expanding prosthesis CoreValve™.

TRIALS IN INTERMEDIATE-RISK PATIENTS

Following the favorable results observed after one year in high-risk patients, the two manufacturers initiated trials in intermediate-risk patients, PARTNER 2 (Edwards Lifesciences) and SURTAVI (Medtronic Inc.).

In PARTNER 2 (mean age 81 years, mean STS score 5.8%), no significant differences were observed in the composite primary outcome of death or disabling stroke at 30 days, at 1 and 2 years. The only significant differences at 2 years were in life-threatening bleeding and atrial fibrillation, both more prevalent in the RQVA group, and vascular complications, more frequent in the TAVI group. In this study, there were no differences in the need for pacemaker implantation between the two types of treatment⁷. At 5 years, there were no significant differences in the incidence of death from any cause or disabling stroke between the TAVI group and the surgery group. More patients in the TAVI group than in the TAVR group had at least mild paravalvular aortic regurgitation. Hospital readmissions, such as aortic valve reoperations, were more frequent after TAVI than after surgery. The improvement in health status at 5 years was similar in both⁸.

In SURTAVI (mean age 79 years, mean STS score 4.5%), 30-day, 1-year, and 2-year mortality were similar in the two groups. The TAVI group had a significantly higher rate than the RQVA group in terms of vascular complications, residual aortic

insufficiency, and need for pacemaker implantation; conversely, the RQVA group suffered more episodes of atrial fibrillation and renal failure and required more transfusions than the TAVI group, with statistically significant differences⁹. At 5 years, no differences were identified in the composite primary outcome of death or disabling stroke between the TAVI and RQVA groups. However, there were more valve-related reinterventions in the TAVI group. The rate of patients requiring pacemaker implantation was 39.1% in patients treated with percutaneous prosthesis¹⁰.

These trials informed the recommendations of the 2017 European Society of Cardiology/European Association for Cardiothoracic Surgery (ESC/EACTS) guidelines on the management of valvular heart disease, in which RQVA was recommended for patients at low surgical risk and without other risk factors such as frailty, porcelain aorta, and sequelae of thoracic radiation. For patients with increased surgical risk (STS or EuroSCORE II $\geq 4\%$ or logistic EuroSCORE I $\geq 10\%$) or with other risk factors such as those described above, the decision between RQVA and TAVI should be made by the cardiology team based on individual patient characteristics, with a preference for TAVI for older individuals with possible femoral access¹¹.

Before the publication of the 2017 European guidelines, a progressive increase in the use of TAVI had already been noticed, especially in patients older than 80 years¹²⁻¹⁴.

TRIALS IN LOW-RISK PATIENTS

However, it was after the publication of the trials in low-risk patients PARTNER 3 (promoted by Edwards Lifesciences) and Evolut LR (promoted by Medtronic Inc.) and the subsequent approval by the Food and Drug Administration (FDA) of the use of TAVI in low-risk patients,¹⁵ when an increase in the use of percutaneous prostheses for the treatment of severe aortic stenosis in younger patients was noted, with a consequent decrease in the RQVA in this group of patients¹⁶.

Given the expansion of percutaneous aortic prostheses in patients with AS,¹⁷ it is essential to deepen the methods and results of both trials, understand their limitations, and evaluate the consequences of the indiscriminate use of TAVI in young, low-risk patients.

PARTNER 3 and Evolut LR are noninferiority trials in which patients were randomized 1:1 to TAVI or RQVA. In PARTNER 3, 1000 patients with severe aortic AS and low surgical risk, with a mean STS score of 1.9%, were randomized to transfemoral

TAVI with a SAPIEN balloon-expandable valve S3™ (Edwards Lifesciences) or RQVA. The impossibility of implanting the percutaneous prosthesis via femoral access (which requires a minimum vessel diameter >5.0 mm for 14 Fr and >5.5 mm for 16 Fr) was an exclusion criterion¹⁸.

On the other hand, in the Evolut LR, 1468 patients with severe AS and low surgical risk (mean STS score of 1.9%) were randomized to TAVI with a self-expandable valve Evolut™ (Medtronic Inc.) or RQVA. A total of 1403 patients underwent the assigned procedure. Almost all TAVI procedures were performed via the transfemoral route (99%)¹⁹.

Patients enrolled in these trials were approximately a decade younger than participants in previous studies (mean age 73 years in PARTNER 3 and 74 years in Evolut LR). Similar primary and secondary outcome variables were established in both studies, providing an opportunity to extrapolate their findings to clinical practice.

In PARTNER 3¹⁸, the primary endpoint was a composite of all-cause mortality, any stroke, and rehospitalization (prosthesis- or procedure-related, including heart failure) 1 year after the procedure. The secondary variables were as follows:

- New-onset atrial fibrillation at 30 days.
- Duration of index hospitalization.
- Death from any cause, any stroke, and rehospitalization at 1 year (primary variable: evidence of superiority).
- Death, Kansas City Cardiomyopathy Questionnaire (KCCQ) score <45 or KCCQ decline ≥ 10 points from baseline to 30 days.
- Death or stroke at 30 days.
- Stroke at 30 days.

Although the baseline characteristics of the patients were similar in both groups, it should be noted that 26.4% of patients in the group randomized to RQVA required an additional procedure (12.8% of the total underwent one or more coronary artery bypass grafts), whereas this was the case in only 7.9% in the TAVI group (6.5% underwent percutaneous coronary intervention).

At 1 year, the composite of death from any cause, stroke, or rehospitalization occurred in 42 patients (8.5%) in the TAVI group compared with 68 patients (15.1%). Noninferiority and superiority were met, with an absolute difference between the TAVI group and the surgery group of -6.6 percentage points (95% confidence interval [CI], -10.8 to -2.5; $P < 0.001$ for noninferiority) and a hazard ratio of 0.54 (95% CI, 0.37 to 0.79; $P = 0.001$ for superiority). Although there were no significant differences in death of any type and stroke between the two groups, there were

substantial differences in the composite variable of death and stroke and other variables, such as rehospitalization and life-threatening bleeding, always in favor of TAVI. In this study, there were no differences in vascular complications or the need for pacemaker implantation (although there were differences in the occurrence of left bundle branch block). The differences above were maintained concerning the primary composite variable and its components in the subgroup of patients in whom concomitant procedures were not performed.

At 1 year, the mean aortic valve gradient was 13.7 mm Hg in the TAVI group and 11.6 mm Hg in the surgical group. The mean aortic valve area was 1.7 cm² and 1.8 cm², respectively. Aortic annulus enlargement was performed in 4.6% of the patients in the TAVI group, and 20.1% of the total had a 19 or 21-mm prosthesis implanted. Fifty-one percent of the prostheses used were Magna Ease™ (Edwards Lifesciences), 8.2% were porcine prostheses, and 16.8% of the patients were implanted with prostheses that were almost obsolete or withdrawn from the market, such as the Trifecta™ (Abbott Vascular, Santa Clara, California, USA) or LivaNova Mitroflow™ and Crown™ (LivaNova, London, United Kingdom)²⁰. The percentage of patients with moderate or severe paravalvular regurgitation did not differ significantly between the TAVI and the surgery groups (0.8% and none, respectively, at 30 days; 0.6% and 0.5% at 1 year). The percentage of patients with mild paravalvular regurgitation at 1 year was higher with TAVI than with surgery (29.4% vs. 2.1%). There were no episodes of valve thrombosis associated with clinical events, although 6 asymptomatic patients (5 in the TAVI group and 1 in the RQVA group) had findings suggestive of valve thrombosis¹⁹.

In PARTNER 3, the results at 5 years were less advantageous for the TAVI group²⁰. The superiority in the primary variable had disappeared. Concerning the number of deaths from any cause and stroke, both were more frequent in the TAVI group than in the surgical group, although without significant differences. The only variable that reached substantial differences in favor of RQVA was that of valvular thrombosis adjudicated according to VARC 3 criteria. At this point, it is essential to note that while, at hospital discharge, 45.8% of patients in the RQVA group and 21.2% of patients in the TAVI group were on treatment with anticoagulants, at 5 years, the rate was 24.9%, and 24.8%, respectively. Importantly, for the composite variable of death from any cause and disabling stroke, the risk ratio (RR) was 1.6 (95%CI: 1.00-2.55).

In the Evolut LR, the primary hypothesis was that the incidence of the primary endpoint (death from any cause or disabling stroke at 24 months) with TAVI is non-inferior to surgery, with a margin of 6%²¹.

The following secondary objectives were tested in order, and testing continued if and only if all previous objectives had met the designated success criterion:

- Mean transvalvular gradient at 1 year (noninferiority).
- Effective orifice area at 1 year (noninferiority).
- Change in New York Heart Association (NYHA) classification from baseline to 1 year (noninferiority).
- Change in KCCQ score from baseline to 1 year (noninferiority).
- Mean transvalvular gradient at 1 year (superiority).
- Effective orifice area at 1 year (superiority).
- Change in KCCQ score from baseline to 30 days (superiority).

Additional secondary safety endpoints included:

- A composite of death, disabling stroke, life-threatening bleeding, major vascular complication, or stage 2 or 3 acute kidney injury at 30 days.
- Prosthetic valve endocarditis.
- Prosthetic valve thrombosis.
- Prosthetic valve dysfunction requiring a repeat procedure.
- Stroke.
- Life-threatening bleeding at 12 months.

Other procedures were performed in 26% of patients in the treatment group. For example, in this group, 92 (13.1%) patients received coronary artery bypass grafts, and 24 (3.5%) underwent surgical ablation of atrial fibrillation.

The incidence of death or disabling stroke at 24 months was 5.3% in the TAVI group and 6.7% in the surgery group. The prespecified criterion of noninferiority was met, but the prespecified criterion of superiority was not met.

Concerning the incidence of de novo atrial fibrillation at 30 days, it was found in 7.7% of patients in the TAVI group and 35.4% in the surgery group. In contrast, definitive pacemaker implantation was performed in 17.4% of patients in the TAVI group and 6.1% in the surgery group. Hospitalization for heart failure during the 12-month follow-up period occurred in 3.2% of patients in the TAVI group and 6.5% in the surgery group. The overall summary score (\pm DE) of the KCCQ measuring the quality of life was 88.7 \pm 14.2 in the TAVI group and 78.6 \pm 18.9

in the surgery group at 30 days, with no differences between groups observed at 12 months. Differences in the rest of the secondary variables were not statistically significant.

Although there is information on the size of the surgical prostheses used in Evolut LR (22% of patients received prostheses of size 19 or 21 mm), the type or manufacturer of the prostheses was not specified.

Four-year outcomes could be assessed in 94.7% of patients in the TAVI group and 89.2% of patients in whom AVR was indicated. The primary endpoint of all-cause mortality or disabling stroke at 4 years was 10.7% in the TAVI group and 14.1% in the SAVR group (RR: 0.74; 95%CI: 0.54-1.00; P = 0.05), representing a 26% relative reduction in the risk of death or disabling stroke with TAVI compared with RQVA. The absolute difference between treatment groups for the primary endpoint continued to increase over time: -1.8% at 1 year, -2.0% at 2 years, -2.9% at 3 years, and -3.4% at 4 years. Rehospitalization for heart failure was 10.3% with TAVI versus 12.1% in the RQVA group. The percentage of patients requiring new permanent

pacemaker implantation was significantly higher in the TAVI group (24.6% vs. 9.9%; P <0.001). Reintervention on the aortic valve prosthesis, clinical or subclinical valve thrombosis, and prosthetic endocarditis were also low in both groups.

Regarding valve hemodynamics, TAVI patients had significantly lower mean aortic valve gradients (9.8±5.5 mmHg in the TAVI group versus 12.1±5.4 mmHg in the RQVA group; P<0.001) and a larger effective area (2.1±0.6 cm² in the TAVI group versus 2.0±0.6 cm² in the RQVA group; P <0.001). Although there were no differences in the incidence of moderate or severe paravalvular regurgitation, mild regurgitation was detected in 14.9% of patients in the TAVI group and 1.6% of those in the RQVA group²².

In summary and concerning the two studies in low-risk patients, it can be said that in the medium term (5 years in the PARTNER 3 and 4 years in the Evolut LR), the differences in the outcome variables indicate that these were more positive for the Evolut prosthesis than the Sapiens 3 compared to the RQVA. This was observed for most variables, except the need for pacemaker implantation (*Table 1*).

Variable	PARTNER 3 (5 years)		EVOLUT LR (4 years)	
	TAVI	RQVA	TAVI	RQVA
Primary ^a	22.8%	27.2%	10.7%	14.1%
Death + incapacitating stroke	12.9%	10.9%	10.7%	14.1%
Rehospitalization	13.7%	17.4%	10.3%	12.1%
Need of pacemaker	13.5%	10.4%	24.6%	9.9% ^b
Mild paravalvular insufficiency	19.9%	3.2% ^b	14.9%	1.6% ^b
Valvular thrombosis	2.5%	0.2% ^b	0.7%	0.6%

TABLE 1. Comparison of results between the PARTNER 3 and EVOLUT LR trials

CVA: cerebrovascular accident; AVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve implantation.

^aEvolut LR: death from any cause or disabling stroke. PARTNER 3: All-cause mortality, any stroke, and rehospitalization.

^bSignificant difference.

Based on the above data, we conclude that, in the population studied, the mid-term results are similar between both techniques (TAVI and RQVA), with the only difference being the number of patients requiring permanent pacemaker implantation if treated with a Medtronic Evolut™ prosthesis. It is not surprising then that the FDA approved the use of TAVI in patients with low-risk patients and that the performance of percutaneous aortic valve implantation has grown almost exponentially in some countries. At the 60th Annual Congress of the US STS, data on the use of TAVI in California were presented, showing that nearly 50% of patients

under 60 years of age choose TAVI over TAVR for treating AS²³.

STRUCTURAL DETERIORATION OF BIOLOGICAL PROSTHESES

This increasing trend in the use of percutaneous biological prosthesis implantation in patients with a life expectancy of more than 10 years will lead to a growing number of patients with degraded percutaneous prostheses requiring treatment.

Advances in materials biotechnology, transcatheter prosthesis designs, and tissue preservation and folding techniques promise to increase the durability of these

prostheses. However, it is also true that, although the anti-calcification treatments of conventional prostheses are similar to those used for percutaneous prostheses, in the latter, the manipulation required for valve folding and post-dilatation maneuvers can cause microtrauma at the level of the leaflets, which can contribute to prosthetic degeneration^{24,25}.

In a study with finite element analysis in a computational model of soft tissue fatigue damage, investigating the fatigue of surgical and percutaneous prosthesis leaflets, it was observed that percutaneous prosthesis leaflets suffer more significant stress, deformation, and fatigue damage compared to surgical prosthesis leaflets. Simulation results suggest that the durability of percutaneous prostheses can be significantly reduced compared to surgical prostheses to 7.8 years²⁶.

Beyond the technical peculiarities of prosthesis manipulation during implantation, and far from the non-touch approach used with conventional surgical prostheses, it should be considered that the permanence of the native aortic valve increases perivalvular turbulent flows, which is likely to accelerate the degeneration process^{27,28}.

Subclinical leaflet thrombosis, defined as hypoattenuating thickening on cardiac tomography appears more frequently in patients who have undergone TAVI than in those treated with TAVI²⁹. This phenomenon may be related to the stagnation of blood flow in the aortic root after percutaneous valve implantation³⁰.

In the PARTNER 3 4D cardiac computed tomography (CT) substudy, 435 patients with severe AS and low surgical risk were randomized to TAVI (n = 214) versus SAVORY (n = 221) and underwent 4D cardiac CT at 30 days and 1 year after surgery. Subclinical thrombosis at 30 days was significantly more frequent in patients treated with TAVI (13% vs. 5%, P = 0.03), although this difference disappeared at 1 year³¹.

Although a causal relationship between subclinical thrombosis and altered valve hemodynamics or thromboembolic risk has not been demonstrated, analysis of 890 patients included in the Registry for Evaluation of Transcatheter and Surgical Aortic Bioprosthetic Aortic Valve Thrombosis and Anticoagulation Therapy (RESOLVE, (RESOLVE) registry) and of 264 patients included in the registry of subclinical aortic bioprosthetic valve thrombosis evaluated with 4-dimensional computed tomography (SAVORY) who had 4D cardiac CT, has shown a significant increase in the incidence of transient cerebral ischemic attacks as well as a higher proportion of increased valve gradients in patients

with subclinical thrombosis. Thus, Subclinical thrombosis represents valvular dysfunction and may progress to impaired leaflet motion^{32,33}.

The long-term clinical impact of this phenomenon is unknown. There is insufficient evidence on its implications in young patients: the increased risk of prosthetic degeneration in young people is a well-documented phenomenon in TAVI, and although there is no comparable evidence for the TAVI population, it can be expected to represent a potential problem in the long term. Furthermore, as has been the case with some prosthetic valves used in TAVI and subsequently withdrawn from the market, it is expected that some transcatheter bioprostheses' durability may be disappointing at follow-up.

When percutaneous treatment is considered in the low-risk population, which is therefore also eligible for AVR, a reflection on the durability and results of the treatment offered is mandatory.

EXPLANTATION OF PERCUTANEOUS PROSTHESES

The increasing choice of using biological valves by transcatheter implantation, as has occurred in conventional surgery, implies the assumption that patients are likely to require more than one intervention on the aortic valve during the patient's lifetime. It is to be expected that percutaneous prosthesis explantation surgery will experience an exponential increase in demand in the coming years³⁴.

In the EXPLANT-TAVR, an international multicenter retrospective registry including 269 patients who underwent transcatheter prosthesis explantation, 43.1% of patients required the intervention due to the development of endocarditis. Other causes of explantation were prosthetic degeneration (20.1%), perivalvular leak (18.2%), and prosthesis-patient mismatch (10.8%). The results reveal a non-negligible risk associated with explant surgery, with in-hospital, 30-day, and 1-year mortality of 11.9%, 13.1%, and 28.5%, respectively³⁵.

Explanting a percutaneous prosthesis is a surgery that can have complications; it is often associated with urgent or emergencies (53.1% of the patients included in the EXPLANT-TAVR) and can require extensive endarterectomies due to neoendothelialization of the prostheses.

In the EXPLANT-TAVR registry, the mortality of surgical explant of a transcatheter prosthesis had high mortality (13.6%) at 30 days, compared to the mortality in the TAVI-in-TAVI group, which was 3.6%. This difference was still significant at 1 year (32.4% vs. 15.4%). However, the difference in mortality after 30 days was not significant³⁶.

The alternative to the surgical explant of a percutaneous prosthesis is the implantation of a second transcatheter prosthesis. The "valve-in-valve" or "TAVI-in-TAVI" techniques are under development and do not currently represent a safe and viable solution in all patients, especially when the cause of reintervention is of infectious etiology or when the size of the implanted prostheses is small. Moreover, there are compelling reasons to doubt the possibility of applying this strategy in a generalized manner.

The so-called sequestration of the sinuses of Valsalva by the prostheses can obstruct the coronary ostia and make their cannulation almost impossible for percutaneous coronary procedures should these be necessary in the future^{37,38}. The absence of data on the incidence of thrombosis or patient-prosthesis mismatch in patients with TAVI-in-TAVI precludes recommending this technique to support a TAVI treatment strategy in patients with a life expectancy of more than 10 years.

The development of TAVI is a revolutionary event in our milieu and opens the doors of AS treatment for patients with high surgical risk who lack options. However, the growing use of the transcatheter option and the continuous development of implantation techniques mean that the therapeutic plan will be increasingly individualized shortly.

The long-term approach must consider comorbidities, anatomy, and the relative advantages and disadvantages of the two therapies, not only about the index surgery but also all possible combination scenarios of the two treatments throughout the patient's lifetime.

Therefore, in low-risk patients, TAVI should be the option of choice only for those with a life expectancy of less than 10 years. In the remainder, TAVI is the safest long-term alternative.

Declarations

The authors declare no conflict of interest.

REFERENCES

- Cribier AG. The odyssey of TAVR: From Concept to Clinical Reality. Vol. 41, Texas Heart Institute Journal 2014;41(2): 125–30.
- Cribier A, Eltchaninoff H, Bash A, Borenstein N, Tron C, Bauer F, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: First human case description. *Circulation* 2002;106(24):3006–3008.
- Smith CR, Leon MB, Mack MJ, Craig D, Moses JW, Svensson LG, et al. Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients. *N Engl J Med* 2011;364(23):2187–2198.
- Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, et al. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): A randomised controlled trial. *The Lancet* 2015;385(9986):2477–2484.
- Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis. *New England Journal of Medicine*. 2014 May 8;370(19):1790–1798.
- Gleason TG, Reardon MJ, Popma JJ, Deeb GM, Yakubov SJ, Lee JS, et al. 5-Year Outcomes of Self-Expanding Transcatheter Versus Surgical Aortic Valve Replacement in High-Risk Patients. *J Am Coll Cardiol*. 2018 Dec 4;72(22):2687–2696.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med* 2016 ;374(17):1609–1620.
- Makkar RR, Thourani VH, Mack MJ, Kodali SK, Kapadia S, Webb JG, et al. Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement. *N Engl J Med* 2020;382(9):799–809.
- Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, et al. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med* 2017;376(14):1321–1331.
- Van Mieghem NM, Deeb GM, Søndergaard L. Self-expanding Transcatheter vs Surgical Aortic Valve Replacement in Intermediate-Risk Patients: 5-Year Outcomes of the SURTAVI Randomized Clinical Trial. *JAMA Cardiol* 2022;7(10):1000–1008.
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38(36):2739–86.
- Lundahl C, Kragholm K, Tayal B, Karasoy D, Andersen NH, Strange JE, et al. Temporal Trends in Patient Characteristics and Outcomes of Transcatheter Aortic Valve Implantation and Surgical Aortic Valve Replacement: A Nationwide Study. *Am J Cardiol* 2024;211:299–306.
- Burke CR, Kirkpatrick JN, Otto CM. Goals of care in patients with severe aortic stenosis *Eur Heart J* 2020;41(8):929–932.
- Carroll JD, Mack MJ, Vemulapalli S, Herrmann HC, Gleason TG, Hanzel G, et al. STS-ACC TVT Registry of Transcatheter Aortic Valve Replacement. *Ann Thorac Surg* 2021;111(2):701–722
- Coylewright M, Forrest JK, McCabe JM, Nazif TM. TAVR in Low-Risk Patients: FDA Approval, the New NCD, and Shared Decision-Making. *J Am Coll Cardiol* 2020;75(10):1208–11.
- Sharma T, Krishnan AM, Lahoud R, Polomsky M, Dauerman HL. National Trends in TAVR and SAVR for Patients With Severe Isolated Aortic Stenosis. *J Am Coll Cardiol*. 2022;80(21):2054–6.
- Ando T, Akintoye E, Pahuja M, Briasoulis A, Javed AA, Takagi H, et al. Transcatheter Versus Surgical Valve Replacement in Non-elderly (age less than 65): In-hospital Outcomes from the National Inpatient Sample. *J Am Coll Cardiol*. 2018;71(11):A998.
- Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med*. 2019;380(18):1695–1705.
- Pibarot P, Salaun E, Dahou A, Avenatti E, Guzzetti E, Annabi MS, et al. Echocardiographic Results of Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients: The PARTNER 3 Trial. *Circulation*. 2020;141(19):1527–37.
- Mack MJ, Leon MB, Thourani VH, Pibarot P, Hahn RT, Genereux P, et al. Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years. *N Engl J Med*. 2023;389(21):1949–1960.
- Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *N Engl J Med*. 2019;380(18):1706–1715.
- Forrest JK, Deeb GM, Yakubov SJ, Gada H, Mumtaz MA, Ramlawi B, et al. 4-Year Outcomes of Patients With Aortic Stenosis in the Evolut Low Risk Trial. *J Am Coll Cardiol*. 2023;82(22):2163–5.
- The Society of Thoracic Surgeons. Press release. 2024. Almost 50% of Patients Under 60 Years Choose TAVR Over SAVR with Worse Outcomes. <https://www.sts.org/press-releases/almost-50-patients-under-60-years-choose-tavr-over-savr-worse-outcomes>.
- Alavi SH, Groves EM, Kheradvar A. The effects of transcatheter valve crimping on pericardial leaflets. *Ann Thorac Surg*. 2014;97(4):1260–6.
- Kiefer P, Gruenwald F, Kempfert J, Aupperle H, Seeburger J, Mohr FW, et al. Crimping may affect the durability of transcatheter valves: An experimental analysis. *Ann Thorac Surg*. 2011;92(1):155–60.

26. Martin C, Sun W. Comparison of transcatheter aortic valve and surgical bioprosthetic valve durability: A fatigue simulation study. *J Biomech.* 2015;48(12):3026–34.
27. Becsek B, Pietrasanta L, Obrist D. Turbulent Systolic Flow Downstream of a Bioprosthetic Aortic Valve: Velocity Spectra, Wall Shear Stresses, and Turbulent Dissipation Rates. *Front Physiol.* 2020 ;11: 577188.
28. Pietrasanta L, Zheng S, De Marinis D, Hasler D, Obrist D. Characterization of Turbulent Flow Behind a Transcatheter Aortic Valve in Different Implantation Positions. *Front Cardiovasc Med.* 2022;8: 804565.
29. Yanagisawa R, Tanaka M, Yashima F, Arai T, Jinzaki M, Shimizu H, et al. Early and late leaflet thrombosis after transcatheter aortic valve replacement: A multicenter initiative from the OCEAN-TAVI registry. *Circ Cardiovasc Interv.* 2019;12(2):e007349.
30. Trusty P, Bath SS, Sadri V, Makkar R. The role of flow stasis in transcatheter aortic valve leaflet thrombosis. *J Thorac Cardiovasc Surg.* 2020;164(3):e105–17.
31. Makkar RR, Blanke P, Leipsic J, Thourani V, Chakravarty T, Brown D, et al. Subclinical Leaflet Thrombosis in Transcatheter and Surgical Bioprosthetic Valves: PARTNER 3 Cardiac Computed Tomography Substudy. *J Am Coll Cardiol.* 2020;75(24):3003–15.
32. Chakravarty T, Søndergaard L, Friedman J, De Backer O, Berman D, Kofoed KF, et al. Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study. *The Lancet.* 2017;389(10087):2383–92.
33. Søndergaard L, De Backer O, Kofoed KF, Jilaihawi H, Fuchs A, Chakravarty T, et al. Natural history of subclinical leaflet thrombosis affecting motion in bioprosthetic aortic valves. *Eur Heart J.* 2017;38(28):2201–7.
34. Fukuhara S, Brescia AA, Shiomi S, Rosati CM, Yang B, Kim KM, et al. Surgical explantation of transcatheter aortic bioprostheses: Results and clinical implications. *Journal of Thoracic and Cardiovascular Surgery.* 2021;162(2):539-547.e1.
35. Bapat VN, Zaid S, Fukuhara S, Saha S, Vitanova K, Kiefer P, et al. Surgical Explantation After TAVR Failure: Mid-Term Outcomes From the EXPLANT-TAVR International Registry. *JACC Cardiovasc Interv.* 2021;14(18):1978–91.
36. Tang GHL, Zaid S, Kleiman NS, Goel SS, Fukuhara S, Marin-Cuartas M, et al. Explant vs Redo-TAVR After Transcatheter Valve Failure: Mid-Term Outcomes From the EXPLANTORREDO-TAVR International Registry. *JACC Cardiovasc Interv.* 2023;16(8):927–41.
37. Rogers T, Khan JM, Satler LF, Greenbaum AB, Lederman RJ. TAVR-in-TAVR?: Don't Bank on It! *J Am Coll Cardiol.* 2020;76(8):1003.
38. Ochiai T, Yamanaka F, Yamabe T, Miyashita H, Moriyama N, Shishido K, et al. Late Sinus Sequestration After TAVR-in-TAVR Rescued by Coronary Artery Bypass Grafting. *JACC Cardiovasc Interv JACC Cardiovasc Interv.* 2024 Feb 17;17(6):810-813. doi: 10.1016/j.jcin.2024.01.277.

MASSIVE LATE ENDOLEAK TYPE IA, ASSOCIATED WITH SHOCK AND ACUTE ANEMIA: CONSERVATIVE SURGICAL TREATMENT

ABSTRACT

We present a case of type 1 endoleaks associated with massive hemorrhage and shock, treated with traditional open surgery. We present a 74-year-old male patient with a history of endovascular repair of abdominal aortic aneurysm 6 years ago, was admitted to the emergency department in shock and acute anemia, showing a type IA endoleak associated with retroperitoneal hematoma. Open repair was performed with the interposition of a Dacron™ prosthesis with preservation of the aortic endoprosthesis. Although in these cases of extreme urgency, it has been proposed the extraction of the endoprosthesis, which involves a procedure associated with high mortality, in this case, it was feasible a simple repair as was the interposition of prosthesis between proximal aorta and endoprosthesis. Endovascular repair of aortic aneurysm requires strict monitoring and a good selection of patients for this procedure since this late complication has a high mortality rate.

Keywords: endoprosthesis, endoleak, abdominal aortic aneurysm.

Authors:

Juan Marín P.¹, Daniel Gutiérrez V.² and Claudia Marín H.³

¹*Surgery Service, Hospital de Urgencia de la Asistencia Pública, Santiago, Región Metropolitana, Chile.*

²*Surgical Residency, Hospital de Urgencia de la Asistencia Pública, Santiago, Región Metropolitana, Chile.*

³*Surgical Residency, Pontificia Universidad Católica de Chile, Santiago, Chile.*

Corresponding author:

Juan Marín P.

jmarin1953@gmail.com

INTRODUCTION

Abdominal aortic aneurysm represents a major problem due to the risk of rupture. Until 1991, the treatment was traditional open surgery, with high morbidity and mortality rates, especially in the case of rupture¹. Even some patients who met the criteria for this procedure presented a high risk of complications, which precluded surgery. In that year, the era of endovascular therapy began, with stents to exclude the aneurysm, achieve sac thrombosis, and, later, reduce the sac size and the risk of rupture². Endovascular aneurysm repair (EVAR) is less invasive than traditional surgery; in addition, it has lower mortality and shorter hospital stay, is associated with a shorter intensive care unit (ICU) stay, shorter surgery time, and, above all, is accessible to patients who are at high risk for traditional open surgery³.

This technique, however, is not free of serious complications, which occur in 16 to 36% of cases. For this reason, several reinterventions are performed during patient follow-up to reduce the size of the aneurysm and the risk of rupture, which can reach up to 19%⁴.

With this new technique, endoleaks arise that repressurize the aneurysm in the long term, leading to its rupture, so it is recommended to follow up strictly and lifelong through different modalities of imaging studies.

We present a clinical case of late-type I A endoleak associated with shock and acute anemia that required traditional open surgery to resolve this severe complication.

CLINICAL CASE

A 74-year-old male patient with a history of EVAR in 2017, arterial hypertension, obstructive pulmonary disease, and cessation of smoking. In May 2023, he

went to the polyclinic of the sector for presenting hypotension and lipotimia. He was immediately referred to our emergency department, where he arrived with hypotension and unconscious, vasoactive drugs and a massive blood transfusion were administered. An angiotomography showed a large aneurysm with contrast leakage into the sac, associated with retroperitoneal hematoma, reported as endoleak type I A (*Figure 1*). No elements were available to treat this endoleak endovascularly, and given the extreme severity of the clinical picture, it was decided to take him to the surgical ward. A laparotomy was performed, and a retroperitoneal hematoma was found with active bleeding and an intact aneurysm with no reduction in size.

To stop the bleeding, the suprarenal aorta was clamped. Once the bleeding was controlled, the aneurysm sac was opened, and a wide space was found between the aorta and the stent, attached to the proximal aorta only with the hooks of the free-flow device. The distal aorta was prepared, and a useful area was left flush with the renal arteries. The endoleak was repaired by the interposition of a 16 mm Dacron™ prosthesis joining the normal wall aorta after the removal of the wires of the free-flow device and the endoprosthesis. The sac and retroperitoneum were closed in two planes (*Figure 2*).

RESULT

The patient is maintained on vasoactive drugs and a massive transfusion protocol, both in the operating room and in the ICU. During the hospital stay, a right renal infarction was confirmed; the left kidney had normal circulation. However, dialysis was required to improve conditions. Another complication was pneumonia associated with mechanical ventilation that required broad-spectrum and second-line antibiotics. During

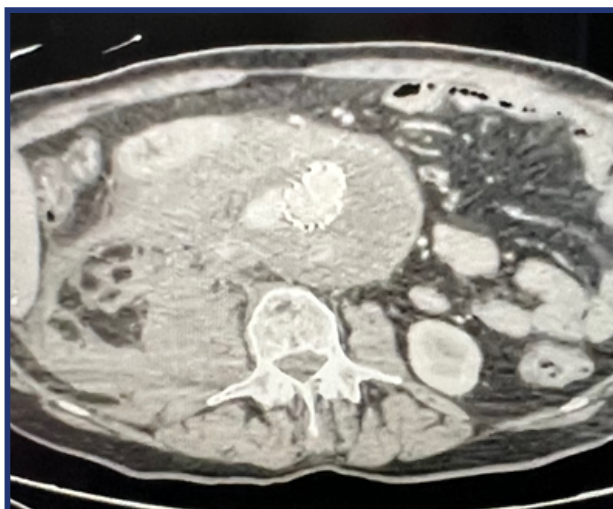


FIGURE 1. Angiotomography shows a type 1A endoleak with aneurysm reproduction associated with a retroperitoneal hematoma.

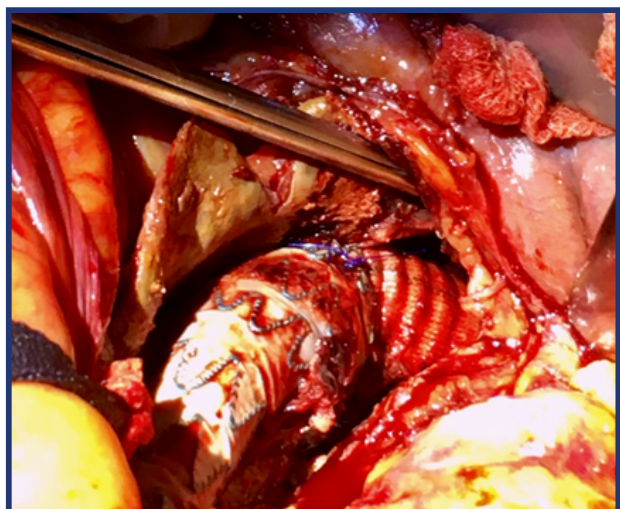


FIGURE 2. Interposition of Dacron™ prosthesis between the proximal aorta and the aortic endoprosthesis, with the release of the aorta from the wires of the free flow device.

follow-up, the original aneurysm presented thrombosis and no endoleaks (Figure 3). However, the patient died due to a hiatal hernia with the entire stomach in the chest associated with aspiration pneumonia, it was almost impossible to resolve the possibility of enteral feeding and hiatal hernia, which prevented this type of feeding (Figure 4).

DISCUSSION

Although EVAR is a widely accepted technique for the repair of infrarenal aneurysms, endoleaks are a very frequent complication affecting 15-52% of all patients in whom it was used. Type 1A is infrequent (1-3%) but is associated with a high risk of expansion and rupture of the aneurysmal sac. There are several endovascular options for its solution, including the use of Palmaz stent XL™ and the use of Heli-Fx system R™ (Aptus, Medtronic)⁵, and the possibility of adding a fenestrated stent. If the latter fails, the only option is open surgery, with removal of the stent and reconstruction of the original type with a bifurcated prosthesis, which is associated with high morbidity and mortality⁶. It is important to mention

that these endovascular techniques are not universally accepted recommendations.

In our case, the elements could not solve the endoleak endovascularly. In addition to the patient's shock, we were forced to repair it using an open technique, with good results, such as the interposition of Dacron™ between the proximal aorta and the endoprosthesis. This is a simple and safe technique we have not seen in other publications. As a complication, and due to the proximity of the renal arteries, one of the circulations of the kidney was compromised. In the literature, we have not found this severe acute complication associated with hemodynamic compromise and acute anemia, so we should resolve the situation with traditional surgery and, at the same time, conclude that EVAR requires lifelong imaging surveillance to avoid this severe complication.

Declarations

The authors declare no conflict of interest.

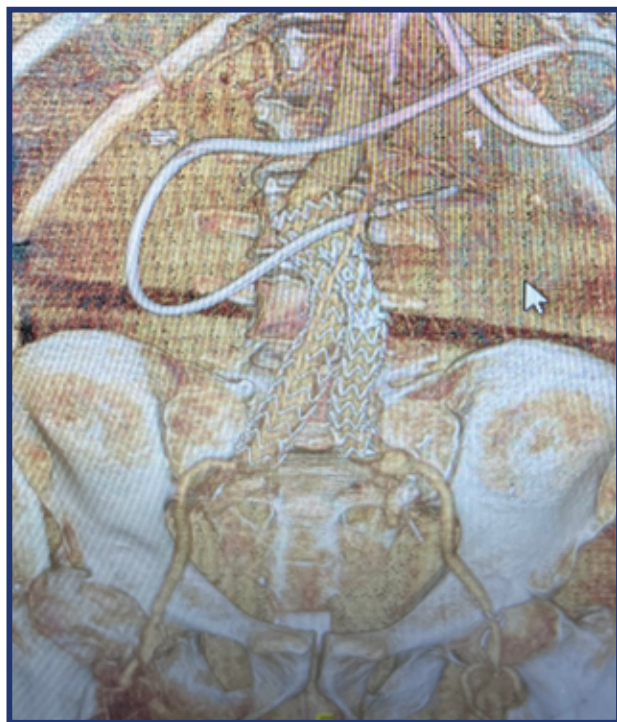


FIGURE 3. Repair control of a type 1A endoleak.

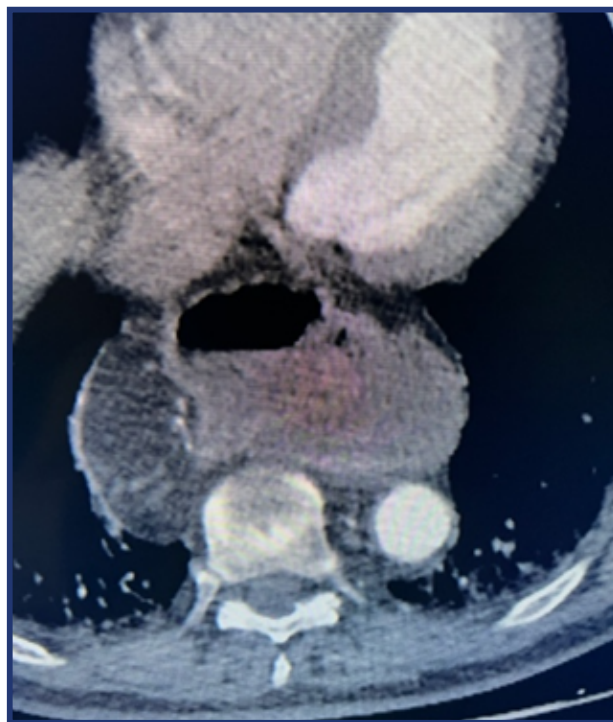


FIGURE 4. Large hiatal hernia with displacement of the stomach into the thorax.

REFERENCES

1. Creech Jr O. Endoaneurismorrhaphy and treatment of aortic aneurysm. *Ann Surg* 1966;164:935.
2. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg* 1991;5:491e9.
3. Participantes en el ensayo EVAR. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomized controlled trial. *Lancet* 2005;365(9478):2179e86
4. Nordon IM, Karthikesalingam A, Hinchliffe RJ, et al. Secondary interventions following endovascular aneurysm repair (EVAR) and

the enduring value of graft surveillance. *Eur J Vasc Endovasc Surg* 2010;39:547-54.

5. Wyss TR, Brown LC, Powell JT, et al. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: data from the EVAR Trials. *Ann Surg* 2010; 252: 805-12.

6. Scali ST, McNally MM, Feezor RJ, et al. Elective endovascular aortic repair conversion for type Ia endoleak is not associated with increased morbidity or mortality compared with primary juxtarenal aneurysm repair [published correction appears in *J Vasc Surg*. 2015 May;61(5):1382]. *J Vasc Surg*. 2014;60(2):286-294.e1. doi:10.1016/j.jvs.2014.02.046.

DEFERRED CLOSURE IN THE SUCCESSFUL TREATMENT OF POST-INFARCTION VENTRICULAR SEPTAL RUPTURE

Authors

Jesús Saucedo-Castillo¹,
Diana L. Labastida-Ramírez¹,
Rutilio D. Jiménez-Espinoza¹,
Ana Hernández-Pérez¹

¹*Surgery Division of the High Specialty Medical Unit, Hospital de Cardiología Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico.*

Corresponding author:

Jesús Saucedo-Castillo
jesussaucedocastillo@me.com

ABSTRACT

Ventricular septal rupture is a rare but highly lethal mechanical complication of acute myocardial infarction. The gold-standard treatment is surgical repair; with conservative treatment, 90% mortality is estimated in the following two months. We present the case of an 81-year-old patient with post-infarction SVR who underwent angioplasty and was later admitted to the intensive care unit to assess hemodynamics to prepare him for delayed closure. Surgical repair of the defect was performed 21 days later, and the patient was discharged to the cardiovascular intensive care unit with adequate postoperative evolution.

Keywords: *mechanical complications of acute myocardial infarction, acute myocardial infarction, ventricular septal rupture, surgical repair ventricular septal rupture.*

INTRODUCTION

Ventricular septal rupture (VSR) is a mechanical complication of acute myocardial infarction (AMI). The gold standard of treatment is surgical intervention; however, it has a very high mortality rate. Early repair is recommended when hemodynamic instability is present; however, the time indicated to establish management has yet to be precisely defined. Due to the low incidence of this condition, most of the information comes from cohorts or national patient registries.

CASE PRESENTATION

We present the case of an 81-year-old male patient referred for acute coronary syndrome of the acute myocardial infarction type with positive ST-segment elevation; he has a history of systemic arterial hypertension of ten years of evolution and receives treatment with angiotensin two receptor antagonists (ARA 2). He has no other chronic degenerative diseases.

The current presentation began at 18:00 hours the day before admission with oppressive chest pain of intensity 10/10 on the visual analog scale, accompanied by a vagal response characterized by diaphoresis and nausea. He came to the general hospital at 19:00 hours with vital signs: blood pressure of 188/83 mmHg, heart rate of 96 beats per minute, respiratory rate of 22 breaths per minute, and oxygen saturation of 96%. The first electrocardiogram (ECG) showed positive ST-segment elevation of V1-V4; acetylsalicylic acid, clopidogrel, atorvastatin, and enoxaparin were administered. The patient was transferred to the coronary intensive care unit with a diagnosis of AMI; he was admitted 5 hours and 50 minutes after the onset of symptoms, hemodynamically stable, with angular pain of intensity 5/10 and no other added symptoms. A new ECG was performed, which confirmed anterior infarction; auscultation showed a bar murmur predominantly in the apex. A transthoracic echocardiogram was requested, showing a rupture of the interventricular (IV) septum of 5 mm in the apical portion, left ventricular ejection fraction of 45%, and mobility alterations (septoapical, lateroapical, inferoapical and anteroapical akinesia; inferoseptal hypokinesia of the middle segment, anterior akinesia of the middle segment and anteroapical akinesia of the middle segment). In the hemodynamics department, coronary angiography showed disease of two main vessels: anterior descending artery (AD) with 99% subocclusive lesion in the middle

segment and posterior descending artery with focal distal segment lesion of 75%. The percutaneous coronary intervention of the LAD was performed with the placement of a 3 x 38 mm XIENCE Sierra™ stent with TIMI 3 end-flow (thrombolysis in myocardial infarction). In the second stage, we worked on the right coronary artery by placing a 3 x 38 mm Resolute Onyx™ stent in the distal segment with normal arterial flow (TIMI 3). He was admitted to the cardiovascular intensive care unit. A new ECG showed a 15 mm IV septum rupture with a left to right shunt and a pressure difference of 3:1. During his stay, a medical-surgical session was held, and it was agreed to close the defect with a pericardial patch three weeks after the AMI. On the 21st day after the IV septum rupture, hemodynamic deterioration, data suggestive of cardiogenic shock, and heart failure refractory to treatment, so vasopressor therapy was initiated. Hemodynamic studies showed evidence of decreased peripheral vascular resistance, so it is considered for emergency surgery.

The patient is admitted to the operating room; the approach is performed by median sternotomy, arterial and bicaval cannulation, the total cardiopulmonary shunt is started, and aortic clamping is performed. A right ventriculotomy is performed with a cut parallel to the IV septum, a 3 x 2 cm defect is identified (*Figure 1*), a bovine pericardium patch is placed (*Figure 2*) and closed with Prolene™ U-stitches 4-0 with pledgets (*Figure 3*). Then a ventriculorrhaphy is performed with a sandwich technique with Prolene™ 2-0 with pledgets (*Figure 4*). Trans-operative findings were global grade III cardiomegaly, a macroscopic trace of infarction in the inferior and anterior face, and an apical fenestrated ventricular septal defect of 3 x 2 cm. After surgery, he was admitted to the intensive care unit, intubated, and with aminergic and vasopressor support; he was decannulated 24 hours later, and vasopressor support was withdrawn 48 hours later. The patient was transferred to the general ward at 72 hours, clinically stable, without mechanical ventilatory support or vasopressor support, with borderline mean arterial pressure, afebrile, and no evidence of shock. A new control echocardiogram was performed, where the residual defect of the surgical closure was reported as hemodynamically not significant, with a left ventricular ejection fraction of 32% and ischemic cardiomyopathy with moderate myocardial damage. He had a good postoperative evolution and was discharged home without complications.

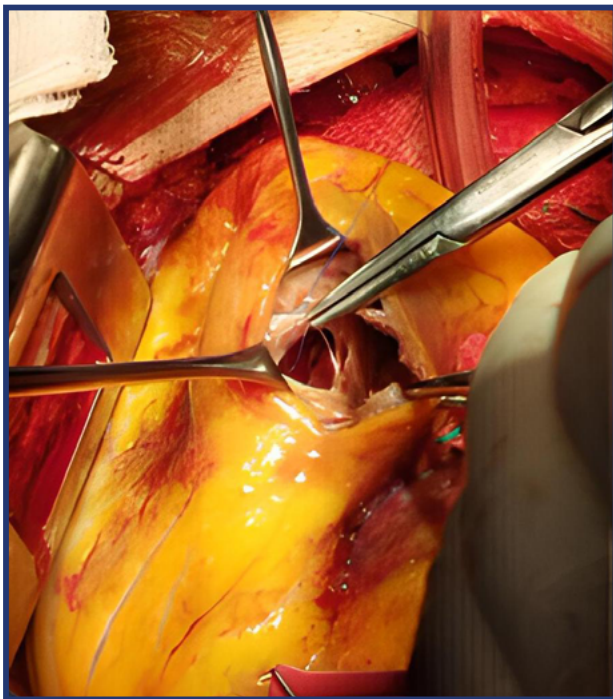


FIGURE 1. Interventricular septal defect.



FIGURE 2. Placement of a bovine pericardium patch in a 3 x 2 cm defect.



FIGURE 3. U-point closure with pledgets.

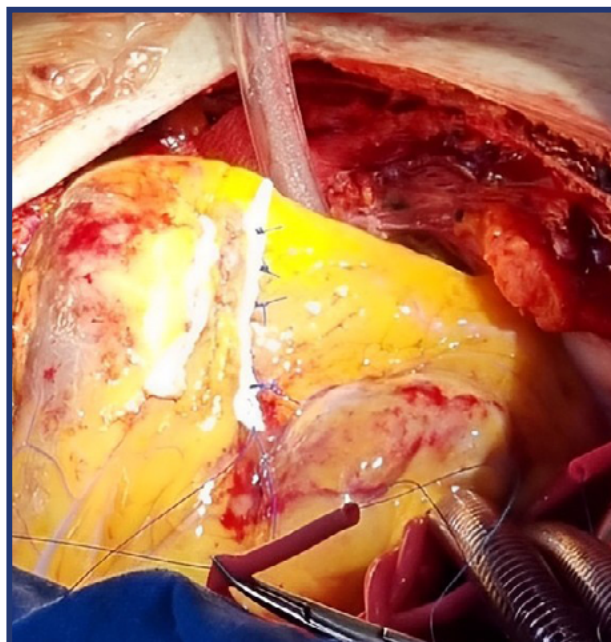


FIGURE 4. Ventriculorrhaphy with sandwich technique with pledgets.

DISCUSSION

SVR is the most common mechanical complication of AMI and carries a very high lethality; it occurs in approximately 0.21% of patients with ST-segment elevation infarctions and 0.04% of those with non-ST-segment elevation infarctions¹.

In this reperfusion era, risk factors for developing post-infarct SVR include older age, female sex, smoking, hypertension, right ventricular infarction, and extensive AMI². The report Elbadawi et al. obtained from the National Inpatient Sample (NIS)

database from 2003 to 2015 evaluated mechanical complications arising from ST-segment elevation and non-ST-segment elevation AMI. The sample included 13,767 patients who had mechanical complications; 10,344 (75%) developed SVR, and the remaining patients had acute mitral insufficiency due to papillary muscle rupture (19%) or free wall rupture (6%)³. ST-segment elevation infarcts are more likely to be associated with transmural infarction than non-elevation infarction. A transmural AMI is a prerequisite for SVR and is, therefore, more

common after ST-segment elevation infarction¹. This mechanical complication usually occurs between day 2 and day 6, although it can occur at any time in the 2 weeks following acute infarction. The average time to onset was one day in the GUSTO-I study (Global Utilization of Tissue Plasminogen Activator and Streptokinase for Coronary Artery Occlusion), four days in the American Heart Association Study of Mechanical Complications of AMI, and 16 hours in the SHOCK study^{4,5}. Depending on the presentation of the septal rupture (the size of the infarct, the degree of shunt present, and the associated right ventricular failure), patients may present with relative hemodynamic stability or frank cardiogenic shock. The most important determinant of the outcome of SVR management is the development of heart failure (left, right, or both) and cardiogenic shock. The severity of heart failure is related to the extent of myocardial necrosis and left-to-right shunt¹. Today, surgical closure is the definitive treatment for post-infarct ventricular septal rupture. Management usually includes excision of all necrotic tissue, patching of the defect, and myocardial revascularization⁶. Without surgical treatment, 90% of patients will die within two months⁴. Arnaoutakis et al. published results obtained from the 1999-2000 cohort of the STS (Society of Thoracic Surgeons) National Database, where they studied 2,876 patients who underwent surgical repair for post-infarction SVR. They reported an overall 30-day in-hospital mortality rate of 42.9%, with a marked decrease with deferred closure (54.1% mortality with surgical repair in the first seven days versus 18.4% after this time). Risk factors that increased trans-operative mortality included age, female sex, shock, inferior infarction, use of intra-aortic balloon counterpulsation, dialysis, mitral insufficiency, reoperation, emergency surgery, and time to repair⁴. Other investigators found that mortality was higher (60%) in patients who underwent surgery within the first 24 hours^{7,8}.

The international multicenter retrospective multicenter retrospective cohort study CAUTION (Mechanical Complications of Acute Myocardial Infarction) included patients who received surgical treatment for mechanical complications arising from acute myocardial infarction. The study included 475 patients who underwent surgery for post-infarction SVR from 26 centers in different countries from January 2001 to December 2019. The main findings of this study were as follows:

- The early mortality rate was 40.4%.
- Advanced age, preoperative cardiac arrest, percutaneous revascularization, and postoperative requirement of intraaortic balloon

counterpulsation or extracorporeal membrane oxygenation were independently associated with early mortality.

- Longer times between AMI and SVR and between SVR and surgery were associated with lower mortality.
- Recurrent SVR was not associated with increased mortality⁹.

It is still difficult to determine the optimal time for definitive surgical repair. The American College of Cardiology and the American Heart Association guidelines recommend emergency surgical repair regardless of the patient's hemodynamic status, so the ideal timing is also controversial and should be individualized. Early repair should be considered in stable patients without organ failure and favorable anatomy. In stable patients with complex anatomy or friable tissues, delayed intervention should be considered⁵.

The pathophysiological mechanism involves excessive transmural myocardial necrosis followed by rupture or extensive scarring of the affected tissue. The conventional mechanism of SVR involves coagulation necrosis of ischemic tissue with neutrophil infiltration, which causes thinning and weakness of the septal myocardium; this subacute process requires three to five days. On the other hand, rupture occurring within 24 hours of presentation is more likely to result from dissection of an intramural hematoma or hemorrhage in the ischemic myocardium⁸.

In early repair, the intervention is performed around the infarcted area in friable myocardial tissue, which increases the possibility of expanding the size of the SVR. This would explain the high in-hospital mortality rate compared to delayed closure⁶.

The intervention delay has a mechanistic rationale: after infarction, metalloproteinase activity and tissue degradation peak on day seven, whereas new collagen deposition begins between days two and four, and necrotic myocytes are entirely replaced by collagen by 28 days. Therefore, deferral could facilitate successful closure by allowing friable tissue to organize, strengthen, and differentiate well from surrounding healthy tissue activity, allowing peak tissue breakdown to occur on day 7. The connective tissue and scar formation around the defect promote better anchorage for the suture material and decrease the potential for patch dehiscence⁵. In surgical repair, myocardial revascularization should be performed first to prioritize myocardial protection. Techniques include Dagget's technique, primary closure of the defect, and David's technique, which consists of endocardial patch placement with infarct

exclusion and is currently the most widely used in the world⁵. For anterior SVR, the infarcted area of the anterolateral left ventricle should be incised parallel to the LAD, as the septal defect is usually located below the incision. A patch of pericardium or synthetic material with U-sutures with pledgets should be used in the non-infarcted area of the right ventricle to exclude the entire portion of the LV septum from the mitral annulus to the anterolateral LV wall. True apical SVRs can be repaired, and primary closure can be performed by amputating the apex. Posterior SVRs are approached via ventriculotomy on the infarcted posterior LV wall parallel to the posterior descending, with patch suturing to the LV side of the non-infarcted septum with patch closure, primary closure, or infarct exclusion, depending on how much of the LV free wall is involved⁵. If deferred closure is chosen, ventricular assist devices (VADs) are a valuable bridge to surgery; decreasing afterload and preload helps to increase coronary perfusion in the affected myocardium. Venoarterial extracorporeal membrane oxygenation has also demonstrated numerous benefits compared to VADs, as it prevents sternotomy, provides oxygenation support, and is easily reversible; it also allows hemodynamic stabilization, recovery or prevention of organ failure and washout of the dual antiplatelet effect, and is a decision-making strategy⁴. Presently, percutaneous closure devices allow less invasive management in this type of patient; in selected cases (defects <1.5cm, subacute stage, and patients who are not good candidates for surgery), they are viable. However, in a case series of 29 patients with this type of management, 41% experienced procedure-related complications, and the overall survival rate at 30 days was 35%, with higher mortality in patients with cardiogenic shock⁶.

CONCLUSIONS

Post-infarct SVR is a severe condition with challenging medical and surgical treatment; despite multiple advances in infarct management and surgical repair techniques, the mortality rate has not changed significantly for decades. According to the databases and cohorts reviewed, a better prognosis has been observed with deferred closure; however, more prospective studies are required that include improved surgical techniques and preoperative management to enhance the current suboptimal early mortality rate. In our Institute, and based on literature reports and our center's experience, the management algorithm for this mechanical complication consists of admitting

the patient to the coronary intensive care unit, optimization of pharmacological management, support with ventricular support, and performing surgical repair after 14 days following the event. In case of hemodynamic instability, intervention with mechanical circulatory support and surgical correction after seven days is considered since satisfactory results are obtained.

Declarations

The authors declare no conflict of interest.

Acknowledgments

The authors would like to thank the Cardiothoracic Surgery Service of the Unidad Médica de Alta Especialidad, Hospital de Cardiología Centro Médico Nacional Siglo XXI, for sharing the information requested for the clinical case.

REFERENCES

1. David TE. Post-infarction ventricular septal rupture. *Ann Cardiothorac Surg* 2022;11(3):261-267.
2. Shahreyar M, Akinseye O, Nayyar M, Ashraf U, Ibebuogu U. Post-myocardial infarction ventricular septal defect: A comprehensive review. *Cardiovascular Revascularization Medicine*. 2020; 21:1444-1449.
3. Elbadawi A, Elgendy IY, Mahmoud K, Barakat A, Mentias A, Mohamed A, et al. Temporal Trends and Outcomes of Mechanical Complications in Patients With Acute Myocardial Infarction. *JACC Cardiovasc Interv* 2019;12:1825-36.
4. Goyal A, Menon V. Contemporary Management of Post-MI Ventricular Septal Rupture, American College of Cardiology. 2018.
5. Damluji A, van Diep S, Katz J, Menon V, Tamis-Holland J, Bakitas M, et al. Mechanical Complications of Acute Myocardial Infarction. A Scientific Statement From the American Heart Association. *Circulation*. 2021;144:e16-e35
6. Khazi FM, Al-Safadi F, Karaly Y, Siddiqui NR, Al-Zamkan B, Aljassim O. Management issues during postinfarction ventricular septal defect and role of perioperative optimization: A case series. *Ann Card Anaesth* 2019;22:30-4.
7. Arnaoutakis GJ, Zhao Y, George TJ, Sciortino CM, McCarthy PM, Conte JV. Surgical repair of ventricular septal defect after myocardial infarction:outcomes from the Society of Thoracic Surgeons National Database. *AnnThorac Surg* 2012;94:436-43.
8. Jones BM, Kapadia SR, Smedira NG, Robich M, Tuzcu EM, Menon V, et al. Clinical update Ventricular septal rupture complicating acute myocardial infarction: a contemporary review. *Eur Heart J*. 2014;35:2060-8.
9. Ronco D, Matteucci M, Kowalewski M, De Bonis M, Formica F, Jiritano F, et al. Surgical Treatment of Postinfarction Ventricular Septal Rupture. *JAMA Netw Open*. 2021;4(10):e2128309.

ASCENDING AORTIC ANEURYSM, EXPERIENCE IN A PUBLIC HOSPITAL IN THE PROVINCE OF BUENOS AIRES

ABSTRACT

An ascending aortic aneurysm is a permanent dilatation in that artery region. Their natural history depends on their size and the weakness of the arterial wall. The surgical indication is defined based on the risk of rupture.

A retrospective analysis of the surgically treated cases in our department considers the surgical technique and postoperative complications.

Keywords: *ascending aortic aneurysm, surgical technique, Bentall surgery, hybrid or debranching method, Wheat surgery, David surgery, Yacoub surgery, Cabrol surgery.*

Authors:

Gisele Mendoza¹, Carlos Salomon¹, Pablo Arenaza¹, José Acosta¹, Miguel Aranibar¹, Luis Soto¹, Carlos Soria¹, Nicolás Patrizi¹, Gabriel Basso¹

¹*Cardiovascular Surgery Service, Hospital Interzonal Especializado de Agudos y Crónicos San Juan de Dios, La Plata, Argentina.*

Corresponding author:

Gisele Mendoza
med06_g@hotmail.com

INTRODUCTION

An ascending aortic aneurysm is a permanent dilatation in that region of the artery involving all three wall layers that equals or exceeds 50% of the diameter considered normal for a person of comparable age, sex, and height¹.

The natural history of aortic aneurysms depends on their size and the weakness of the arterial wall. The incidence of rupture of aortic aneurysms less than 5 cm in diameter is 1% to 2% per person per year, with a rate of progression of 0.2 cm/year; when the aneurysm is larger than 5 cm, the incidence of rupture is approximately 20%, with a rate of disease progression of 0.3 to 0.8 cm/year².

Ascending aortic aneurysms that cause symptoms have a higher incidence of rupture (27% survival at five years compared to 58% for asymptomatic

ones). Patients are usually asymptomatic, although subcostal burning chest pain may occur because of its progression and/or expansion. Rarely, dyspnea or cough due to erosion of the bronchial tree; superior vena cava compression has also been reported with a mediastinal syndrome.

In aortic dissection, separation of the wall of the aortic layers occurs, with the formation of a false lumen that runs parallel to the normal lumen. The natural history of untreated type A dissections (according to the Stanford classification) has a very high mortality rate. In the first 24 to 48 hours, it approaches 1% to 2% per hour².

The Stanford classification considers the involvement of the ascending aorta independently of the site of the initial lesion (type A, involved ascending aorta; type B, not involved) (Figure 1).

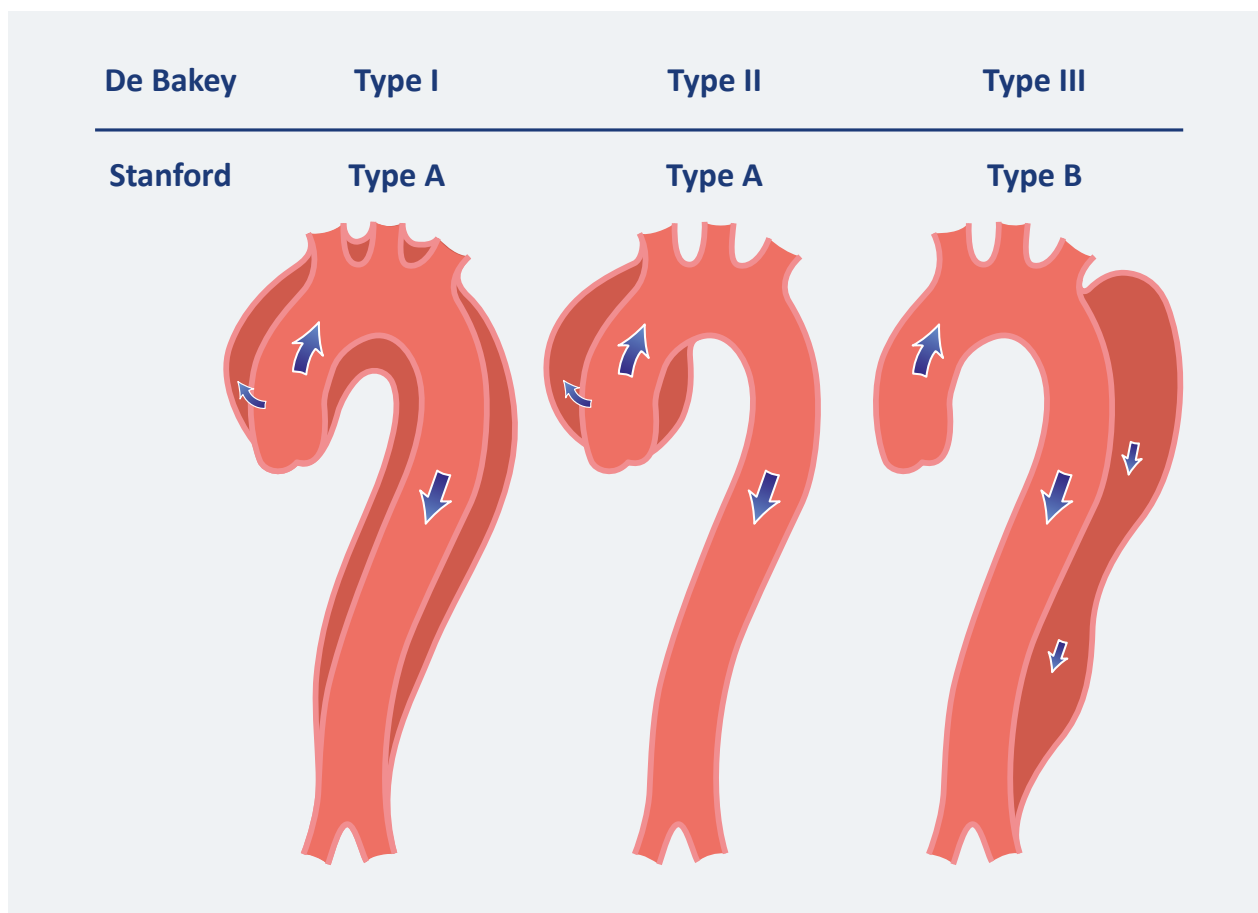


FIGURE 1. Stanford classification of aortic dissections.

From: ³Erbel R y cols., 2014:2899

Due to the high mortality per se, these cases are not included in this analysis.

According to the Argentine Society of Cardiology, surgery is indicated for ascending aortic aneurysms with a diameter greater than 5 cm and symptomatic;

if the diameter is larger, surgery is performed whether the patient has symptoms or not². If the patient is asymptomatic and the aneurysm has a diameter of less than 5 cm, echocardiographic control is indicated every 3 to 6 months.

For European guidelines, the cut-off point is 55 mm in ascending aorta dilatation and 50 mm if the valve is bicuspid¹.

In aneurysms of the ascending aorta accompanying Marfan syndrome, the surgical indication is a diameter greater than 45 mm.

The basic surgical technique for treating ascending aortic aneurysms is replacing the dilated aorta with a tubular prosthetic Dacron™ graft.

Different criteria can be used to classify the possible surgical techniques used in this pathology: the extent of the aneurysm, the type of aortic substitute used, or the anastomotic technique:

1. Extent of the area affected by the aneurysm: The extent of surgery may vary depending on the involvement of regions adjacent to the tubular portion of the ascending aorta. In case of proximal involvement and dilatation of the aortic root, with or without involvement of the aortic valve, the aorta should be replaced in its sinus portion, with or without valve surgery for the replacement or preservation-repair of the aortic valve. It can extend to the distal aorta, involving the supra-aortic vessels.
2. Type of aortic substitute: Depending on the proximal extent of aortic pathology, a synthetic valved Dacron™ graft may or may not be used.
3. The main specific procedures on the ascending aorta and aortic root depend mainly on the extent of the aneurysm and the condition of the aortic root and valve, but also on other factors such as the underlying pathology, the patient's life expectancy, the possibility of anticoagulation and the surgeon's preferences.

SURGICAL TECHNIQUE

In ascending aortic aneurysms with sinuses of Valsalva and normal valvular annulus, only the ascending aorta from the sinotubular junction to the beginning of the aortic arch must be replaced. If the valve is pathological, it can be replaced separately (Wheat technique).

In valve, root, and ascending aorta replacement with aortovalvular grafting (Bentall-type operation), the coronary arteries are reimplanted as coronary "buttons" on the Dacron™ graft. In some cases, coronary reimplantation requires prolongation by Dacron™ tubes (Cabrol technique).

Valve-sparing aortic root replacement procedures can be classified into two major groups: the remodeling or Yacoub technique and the reimplantation technique or the David technique. In both procedures, the aortic valve cusps must be normal, and valve insufficiency is secondary to aortic root dilatation.

A hybrid approach, known as debranching³, can address the aortic arch by surgical bypass of the neck vessels and subsequent exclusion of the aneurysm with an endoprosthesis.

The surgeon chooses the technique. In our service, we do not have a stock of supplies, but we depend on the provision by the State or social security. Endoprostheses are often unavailable for emergency use, so they are performed in a second stage. However, patients in our center would have required endoprosthesis in a second stage (hybrid method or debranching), but they did not reach that stage due to poor clinical evolution.

METHOD

This study evaluates the cases of ascending aortic aneurysms treated in our department in the last four years. We consider the preoperative status, the decision to perform emergency surgery or not, and, depending on the surgical technique chosen, complications and length of hospital stay will be evaluated. The aim is to correlate surgical technique with postoperative morbimortality; immediate complications and hospitalization time are variables.

RESULTS

Table 1 shows the results of this study. Concerning the previous conditions of the patients, it can be appreciated that those with ages below 50 years and arterial hypertension as the only comorbidity presented a lower incidence of complications and less hospitalization time.

In terms of mortality, the highest incidence was seen in cases admitted as emergencies, especially with pathology involving the aortic arch.

In one case (a patient with a history of chronic obstructive pulmonary disease), a longer postoperative intubation time was recorded. Even so, the sample is too small to establish an association.

CONCLUSIONS

There is no relationship between surgical technique and morbimortality, nor is there any relationship between days of hospitalization directly related to postoperative complications.

The involvement of the arch was associated with higher mortality, which reached almost 70%.

The analysis shows that risk factors and factors inherent to the patient would be the determining factors of postoperative evolution, which would not be directly related to the technique chosen.

Declarations

The authors declare no conflict of interest.

Year	N.º of surgeries	Surgical technique (n)	Complications (n)	Days of hospitalization (average)	Age (years)	Comorbidities	Aortic disease
2022	5	Ascending aorta replacement (3)	None (3)	10	50	AHT (80%)	Aneurysm
		Bentall surgery (2)	Prolonged intubation (1)		38	Marfan syndrome	Aneurysm
2021	8	Bentall surgery (2)	Mediastinitis (1)	44	41	Marfan syndrome	Dissection
			Prolonged OTI (1)		65	AHT and COPD	Aneurysm
		Ascending aorta replacement (4)	Trombophlebitis (1)	33	51	Marfan syndrome	Dissection
			None (2)		25	Marfan syndrome	Aneurysm
			AV block (1)		56	None	Aneurysm
			Hybrid technique (<i>debranching</i>) (1)		Postoperative death	7	65
		Wheat surgery (1)	None	32	44	AHT	Aneurysm
		2020	4	Aorta replacement (1)	Death due to lower limb ischemia	Intraoperative death	54
Hybrid technique (<i>debranching</i>) (2)	Prolonged OIT and mediastinitis (1)			18	32	None	Aneurysm
	Death (1)			Intraoperative death	44	Acute coronary syndrome	Dissection
Bentall surgery (1)	None			8	77	AHT	Aneurysm
2019	10	Bentall surgery (7)	None (4)	7	50	AHT (80%) and MRS (1)	Aneurysm
			Death (3)	Intraoperative death	58	AHT and CRF	Aneurysm
				Intraoperative death	34	AHT	Dissection
				Intraoperative death	32	None	Aneurysm
		Hybrid technique (<i>debranching</i>) (2)	None (1)	9	52	AHT	Dissection
			Death (1)	Intraoperative death	56	Emergency and IDH	Dissection
		Ascending aorta replacement (1)	Death (1)	Intraoperative death	59	Haematoma of the ascending aorta	Dissection

TABLE 1. Results of the retrospective analysis of aortic aneurysm surgeries in a public hospital in the province of Buenos Aires, Argentina

AHT: arterial hypertension, AV: atrioventricular, COPD: chronic obstructive pulmonary disease, CRF: chronic renal failure, IDH: intramyocardial dissecting haematoma, MRS: myocardial revascularization surgery, OIT: orotracheal intubation.

REFERENCES

1. García Fuster, R. Aneurisma de aorta ascendente: tratamiento quirúrgico. *Cirugía cardiovascular*. 2015; 22(4):195-199.
2. Guevara E, Bagnati, R, Bastianelli G, Baratta S, Battu C, Bluro I, y cols. Consenso de Patología de la Aorta. *Rev Argent Cardiol* 2023;91 (Suplemento 1):1-97. <http://dx.doi.org/10.7775/rac.es.v91.s1>
3. Erbel R, Aboyans V, Boileau C, Bossone E, di Bartolomeo R, Eggebrecht H, y cols. ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). *Eur Heart J*. 2014;35:2873-2926.

daflon®

fracción flavonoide purificada micronizada

Sentirse imparable

Líder indiscutible en flebología*

Último prospecto
aprobado de Daflon
en código QR



SERVIER
moved by you

*IGVIA C05C Unidades. Nivel Nacional. MAT 03-2023

SERVIER ARGENTINA S.A. Av. Castaños 3222 - C.A.B.A. • Tel: 0800-777 SERVIER (7378437) • www.servier.com.ar