

Editorials

FFR post-PCI: what we learned from the FFR-SEARCH study

In search of excellence in transcatheter and surgical aortic valve implantation

Left atrial appendage occlusion: a decade of evidence

Original articles

Predictors of postprocedural fractional flow reserve: insights from the FFR-SEARCH study

Angiographic and clinical results of the STENTYS Xposition S self-apposing stent. A single-center experience

Percutaneous and surgical aortic valve replacement. Impact of volume and type of center on results

A decade of left atrial appendage closure: from procedural data to long-term clinical benefit

Review article

Percutaneous treatment of pulmonary valve and arteries for the management of congenital heart disease

Debate

Debate: Percutaneous left atrial appendage closure

Perspective from the clinic

Perspective from interventional cardiology

Letters to the Editor

Utility of balloon-assisted tracking in radial arterial access

Prognostic impact of zero coronary calcium score in stable patients

Thrombus aspiration in the left atrial appendage: an option or a walk on the tightrope?

COVID-19 and spontaneous coronary artery dissection: causality?

Clinical case

Shock after immediate TAVI implantation. Do we know what we are dealing with?

How would I approach it?

Case resolution

Images in cardiology

TAVI and compromised left main coronary artery. IVUS-guided "ping-pong" resolution

Complicating a very late stent thrombosis

Percutaneous closure of coronary fistulae using different devices

CONTENTS

VOLUME 3, ISSUE 2, APRIL-JUNE 2021

EDITORIALS

FFR post-PCI: what we learned from the FFR-SEARCH study
Nico H.J. Pijls and Lokien X. van Nunen 83

In search of excellence in transcatheter and surgical aortic valve implantation
Eduardo Pinar Bermúdez 87

Left atrial appendage occlusion: a decade of evidence
Ignacio Cruz-González and David González-Calle 89

ORIGINAL ARTICLES

ISCHEMIC HEART DISEASE

Predictors of postprocedural fractional flow reserve: insights from the FFR-SEARCH study
Laurens J.C. van Zandvoort, Kaneshka Masdjedi, Tara Neleman, María Natalia Tovar Forero, Jeroen Wilschut, Wijnand Den Dekker, Roberto Dietti, Felix Zijlstra, Nicolas M. van Mieghem, and Joost Daemen 91

Angiographic and clinical results of the STENTYS Xposition S self-apposing stent. A single-center experience
Ainhoa Pérez Guerrero, Georgina Fuertes Ferré, Isabel Caballero Jambrina, Juan Sánchez-Rubio, Gabriel Galache Osuna, María Cruz Ferrer Gracia, María Rosario Ortas Nadal, and José Antonio Diarte de Miguel 98

VALVULOPATHY

Percutaneous and surgical aortic valve replacement. Impact of volume and type of center on results
Iván J. Núñez-Gil, Javier Elola, María García-Márquez, José L. Bernal, Cristina Fernández-Pérez, Andrés Íñiguez, Luis Nombela-Franco, Pilar Jiménez-Quevedo, Javier Escaned, Carlos Macaya, and Antonio Fernández-Ortiz 103

STRUCTURAL INTERVENTION

A decade of left atrial appendage closure: from procedural data to long-term clinical benefit
Rafael J. Ruiz-Salmerón, María Ronquillo-Japón, Carlos Robles-Pérez, Manuel Iglesias-Blanco, Carlos Rubio-Iglesias, Rafael García de la Borbolla, César Carrascosa-Rosillo, Sergio Rodríguez de Leiras, Manuel Vizcaíno-Arellano, Irene Méndez-Santos, and Juan Polo-Padillo 112

REVIEW ARTICLE

Percutaneous treatment of pulmonary valve and arteries for the management of congenital heart disease
Federico Gutiérrez-Larraya Aguado, César Abelleira Pardeiro, and Enrique José Balbacid Domingo 119

DEBATE

Debate: Percutaneous left atrial appendage closure. The clinical cardiology perspective
Juan Cosin-Sales 129

Debate: Percutaneous left atrial appendage closure. The interventional cardiology perspective
Tomás Benito-González 131

LETTERS TO THE EDITOR

Utility of balloon-assisted tracking in radial arterial access
Pau Federico Zaragoza, Francisco Pomar Domingo, Teresa Castelló Viguier, Luis Martínez Ortiz de Urbina, and Enrique Peris Domingo 134

Prognostic impact of zero coronary calcium score in stable patients
Víctor Manuel Becerra-Muñoz, Mercedes Millán-Gómez, Germán Berteli-García, José Algarra-García, Nieves Alegre-Bayo, and Manuel Jiménez-Navarro 136

Thrombus aspiration in the left atrial appendage: an option or a walk on the tightrope?
Rafael J. Ruiz-Salmerón, Sergio Rodríguez de Leiras, Rafael García de la Borbolla, César Carrascosa-Rosillo, Manuel Vizcaíno-Arellano, and Carlos Robles-Pérez 139

COVID-19 and spontaneous coronary artery dissection: causality?
Álvaro Aparisi, Cristina Ybarra-Falcón, Pablo Elpidio García-Granja, Aitor Uribarri, Hipólito Gutiérrez, and Ignacio J. Amat-Santos 141

CLINICAL CASE

Shock after immediate TAVI implantation. Do we know what we are dealing with?
M. Isabel Barrionuevo Sánchez, Juan G. Córdoba Soriano, Arsenio Gallardo López, Juan C. García López, Miguel J. Corbí Pascual, and Jesús Jiménez Mazuecos 144

Shock after immediate TAVI implantation. Do we know what we are dealing with? How would I approach it?
Mariano Larman 146

Shock after immediate TAVI implantation. Do we know what we are dealing with? Case resolution
M. Isabel Barrionuevo Sánchez, Juan G. Córdoba Soriano, Arsenio Gallardo López, Juan C. García López, Miguel J. Corbí Pascual, and Jesús Jiménez Mazuecos 148

IMAGES IN CARDIOLOGY

TAVI and compromised left main coronary artery. IVUS-guided "ping-pong" resolution
Iván J. Núñez-Gil, Rafael Vera, Pilar Jiménez-Quevedo, Luis Nombela-Franco, and Antonio Fernández-Ortiz 151

Complicating a very late stent thrombosis
Pablo Salinas, Pedro Martínez-Losas, Hernán Mejía-Rentería, Luis Nombela-Franco, Iván J. Núñez-Gil, and Antonio Fernández-Ortiz 153

Percutaneous closure of coronary fistulae using different devices
Luis Fernández González, Roberto Blanco Mata, Koldobika García San Román, Juan Carlos Astorga Burgo, Aida Acin Labarta, and Josune Arriola Meabe 155

FFR post-PCI: what we learned from the FFR-SEARCH study



RRF tras ICP: ¿qué nos enseña el FFR-SEARCH?

Nico H.J. Pijls,^{a,b} and Lokien X. van Nunen^{a,*}

^a Department of Cardiology, Catharina Hospital Eindhoven, Eindhoven, The Netherlands

^b Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000155>

WHAT DO WE KNOW ABOUT FRACTIONAL FLOW RESERVE AFTER STENTING?

The introduction of the concept of fractional flow reserve (FFR) in the mid 90s moved coronary physiology from experimental science to routine use at the cath lab.¹⁻³ Added to the better understanding of basic physiological mechanisms such as self-regulation and compensatory vasodilation and the coronary flow reserve introduced 20 years earlier by Gould et al.,⁴ FFR has undeniably changed our interpretation of coronary angiograms and had a major influence on the clinical decision-making process, and patient outcomes.^{3,5,6} This has resulted in the unique adoption of FFR as the only physiological index with a class I A indication for use in the clinical practice guidelines produced by the most important cardiologic societies worldwide.^{7,8}

FFR has taught us that coronary angiography and the anatomic images we can acquire at the cath lab only provide moderately reliable measures of the functional significance of coronary artery disease and myocardial ischemia. Also, there is undeniable proof that the decision-making process based on functional measurements leads to better outcomes compared to angiography alone.^{3,5,6}

In contrast, the interpretation of FFR after coronary intervention is still ambiguous. Basically, we should be aware that the status of a coronary artery immediately after a percutaneous coronary intervention (PCI) changes and is prone to much more variability compared to a situation of chronic stable coronary artery disease. An excellent result of a PCI performed today can change rapidly within hours due to thrombus formation, progressive dissection or other unforeseen complications. Therefore, the FFR measured immediately after a PCI should be interpreted with caution. Also, whereas the ischemic FFR threshold (0.80) in the stable angina has been clearly established, FFR values within the first days, weeks or months after a PCI can change quickly due to the healing process in the coronary artery itself, intimal hyperplasia, thrombus formation, etc. This means that by definition, the FFR after a PCI is more dynamic and that an adequate FFR value immediately after a PCI should be considerably higher than 0.80 to compensate for any intravascular changes that may occur in the short-term.

Therefore, it is not surprising to see FFR values of at least 0.90 in medical literature as indicative of an acceptable PCI result.^{9,10} Having said that, at the same time we should realize that most post-stent FFR values in earlier studies were obtained in patients with focal stenosis and without much diffuse disease. It is plausible to think that if diffuse disease is present inside a coronary artery, FFR values ≥ 0.90 will probably not be achieved by just stenting a focal stenosis.

Most likely, in such cases, hyperemic pressure pullback recording (whether motorized or not) or a sophisticated variety called hyperemic pressure pullback gradient will better qualify the functional result after stenting. They will also reveal if the remaining gradients inside the coronary artery are due to insufficient stent deployment or more diffuse disease.¹¹

Despite these limitations, the existence of a clear correlation between the FFR values measured immediately after PCI and long-term outcomes is undeniable. This was first described in the FFR-post-STENT Registry of 750 patients that revealed the existence of an inverse correlation between the FFR values measured immediately after the PCI and the rate of restenosis at the 6-month follow-up (figure 1). Such an inverse correlation between high FFR values post-stenting and the mid-term risk of restenosis has been confirmed ever since.¹² Still, it is not completely clear if suboptimal FFR values after stenting are due to a focal problem in the stented segment or to diffuse disease elsewhere in the artery. Hyperemic pressure pullback recording and pressure pullback gradient recording have proven that a considerable pressure gradient across the stent is often associated with inappropriate deployments as seen on intravascular ultrasounds or optical coherence tomographies.

PATIENT AND VESSEL RELATED PREDICTORS OF POST-PROCEDURAL FFR

At this point, the study conducted by van Zandvoort et al. and recently published on *REC: Interventional Cardiology* comes into perspective.¹⁰ In this study, a large registry of 1000 consecutive

* Corresponding author: Department of Cardiology, Catharina Hospital, P.O. Box 1350, 5602 ZA Eindhoven, The Netherlands.
E-mail address: lokien.v.nunen@catharinaziekenhuis.nl (L.X. van Nunen).

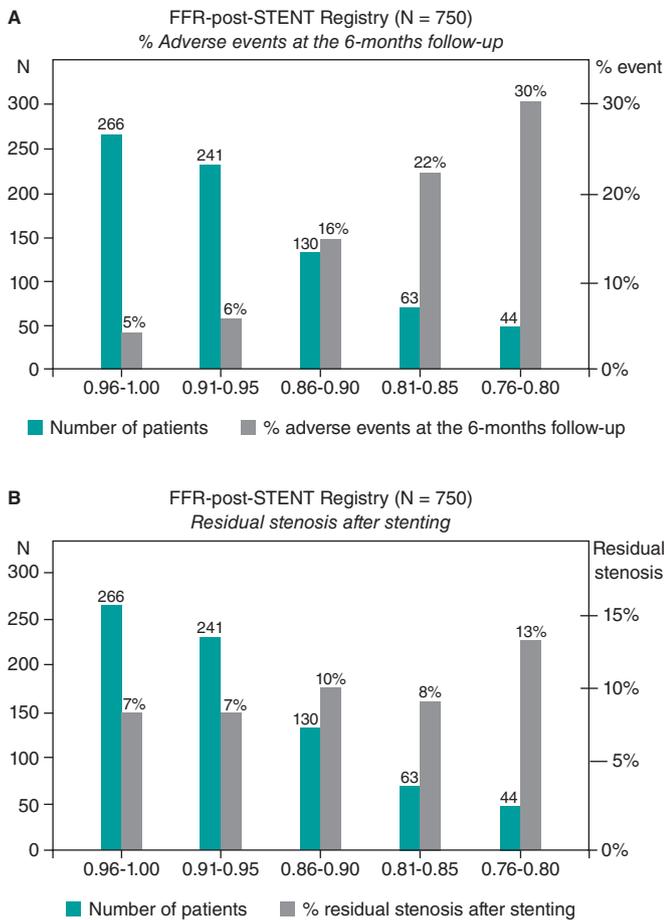


Figure 1. Superiority of functional testing compared to angiography alone to predict the outcomes after stenting. **A:** correlation between post-stenting fractional flow reserve (FFR) and the rate of adverse events at the 6-month follow-up in 750 patients from the FFR-Post-Stent registry. **B:** correlation between post-stenting angiography and the rate of adverse events at the 6-month follow-up. Reproduced with permission from Pijls et al.⁹

patients from 1 large volume cardiac center, the FFR was consistently measured after an angiographically successful PCI without the intention of performing any additional procedures in cases of unexpectedly low FFR values. The authors should be praised for their adherence to this protocol. Afterwards, independent patient and vessel related characteristics were determined as associated with the post-procedural FFR values. Considering that in this study no information was available on the outcomes and that the relationships were not causal *per se* but associative, a few important lessons can be learned.

In the first place, a very strong predictor of lower FFR values was stent implantation in the left anterior descending coronary artery (LAD). In truly normal LADs, the FFR is not different from other arteries and is very close to 1.00.¹³ However, even in cases of mild disease, the FFR values measured in the LAD are often more damaged compared to other arteries. This is explained by the fact that the LAD perfusion territory is large. One of the major advantages of FFR with respect to other methodologies that only address a coronary artery injury is that the FFR does not only measure the stenosis itself, but also the extent of the perfusion territory. If a similar stenosis (with similar angiographic, intravascular ultrasound or optical coherence tomography characteristics) is located in a coronary artery with a larger perfusion territory, the FFR will be lower. In this regard, the FFR is actually the link between stenosis

severity, coronary blood flow, extent of the myocardial perfusion territory, and myocardial ischemia.¹⁴ As such, it is plausible that after a successful PCI, the FFR of the LAD will be somehow lower compared to other coronary arteries.

A second interesting observation is that in women, the FFR measured after apparently successful stenting was often higher compared to the males. Van Zandvoort et al. suggest that this might be due to the fact that in women, microvascular disease plays a more predominant role compared to men. Also, that the generation of a hyperemic gradient within the epicardial coronary artery may be blunted by the presence of microvascular disease.¹⁰ To confirm that position, more detailed studies of coronary microvasculature are needed. For many years, the assessment of microvascular disease in a true quantitative way has been too hard to pin down. However, recently developed methodology has changed that as follows.¹⁵

SIMULTANEOUS ASSESSMENT OF EPICARDIAL AND MICROVASCULAR DISEASE

Recently, the technique for measuring absolute coronary blood flow and microvascular resistance has been introduced as an adjunctive to FFR measurement. This technique is based on the continuous infusion of a saline solution at a low rate and thermodilution. The technique is simple, elegant, accurate, and operator independent.¹⁵

In short, immediately after measuring the FFR, a specifically designed infusion catheter (Rayflow, Hexacath, Paris) is advanced while mounted on the pressure guidewire and placed inside the stent (to study the microvascular resistance of the territory distal to the stent). Then, the infusion of a saline solution at a low rate is started and the absolute coronary blood flow in mL/min is measured in the area of interest using this equation:

$$Q = Q_i \times T/T_i \times 1.08$$

where Q is blood flow in the myocardial territory distal to the stent, Q_i is the infusion rate of the saline solution (mL/min), T_i is the temperature of the infused saline solution ($^{\circ}\text{C}$), and T is the temperature in the distal coronary artery after mixing blood and the saline solution. T and T_i are expressed as the difference with respect to body temperature.

With infusion rates = 8 to 10 mL/min, resting blood flow values are obtained and with infusion rates = 20 mL/min, maximum hyperemic values are obtained since the saline solution itself at that rate induces maximum hyperemia in a matter of seconds (figure 2; unpublished data).

Immediately after the simultaneous measurement of distal coronary pressure and blood flow values, quantitative microvascular resistance R_{μ} (Wood units) is estimated. In this same way, epicardial disease (indicated by FFR) and microvascular disease (indicated by R_{μ}) can be assessed and independently distinguished. The position taken by van Zandvoort et al. suggesting that higher FFR values after PCI are related to a higher microvascular resistance in women could be elegantly validated this way.

WHAT IS THE BEST TECHNIQUE TO MEASURE THE FFR VALUES AFTER A PCI?

In the study conducted by van Zandvoort et al. the FFR values measured after the PCI are only briefly described.¹⁰ The authors do not report if hyperemic pressure pullback recordings were performed or other techniques used to assess the entire artery. Also, we should mention that to measure intracoronary pressure, not a

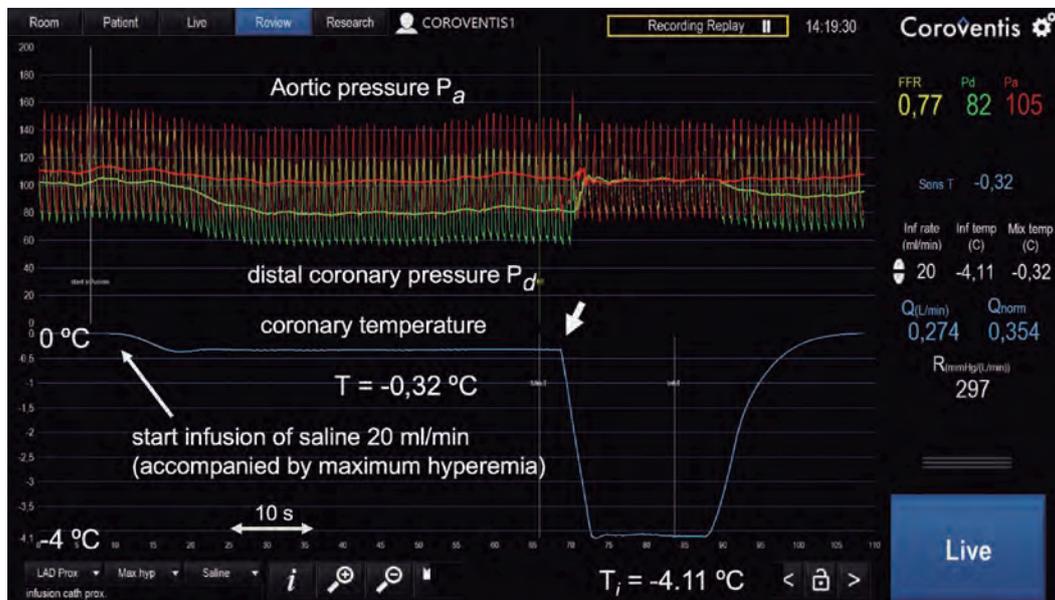


Figure 2. Example of absolute coronary blood flow and microvascular resistance measurement in left anterior descending coronary artery following routine fractional flow reserve measurement. On the figure upper side, aortic pressure (P_a), and distal coronary pressure (P_d) are shown in red and green, respectively. The blue line represents coronary temperature as a difference with respect to body temperature ($T = 0$). After starting the infusion of 20 mL/min of a saline solution (Q) at room temperature through a dedicated infusion catheter, maximum hyperemia occurs within seconds. Then, after a complete mix of blood and saline solution, a steady-state distal coronary temperature T of 0.32 °C below body temperature is achieved. After withdrawing the pressure/temperature sensor from the tip of the infusion catheter, the infusion temperature (T_i) measured is 4.11 °C below body temperature. Absolute flow (Q) in the coronary artery is calculated using the equation shown in this article (274 mL/min). Microvascular resistance is simply calculated now by P_d/Q and equals 297 Wood units, which is a normal value for the anterior wall. Since the fractional flow reserve value is also known, the normal reference value of coronary flow can be calculated. All parameters are shown online supported by dedicated software (Coroventis, Sweden).

single true pressure guidewire was used, but the Navvus system instead (ACIST Medical Systems, Eden Prairie, MN, United States). This system is known to overestimate pressure gradients and underestimate FFR mildly in cases of minimal disease or moderately in cases of more severe disease.¹⁶ Also, this system is not validated against regular pressure guidewires in post-PCI vessels.

Nevertheless, the measurements were taken meticulously using IV adenosine at a rate of 140 $\mu\text{g}/\text{kg}/\text{min}$, giving the opportunity of an easy and reliable estimation of the FFR under stable conditions. We should mention that only 2 out of 1000 patients showed adenosine intolerance, meaning that the infusion of adenosine had to be interrupted due to harmless adenosine-induced, angina-like chest pain. This underlines the safety profile of IV adenosine infusions as seen in tens of thousands of patients in a myriad of other studies.

In future studies on the meaning and interpretation of post-PCI FFR, it would be advisable to perform hyperemic pressure pullback recordings as outlined in the first part of this article or use the even more sophisticated technique for whole vessel evaluation after PCI recently introduced by Collet et al. and called hyperemic pressure pullback gradient.¹¹ Obviously, all pressure analyses performed inside the stented coronary artery should preferably be performed at maximum hyperemia since gradients at rest inside the artery are 2 to 3 times smaller. Consequently, the signal-to-noise ratio of a resting pullback recording is 2 to 3 times less sensitive.

In conclusion, although outcome data were not presented which, by the way, was not the objective of the study, the interesting trial conducted by van Zandvoort et al.¹⁰ teaches us about several interesting patient and vessel related predictors of post-procedural FFR measurement. Also, it anticipates the need for future physiological studies to unravel the different factors involved using new research

methods on coronary circulation like hyperemic pressure pullback gradients and truly quantitative microvascular resistance (R_{μ}) measurements.

FUNDING

No funding whatsoever with regards to this article.

CONFLICTS OF INTEREST

N.H.J. Pijls has received institutional research grants from Abbott and Hexacath. Also, he is a consultant for Abbott, Opsens, and General Electric, and a minor stockholder of Philips, GE, ASML, and Heartflow. L.X. van Nunen declared no conflicts of interest whatsoever.

REFERENCES

1. Pijls NH, van Son JA, Kirkeeide RL, De Bruyne B, Gould KL. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. *Circulation*. 1993;87:1354-1367.
2. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. *N Engl J Med*. 1996;334:1703-1708.
3. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213-224.
4. Gould KL, Lipscomb K, Hamilton GW. Physiologic basis for assessing critical coronary stenosis. Instantaneous flow response and regional

- distribution during coronary hyperemia as measures of coronary flow reserve. *Am J Cardiol.* 1974;33:87-94.
5. De Bruyne B, Fearon WF, Pijls NH, et al. Fractional flow reserve-guided PCI for stable coronary artery disease. *N Engl J Med.* 2014;371:1208-1217.
 6. Zimmermann FM, Omerovic E, Fournier S, et al. Fractional flow reserve-guided percutaneous coronary intervention vs. medical therapy for patients with stable coronary lesions: meta-analysis of individual patient data. *Eur Heart J.* 2019;40:180-186.
 7. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41:407-477.
 8. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for T. *J Am Coll Cardiol.* 2017;69:2212-2241.
 9. Pijls NH, Klauss V, Siebert U, et al. Coronary Pressure Measurement After Stenting Predicts Adverse Events at Follow-Up. *Circulation.* 2002;105:2950-2954.
 10. van Zandvoort LJC, Masdjedi K, Neleman T, et al. Predictors of postprocedural fractional flow reserve: insights from the FFR-SEARCH study. *REC Interv Cardiol.* 2021;3:91-97.
 11. Collet C, Sonck J, Vandelloo B, et al. Measurement of Hyperemic Pullback Pressure Gradients to Characterize Patterns of Coronary Atherosclerosis. *J Am Coll Cardiol.* 2019;74:1772-1784.
 12. Rimac G, Fearon WF, De Bruyne B, et al. Clinical value of post-percutaneous coronary intervention fractional flow reserve value: A systematic review and meta-analysis. *Am Heart J.* 2017;183:1-9.
 13. Pijls NH, Van Gelder B, Van der Voort P, et al. Fractional flow reserve. A useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. *Circulation.* 1995;92:3183-3193.
 14. De Bruyne B, Hersbach F, Pijls NH, et al. Abnormal epicardial coronary resistance in patients with diffuse atherosclerosis but 'Normal' coronary angiography. *Circulation.* 2001;104:2401-2406.
 15. Xaplanteris P, Fournier S, Keulards DC, et al. Catheter-Based Measurements of Absolute Coronary Blood Flow and Microvascular Resistance: Feasibility, Safety, and Reproducibility in Humans. *Circ Cardiovasc Interv.* 2018;11:e006194.
 16. Wijntjens GW, van de Hoef TP, Kraak RP, et al. The IMPACT Study (Influence of Sensor-Equipped Microcatheters on Coronary Hemodynamics and the Accuracy of Physiological Indices of Functional Stenosis Severity). *Circ Cardiovasc Interv.* 2016;9:e004645.

In search of excellence in transcatheter and surgical aortic valve implantation



A la búsqueda de la excelencia en el implante percutáneo de la válvula aórtica... y también en el quirúrgico

Eduardo Pinar Bermúdez*

Sección de Hemodinámica, Servicio de Cardiología, Hospital Clínico Universitario Virgen de la Arrixaca, El Palmar, Murcia, Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000154>

The management of symptomatic severe aortic stenosis is based on surgical aortic valve replacement (SAVR) or transcatheter aortic valve implantation (TAVI).

In an interesting work recently published on *REC: Interventional Cardiology*, Núñez-Gil et al.¹ studied how the type of hospital and volume of cases impacted the results obtained with both techniques. This was a retrospective analysis with data gathered from administrative sources with the limitations associated with studies based on the Minimum Basic Dataset. Nonetheless, it leaves important messages that should be discussed.

In line with other publications,² they describe the correlation between casuistry, case volume, and results in terms of mortality and risk-adjusted hospital stays. This article is original and important because in Spain, no study like this has ever been conducted on the association between the volume of TAVIs performed and results.

Also, they confirm the existence of a favorable correlation between better TAVI results and in-hospital «structural» variables like the availability of cardiac surgery intensive care units (CICU). The authors stress the importance behind the finding that there is a correlation between the presence of a CICU and a lower mortality rate with both techniques. However, this impact is greater with TAVI compared to SAVR. Actually, having defined protocols and staff trained in the rapid detection and management of periprocedural complications like vascular access hemorrhages, atrioventricular blocks, renal failure, etc. would explain this correlation.

Data from this study show that the risk-adjusted in-hospital mortality rate is lower in large volume centers and high-level hospitals («type 4»). It is logical to think that large volume PCI-capable centers with all their resources and wide experience in coronary and structural heart procedures will have good results. Performing a high number of procedures reduces procedural complications. However, achieving a solid learning curve first is essential to have good clinical results and increase the cost-effectiveness of the procedures. However, nowadays, the learning curve is shorter with the new devices available.

On the other hand, they found that large volume centers that perform TAVIs and also quite a few SAVRs have a lower mortality rate with percutaneous procedures. The large casuistry with both procedures

and the extensive experience of interventional cardiologists and surgeons improves the results. This may be explained by the benefits derived from the mutual collaboration between interventional cardiologists and surgeons regarding the selection of the most appropriate cases for each technique or because surgeons who perform more surgeries have a greater expertise to solve eventual TAVI complications. Still, the need for surgery today is very low.^{3,4} It may also be suggested that these hospitals have a greater surgical activity because they receive a large number of patients with severe aortic stenosis (some treated with SAVR and others with TAVI).

Hospitals that perform large volumes of TAVIs but very few surgeries also have good results. Therefore, it does not seem to be a factor directly associated with surgical activity *per se*, but rather with the experience of interventional cardiologists and the writing of proper protocols before, during, and after the procedure.

Consistent with all this, the authors also say that the availability of a CICU is important in the results of TAVI because it guarantees proper treatment after the procedure.

The importance of this article is undeniable, and its findings are very interesting. However, its conclusions should be interpreted with caution. On the one hand, there is too much heterogeneity among the hospitals studied. On the other hand, there may be biases and factors that still remain unstudied. Some of the possible biases may be that patients treated with TAVI in type 3 hospitals without CICU capabilities may have higher comorbidity rates. Also, there are variables not included in the study that may impact the results like the analysis of the valves used or the timeframe of the process analyzed in each hospital, which could also impact the results differently depending on the timing of the learning curve.

The correlation between volume and results has already been proven in other studies.⁵ However, it seems to decrease in time with more experience, better hospital processes, and more advanced technologies.

Also, there are important additional questions that should be taken into consideration like the analysis of other complications that were not included in the study (eg, need for pacemaker, onset of renal failure, etc.).

* **Corresponding author:** Servicio de Cardiología, Hospital Clínico Universitario Virgen de la Arrixaca, Ctra. Madrid-Cartagena s/n, 30120 El Palmar, Murcia, Spain. E-mail address: epbhva@yahoo.es (E. Pinar Bermúdez).

Over 4000 annual TAVIs are performed in Spain every year in nearly 110 hospitals by interventional cardiologists who, in collaboration with clinical cardiologists, imaging specialists, and other health professionals—geriatrician, anesthesiologists, intensivists, surgeons, radiologists—achieve excellent results that have been improving throughout the years.

As a consequence of these and other data published, TAVIs should only be performed after proper training, in large enough numbers, and with good results.^{6,7}

In conclusion, the article of Núñez-Gil et al.¹ is an interesting study that shows the commitment of interventional cardiologists to optimize the results of TAVI. A commitment that is already a reality in many Spanish cath labs.

FUNDING

No funding was received for this work.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Núñez-Gil IJ, Elola J, García-Márquez M, et al. Reemplazo valvular aórtico percutáneo y quirúrgico. Influencia del volumen y del tipo de centro tratante en los resultados. *REC Interv Cardiol.* 2021;3:103-111.
2. Kaier K, Oettinger V, Reinecke H, et al. Volume–outcome relationship in transcatheter aortic valve implantations in Germany 2008–2014: a secondary data analysis of electronic health records. *BMJ Open.* 2018;8:e020204.
3. Cid A, Rodríguez Leor O, Moreno R, Pérez de Prado A. Registro Español de Hemodinámica y Cardiología Intervencionista. XXVIII Informe Oficial de la Sección de Hemodinámica y Cardiología Intervencionista de la Sociedad Española de Cardiología (1990-2018). *Rev Esp Cardiol.* 2019;72:1043-1053.
4. Jiménez-Quevedo P, Muñoz-García A, Trillo-Nouche R, et al. Evolución temporal en el tratamiento transcatheter de la estenosis aórtica: análisis del registro español de TAVI. *REC Interv Cardiol.* 2020;2:98-105.
5. Arora S, Strassle PD, Qamar A, et al. Trends in inpatient complications after transcatheter and surgical aortic valve replacement in the transcatheter aortic valve replacement era. *Circ Cardiovasc Interv.* 2018;11:e007517.
6. Eggebrecht H, Mehta RH, Haude M, et al. Transcatheter aortic valve implantation (TAVI) by centres with and without an on-site cardiac surgery programme: preliminary experience from the German TAVI registry. *EuroIntervention.* 2014;10:602-608.
7. Tamburino CI, Barbanti M, Tamburino C. Transcatheter aortic valve implantation: how to decrease post-operative complications. *Eur Heart J Suppl.* 2020;22(Suppl E):E148-E152.

Left atrial appendage occlusion: a decade of evidence

Cierre percutáneo de la orejuela izquierda: una década de evidencias

Ignacio Cruz-González^{a,b,*} and David González-Calle^{a,b}

^a Servicio de Cardiología, Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Salamanca, Spain

^b CIBER de Enfermedades Cardiovasculares (CIBERCV), Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000187>

Over the last few years, left atrial appendage occlusion (LAAO) has gained traction in patients with nonvalvular atrial fibrillation as an alternative to oral anticoagulation to prevent cerebral infarction, especially in patients with some sort of contraindication to these drugs.¹

In an article published in *REC: Interventional Cardiology*, Ruiz-Salmerón et al.² describe their experience using this technique during the last 10 years. This publication gives us the opportunity to review the cumulative scientific evidence available in this regard that has justified its exponential growth.

In the last national registry published in the United States, the number of physicians and hospitals that perform this intervention has gone from 30 to over 1200 and from 20 to over 400, respectively, within the last 2 years.³ In Spain, according to the registry published by the Interventional Cardiology Association of the Spanish Society of Cardiology, the number of procedures performed within the last 4 years has tripled.⁴

Left atrial appendage isolation started as a surgical technique back in the 1950s,⁵ but it was not until the beginning of 2000 when the development of percutaneous interventional procedures finally put this technique on the map.⁶ However, the turning point was 2009 with the publication of the multicenter and randomized PROTECT AF clinical trial⁷ that compared the LAAO in over 450 patients implanted with the Watchman device (Boston Scientific, United States) vs conventional treatment with warfarin. It proved the non-inferiority of the intervention for the primary composite of stroke, cardiovascular death or systemic embolism.⁵ Five years later, the PREVAIL trial⁸, with a similar design to the PROTECT AF, achieved similar results regarding efficacy, but with success rates over 95% and significantly less common complications (1.9%).

The mid-term follow-up results are even more interesting. At the 3.8-year follow-up, the patients of the PROTECT AF⁹ experienced a significant benefit in the composite primary endpoint (8.4% vs 13.9%; hazard ratio = 0.61; 95% confidence interval, 0.38-0.97; $P = .04$) compared to the control group with warfarin. Actually, even all-cause mortality improved in the LAAO group (12.3% vs 18%; hazard ratio = 0.66; 95% confidence interval, 0.45-0.98; $P = .04$).

Also, the third large randomized clinical trial, the PRAGUE-17,¹⁰ that compared LAAO with direct-acting oral anticoagulants in 400 patients, proved the non-inferiority of this procedure compared to new anticoagulants to prevent cardiovascular, neurological or hemorrhagic events associated with atrial fibrillation.

A meta-analysis of these randomized clinical trials proved that LAAO has similar cerebral infarction rates to those of oral anticoagulation (warfarin or new anticoagulants) with significant reductions of cerebral hemorrhages and cardiac and non-cardiac death.¹¹

Added to this, large scale multicenter registries have proven the efficacy and safety of this intervention in patients with contraindications to oral anticoagulation. The EWOLUTION registry of 1021 patients reported a 62% rate of contraindication to oral anticoagulation, a 98.5% success rate, and a 2.7% rate of complications.¹² At the 2-year follow-up, cerebral infarction rates of 1.3/100 patients-year (a 83% reduction compared to the historic series) and hemorrhage rates of 2.7/100 patients-year (a 46% reduction compared to the historic series) were reported.¹³ In line with this, the multicenter registry of the Amulet device (Abbott, United States) that included 1088 patients of whom 83% had contraindications to oral anticoagulation revealed a 99% success rate and a 3.2% rate of complications.¹⁴ These results are consistent with almost all the studies published over the last decade.

In our setting we have registries like the one published in this issue of *REC: Interventional Cardiology*, where Ruiz-Salmerón et al.² analyze 260 consecutive cases of LAAO in a population of high embolic (CHA₂DS₂-VASC of 4.3 ± 1.6) and hemorrhagic risk (HAS-BLED of 3.7 ± 1.2). They confirmed a 75.5% reduction of embolic risk and a 58.5% reduction of hemorrhagic risk with respect to the risk predicted by both scales. Also, patients with longer follow-up periods (> 4 years in this case) showed a progressive benefit derived from the intervention (rate of events per 100 patients-year: 0.7 vs 2.0, $P = .17$ for embolisms; and 1.7 vs 4.0, $P = .09$ for major hemorrhages) compared to those with shorter follow-up periods.

Studies like this are necessary since we don't have too many studies on long-term experiences with LAAO with mean follow-up periods

* Corresponding author: Servicio de Cardiología, Hospital Universitario de Salamanca, P.º San Vicente 58-182, 37007 Salamanca, Spain.

E-mail address: cruzgonzalez.ignacio@gmail.com (I. Cruz-González).

Online: 18-02-2021.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.



> 2.5 years. It is only from this long-term follow-up perspective that we will be able to understand the impact of an intervention largely, based on the prophylaxis of the thromboembolic complications that may occur during a patient's lifetime.

Finally, we should mention that scientific societies like the European Heart Rhythm Association and the European Association of Percutaneous Cardiovascular Interventions¹⁵ support the benefits of LAAO in situations of contraindication to oral anticoagulation, high risk of bleeding, cerebral infarction under anticoagulation or even in patients who, after being properly informed, reject oral anticoagulation. However, the current clinical practice guidelines published by the European Society of Cardiology¹ still assign a low level of recommendation (IIb-B) for patients with atrial fibrillation contraindicated to long-term courses with oral anticoagulants (eg, patients with intracranial hemorrhages without reversible cause). In any case, the results of 2 ongoing large scale randomized clinical trials of LAAO vs direct-acting oral anticoagulants, the CHAMPION-AF (NCT04394546) and the CATALYST (NCT04226547) will conclusively establish the level of recommendation of this technique in patients without contraindications to oral anticoagulation.

In conclusion, we should assert that the LAAO is an effective and safe technique. With the cumulative data obtained over the last decade, its utility is undeniable in patients with atrial fibrillation who cannot take oral anticoagulation to prevent the occurrence of strokes. Also, clinical trials have proven its advantages vs warfarin, and even the long-term follow-up of these patients has offered significant positive results, even reducing mortality rate compared to oral anticoagulation. The results of the new clinical trials vs direct-acting oral anticoagulants will determine the large-scale future of this procedure.

FUNDING

I. Cruz-González has received research grants from the *Instituto de Salud Carlos III* (PI19/00658) and the regional health management of the Board of Castille and León (GRS 3031/A/19).

CONFLICTS OF INTEREST

I. Cruz-González is a *proctor* for Boston Scientific, Lifetech and Abbott, and a consultant for IHT and Qatnamedical. D. González-Calle declared no conflicts of interest whatsoever.

REFERENCES

- Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2021;42:373-498.
- Ruiz-Salmerón RJ, Ronquillo-Japón M, Carlos Robles-Pérez, et al. Una década de cierre percutáneo de la orejuela izquierda: desde el procedimiento hasta el beneficio a largo plazo. *REC Interv Cardiol.* 2021;3:112-118.
- Freeman JV, Varosy P, Price MJ, et al. The NCDR Left Atrial Appendage Occlusion Registry. *J Am Coll Cardiol.* 2020;75:1503-1518.
- Ojeda S, Romaguera R, Cruz-González I, Moreno R. Spanish Cardiac Catheterization and Coronary Intervention Registry. 29th Official Report of the Interventional Cardiology Association of the Spanish Society of Cardiology (1990-2019). *Rev Esp Cardiol.* 2020;12:927-936.
- Madden JL. Resection of the left auricular appendix; a prophylaxis for recurrent. *J Am Med Assoc.* 1949;140:769-772.
- Sievert H, Lesh MD, Trepels T, et al. Percutaneous left atrial appendage transcatheter occlusion to prevent stroke in high-risk patients with atrial fibrillation: Early clinical experience. *Circulation.* 2002;105:1887-1889.
- Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet.* 2009;374:534-542.
- Holmes DR, Kar S, Price MJ, et al. Prospective randomized evaluation of the watchman left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: The PREVAIL trial. *J Am Coll Cardiol.* 2014;64:1-12.
- Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. *JAMA.* 2014;312:1988-1998.
- Osmancik P, Herman D, Neuzil P, et al. Left Atrial Appendage Closure Versus Direct Oral Anticoagulants in High-Risk Patients With Atrial Fibrillation. *J Am Coll Cardiol.* 2020;75:3122-3135.
- Turagam MK, Osmancik P, Neuzil P, Dukkupati SR, Reddy VY. Left Atrial Appendage Closure Versus Oral Anticoagulants in Atrial Fibrillation. *J Am Coll Cardiol.* 2020;76:2795-2797.
- Boersma LVA, Schmidt B, Betts TR, et al. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. *Eur Heart J.* 2016;37:2465-2474.
- Boersma LV, Ince H, Kische S, et al. Evaluating Real-World Clinical Outcomes in Atrial Fibrillation Patients Receiving the WATCHMAN Left Atrial Appendage Closure Technology: Final 2-Year Outcome Data of the EWOLUTION Trial Focusing on History of Stroke and Hemorrhage. *Circ Arrhythmia Electrophysiol.* 2019;12:e006841.
- Landmesser U, Schmidt B, Nielsen-Kudsk JE, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: Periprocedural and early clinical/echocardiographic data from a global prospective observational study. *EuroIntervention.* 2017;13:867-876.
- Glikson M, Wolff R, Hindricks G, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion — an update. *EuroIntervention.* 2020;15:1133-1180.



Predictors of postprocedural fractional flow reserve: insights from the FFR-SEARCH study

Laurens J.C. van Zandvoort, Kaneshka Masdjedi, Tara Neleman, Maria Natalia Tovar Forero, Jeroen Wilschut, Wijnand Den Dekker, Roberto Diletti, Felix Zijlstra, Nicolas M. van Mieghem, and Joost Daemen*

Department of Cardiology, Erasmus MC, Rotterdam, The Netherlands

SEE RELATED CONTENT:
<https://doi.org/10.24875/RECICE.M20000197>

ABSTRACT

Introduction and objectives: Patients with a low post-percutaneous coronary intervention (PCI) fractional flow reserve (FFR) are at a higher risk for future adverse cardiac events. The objective of the current study was to assess specific patient and procedural predictors of post-PCI FFR.

Methods: The FFR-SEARCH study is a prospective single-center registry of 1000 consecutive all-comer patients who underwent FFR measurements after an angiographically successful PCI with a dedicated microcatheter. Mixed effects models were used to search for independent predictors of post-PCI FFR.

Results: The mean post-PCI distal coronary pressure divided by the aortic pressure (Pd/Pa) was 0.96 ± 0.04 and the mean post-PCI FFR, 0.91 ± 0.07 . After adjusting for the independent predictors of post-PCI FFR, the left anterior descending coronary artery as the measured vessel was the strongest predictor of post-PCI FFR (adjusted $\beta = -0.063$; 95%CI, -0.070 to -0.056; $P < .0001$) followed by the postprocedural minimum lumen diameter (adjusted $\beta = 0.039$; 95%CI, 0.015-0.065; $P = .002$). Additionally, male sex, in-stent restenosis, chronic total coronary occlusions, and pre- and post-dilatation were negatively associated with postprocedural FFR. Conversely, type A lesions, thrombus-containing lesions, postprocedural percent stenosis, and stent diameter were positively associated with postprocedural FFR. The R^2 for the complete model was 53%.

Conclusions: Multiple independent patient and vessel related predictors of postprocedural FFR were identified, including sex, the left anterior descending coronary artery as the measured vessel, and postprocedural minimum lumen diameter.

Keywords: Percutaneous coronary intervention. Post-PCI FFR. Predictors.

Predictores de la reserva de flujo fraccional posprocedimiento: subanálisis del estudio FFR-SEARCH

RESUMEN

Introducción y objetivos: Los pacientes con una reserva fraccional de flujo (FFR) posintervención coronaria percutánea (ICP) baja tienen mayor riesgo de futuros eventos cardíacos adversos. El objetivo del presente estudio fue evaluar predictores específicos de pacientes y procedimientos de FFR tras una ICP.

Métodos: El estudio FFR-SEARCH es un registro prospectivo de un solo centro que incluyó 1.000 pacientes consecutivos que se sometieron a una evaluación de la FFR tras una ICP con éxito angiográfico utilizando un microcatéter específico. Se utilizaron modelos de efectos mixtos para buscar predictores independientes de FFR tras la ICP.

Resultados: La media de presión distal dividida entre la presión aórtica tras la ICP fue de $0,96 \pm 0,04$, y la media de la FFR tras la ICP fue de $0,91 \pm 0,07$. Tras ajustar por predictores independientes de FFR tras la ICP, la arteria descendente anterior izquierda como vaso medido fue el predictor más fuerte (β ajustado = $-0,063$; IC95%, $-0,070$ a $-0,056$; $p < 0,0001$), seguida del diámetro luminal mínimo posprocedimiento (β ajustado = $0,039$; IC95%, $0,015$ a $0,065$; $p = 0,002$). Además, el sexo masculino, la reestenosis del *stent*, las oclusiones totales crónicas y la pre- y posdilatación se correlacionaron negativamente con la FFR posprocedimiento. Por el contrario, las lesiones de tipo A, las lesiones con trombos, el porcentaje de estenosis posprocedimiento y el diámetro del *stent* se correlacionaron positivamente con la FFR posprocedimiento. El R^2 para el modelo completo fue del 53%.

* **Corresponding author:** Department of Cardiology, Room Rg-628, Erasmus University Medical Center, P.O. Box 2040. 3000 CA Rotterdam, The Netherlands. E-mail address: j.daemen@erasmusmc.nl (J. Daemen).

Received 21 May 2020. Accepted 10 July 2020. Online: 27-10-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Conclusiones: Se identificaron diversos predictores independientes relacionados con los pacientes y con los vasos para la FFR posprocedimiento, incluyendo el sexo, la arteria descendente anterior izquierda como vaso medido y el diámetro luminal mínimo posprocedimiento.

Palabras clave: Intervención coronaria percutánea. FFR post-ICP. Predictores.

Abbreviations

FFR: fractional flow reserve. **LAD:** left anterior descending coronary artery. **MLD:** minimum luminal diameter. **PCI:** percutaneous coronary intervention.

INTRODUCTION

The limitations of an accurate assessment of the hemodynamic significance of coronary artery lesions through angiographic guidance alone are well-known.¹ Instead, the fractional flow reserve (FFR) has proven to be a useful technique to address the coronary physiology and the hemodynamic significance of coronary segments before and after performing an intervention.²⁻⁴ Also, measuring FFR post-stenting has proven to be a strong and independent predictor of major adverse cardiovascular events at the 2-year follow-up.³⁻⁵

While FFR primarily takes into account the relative luminal narrowing and the amount of viable myocardium perfused by a specific vessel, several factors have been shown to impact the FFR values prior to performing a percutaneous coronary intervention (PCI). Therefore, longer lesion length, high syntax scores, calcifications, and tortuosity are associated with significantly lower FFR values. Conversely, the presence of microvascular dysfunction, chronic kidney disease and female gender have been associated with higher FFR values.⁶⁻¹¹

At the present time, there is lack of data on independent predictors of post-PCI FFR. Therefore, the objective of the present study was to assess the patient and procedural characteristics associated with low post-PCI FFR in an all-comer patient population.

METHODS

The FFR-SEARCH study is a prospective single-center registry that assessed the routine distal pressure divided by the aortic pressure (Pd/Pa) and FFR values of all consecutive patients after an angiographically successful PCI. The primary endpoint was to study the impact of post-PCI FFR on the rate of major adverse cardiovascular event at the 2-year follow-up. Accordingly, no further actions were taken to improve post-PCI FFR. The study was performed in full compliance with the Declaration of Helsinki. The study protocol was approved by the local ethics committee. All patients gave their written informed consent to undergo the procedure. Also, anonymous datasets for research purposes were used in compliance with the Dutch Medical Research Act. A total of 1512 patients treated between March 2016 and May 2017 at the Erasmus Medical Center were eligible to enter our study. A total of 504 of these patients were excluded due to hemodynamic instability (156), a rather small distal outflow (129), the operator's decision not to proceed with post-PCI hemodynamic assessment (148) or other reasons (79). A total of 1000 patients were included in the study. The microcatheter could not cross the treated lesion in 28 patients, technical issues with the catheter prevented post-PCI assessments in 11 patients,

and in 2 patients the post-PCI FFR measurements had to be aborted prematurely due to adenosine intolerance. This left 959 patients whose post-PCI FFR values were measured in at least 1 angiographically successfully treated lesion.

Quantitative coronary angiography

The preprocedural lesion type was defined according to the ACC/AHA guidelines¹² and divided into 4 categories: A, B1, B2, and C. Comprehensive quantitative coronary angiography analyses were performed pre- and post-stent implantation in all the treated lesions. An angiographic view with minimal foreshortening of the lesion and minimal overlapping with other vessels was selected. Similar angiographic views were used pre- and post-stent implantation. Measurements included pre- and postprocedural percent diameter stenosis, reference vessel diameter, lesion length, and minimum luminal diameter (MLD). In case of a total occlusion in patients presenting with ST-segment elevation myocardial infarction (STEMI) or chronic total coronary occlusion (CTO), the MLD was considered zero and the percent diameter stenosis, 100%. The reference vessel diameter and the lesion length were measured from the first angiographic view with restored flow. All measurements were taken using CAAS for Windows, version 2.11.2 (Pie Medical Imaging, The Netherlands).

Fractional flow reserve measurements

All FFR measurements were acquired using the Navvus RXi system (ACIST Medical Systems, United States), a dedicated FFR microcatheter with optical pressure sensor technology.^{13,14} Measurements were performed after an intracoronary bolus of nitrates (200 µg). The catheter was advanced while mounted over the previously used guidewire approximately 20 mm distal to the most distal border of the stent. The FFR was defined as the mean distal coronary artery pressure divided by the mean aortic pressure during maximum hyperemia achieved by the continuous IV infusion of adenosine at a rate of 140 µg/kg/min via the antecubital vein. In this study no vessels were assessed using intracoronary adenosine.

Statistical analysis

At baseline, the categorical variables were expressed as counts (percentage) and the continuous ones as mean ± standard deviation. To assess the independent predictors of post-PCI FFR, all the patient and vessel characteristics were primarily assessed through an univariate test using a mixed effects model (LME-model) with a random effect for the patients and a fixed effect for the post-PCI FFR. All

Table 1. Baseline patient and vessel characteristics

Variable	Total FFR-SEARCH registry	Variable	Total FFR-SEARCH registry
Patient characteristics	(N = 1000)	<i>Bifurcation</i>	138 (12)
<i>Age</i>	64.6 ± 11.8	<i>Calcified</i>	402 (35)
<i>Sex, male</i>	725 (73)	<i>In-stent restenosis</i>	39 (3)
<i>Hypertension</i>	515 (52)	<i>Thrombus</i>	214 (18)
<i>Hypercholesterolemia</i>	451 (45)	<i>Stent thrombosis</i>	14 (1)
<i>Diabetes</i>	191 (19)	<i>Ostial</i>	97 (8)
<i>Smoking history</i>	499 (50)	<i>CTO</i>	42 (4)
<i>Previous stroke</i>	77 (8)	<i>Stenosis pre procedural</i>	69 ± 22
<i>Peripheral arterial disease</i>	76 (8)	<i>Reference diameter pre procedural (mm)</i>	2.6 ± 0.6
<i>Previous myocardial infarction</i>	203 (20)	<i>Length pre procedural (cm)</i>	21 ± 11
<i>Previous PCI</i>	264 (26)	<i>MLD pre (mm)</i>	0.9 ± 0.6
<i>Previous CABG</i>	57 (6)	<i>Predilatation</i>	769 (66)
<i>Indication for PCI</i>		<i>Postdilatation</i>	691 (59)
Stable angina	304 (30)	<i>Stenosis post procedural</i>	44 ± 13
NSTEMI	367 (37)	<i>Reference diameter post procedural (mm)</i>	2.7 ± 0.5
STEMI	329 (33)	<i>Length post procedural (cm)</i>	24 ± 13
Vessel characteristics	(N = 1165)	<i>MLD post procedural (mm)</i>	2.6 ± 0.5
<i>Lesion type</i>		<i>Number of stents</i>	1.4 ± 0.6
A	125 (11)	<i>Stent length (cm)</i>	29 ± 17
B1	233 (20)	<i>Stent diameter (mm)</i>	3.2 ± 0.5
B2	379 (33)	<i>Mean post-PCI Pd/Pa</i>	0.96 ± 0.04
C	428 (37)	<i>Mean post-PCI FFR</i>	0.91 ± 0.07
<i>LAD</i>	593 (51)		

CABG, coronary artery bypass graft; CTO, chronic total coronary occlusion; FFR, fractional flow reserve; LAD, left anterior descending artery; MLD, minimum luminal diameter; NSTEMI, non-ST segment elevation acute myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; Pd/Pa, ratio of mean distal coronary artery pressure to mean aortic pressure; Values are expressed as mean ± standard deviation or no. (%).

variables were subsequently inserted in a multivariate LME-model using the enter method that resulted in all the significant independent predictors of post-PCI FFR values. A forest plot was developed to depict all variables with the corresponding 95% confidence intervals (95%CI). Beta (β) values show the average increase or decrease of the FFR values in the case of dichotomous variables or the increment per unit increase in the case of continuous variables. Statistical analyses were performed using the statistical software package R (version 3.5.1, packages: Hmisc, lme4 and nlme, RStudio Team, United States).

RESULTS

Demographic characteristics

The mean age was 64.6 ± 11.8 years and 72.5% were males. In 959 patients, at least, 1 lesion was measured with an overall 1165 successfully treated and measured lesions. The patient demographics and baseline characteristics are shown on [table 1](#). Up to 70% of the patients presented with an acute coronary syndrome, and 18% had confirmed thrombus as seen on the angiography. Intravascular

imaging modalities were used in 9.6% of the patients to guide the procedure. Overall, 1.4 ± 0.6 lesions were treated per patient and in 1.2 ± 0.5 lesions per patient the post-PCI FFR was successfully assessed. The average overall stent length per vessel was 29 mm ± 17 mm with an average stent diameter of 3.2 mm ± 0.5 mm.

The mean post-PCI FFR was 0.91 ± 0.07 and 7.7% of vessels had a post-PCI FFR ≤ 0.80. In the LME-model and after adjusting for independent predictors of post-PCI FFR, the left anterior descending coronary artery (LAD) as the measured vessel was the strongest predictor of post-PCI FFR (adjusted β = -0.063; 95%CI, -0.070 to -0.056; P < .0001) followed by the postprocedural MLD (adjusted β = 0.039; 95%CI, 0.015-0.065; P = .002). Additionally, male sex, in-stent restenosis, CTO, and pre- and post-dilatation were negatively correlated with postprocedural FFR. Conversely, type A lesions, thrombus-containing lesions, postprocedural percent diameter stenosis, and stent diameter were positively correlated with postprocedural FFR. The R^2 for the entire model was 53%. [Figure 1](#) shows all significant and non-significant adjusted predictors included in the LME-model. [Table 2](#) shows all adjusted and unadjusted predictors with corresponding β values and 95%CI. The most important predictors are shown on [figure 2](#).

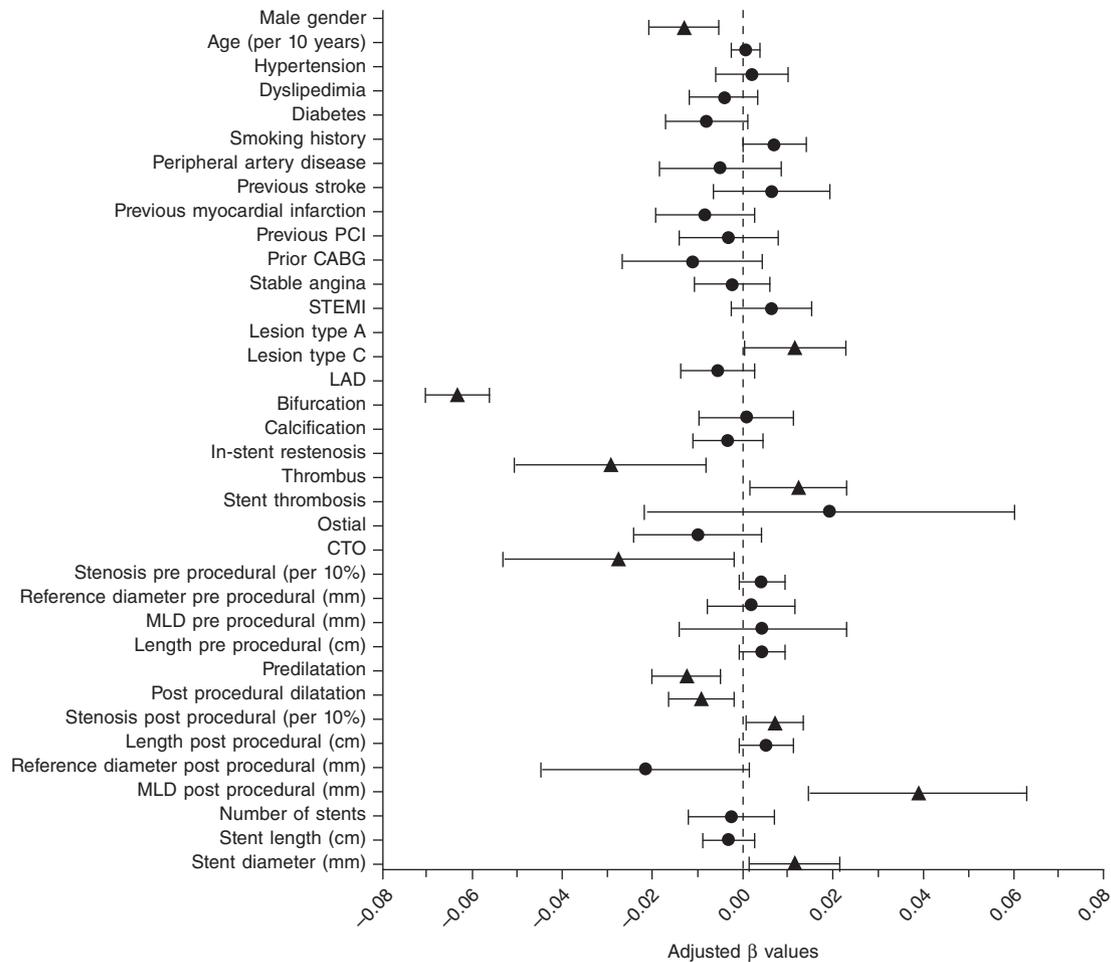


Figure 1. Forest plot of independent predictors of post-PCI FFR. Adjusted beta values with 95% confidence intervals. Triangles indicate significant predictors while circles are indicative of non-significant predictors in the multivariate generalized mixed model to predict post-PCI FFR. ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; LAD, left anterior descending coronary artery; CTO, chronic total coronary occlusion; MLD, minimum lumen diameter.

DISCUSSION

This study is the largest report to this day of predictors of post-PCI FFR. Based on data derived from the FFR-SEARCH registry, we could identify several patient and procedural predictors of post-PCI FFR. These predictors will bring more in-depth interpretations of post-PCI FFR values to be able to identify correctly which vessels are prone to future events. At first, male gender appeared to be negatively correlated with postprocedural FFR. This finding is consistent with the findings of former studies that focused on the impact of gender on pre-PCI FFR measurements.^{6,11,15,16} Compared to females, males are known to have a lower prevalence of microvascular dysfunction.^{8,17} The concept of FFR is based on drug-induced maximal hyperemia to minimize microvascular resistance. Microvascular dysfunction may hamper this vasodilator response and consequently result in a dampened flow response and high FFR.¹⁵ Subsequently, on average, males have larger myocardial masses and myocardial perfusion territories compared to females.^{18,19} The importance of the latter is illustrated by the second and strongest predictor of post-PCI FFR in this study, the FFR measurements in the LAD. FFR values are associated with the myocardial mass and the outflow territory of the measured vessel. As such, the LAD—the vessel with the largest perfusion area—has previously been associated with lower pre- and postprocedural FFR values.²⁰⁻²²

The diameters of the stents implanted in the RCA are larger, on average, but the outflow territory of the LAD is even larger.²³ This discrepancy between luminal dimensions and myocardial mass may explain why the optimal improvement of the FFR measurements in the LAD is difficult to achieve.²³

Thirdly, larger stent diameters and larger post-PCI MLDs were associated with higher post-PCI FFR values. However, higher postprocedural percent stenosis was also associated with higher post-PCI FFR values. While these findings may seem contradictory, postprocedural percent stenosis was not associated with post-PCI physiology in the DEFINE PCI study either.²⁴

In the intravascular ultrasound substudy of the FFR-SEARCH registry, van Zandvoort et al. showed that evident signs of residual luminal narrowing including focal lesions, underexpansion, and malapposition were present in a significant amount of vessels with post-PCI FFR values ≤ 0.85 . These findings were not readily apparent on the comprehensive quantitative coronary angiography.²⁵ Percent diameter stenosis was 20% in the cohort of patients with post-PCI FFR values ≤ 0.85 and > 0.85 .²⁶

Together with the latter predictors of post-PCI FFR we identified several others. A dedicated analysis of 26 CTOs recently showed that postprocedural FFR values are typically low initially; however they

Table 2. Predictors for post-PCI FFR

Variable	Unadjusted		Adjusted	
	P	β (95%CI)	P	β (95%CI)
Patient characteristics				
Male sex	.214	-0.006 (-0.015 – 0.003)	.001	-0.013 (-0.021 – -0.005)
Age (per 10 years)	.976	0.000 (-0.03 – 0.03)	.724	0.001 (-0.002 – 0.003)
Hypertension	.013	-0.010 (-0.018 – -0.002)	.610	0.002 (-0.006 – 0.010)
Hypercholesterolemia	< .001	-0.019 (-0.027 – -0.011)	.287	-0.004 (-0.012 – 0.004)
Diabetes	< .001	0.018 (0.008 – 0.042)	.081	-0.008 (-0.017 – 0.001)
Smoking history	.007	0.020 (0.010 – 0.019)	.054	0.007 (-0.0001 – 0.014)
Previous stroke	.831	-0.002 (-0.017 – 0.013)	.342	0.006 (-0.0007 – 0.019)
Peripheral arterial disease	.022	-0.017 (-0.032 – -0.003)	.460	-0.005 (-0.018 – 0.008)
Previous myocardial infarction	.002	-0.016 (-0.026 – -0.006)	.137	-0.008 (-0.019 – 0.003)
Previous PCI	< .001	-0.016 (-0.025 – -0.007)	.569	-0.032 (-0.014 – 0.008)
Previous CABG	.896	-0.001 (-0.019 – 0.017)	.166	-0.011 (-0.014 – 0.004)
Indication for PCI				
Stable angina	< .001	-0.025 (-0.034 – -0.016)	.563	-0.002 (-0.011 – 0.005)
STEMI	< .001	0.032 (0.025 – 0.041)	.171	0.006 (-0.003 – 0.015)
Vessel characteristics				
Lesion type				
A	<.001	0.022 (0.009 – 0.035)	.040	0.012 (0.0005 – 0.023)
C	.045	-0.008 (-0.016 – -0.0002)	.172	-0.006 (-0.014 – 0.002)
LAD	<.001	-0.070 (-0.077 – -0.064)	<.001	-0.063 (-0.070 – -0.056)
Bifurcation	< .001	-0.024 (-0.036 – -0.012)	.883	0.001 (-0.010 – 0.011)
Calcified	< .001	-0.025 (-0.033 – -0.017)	.409	-0.003 (-0.011 – 0.005)
In-stent restenosis	.006	-0.031 (-0.053 – -0.009)	.007	-0.029 (-0.051 – -0.008)
Thrombus	< .001	0.031 (0.021 – 0.042)	.026	0.012 (-0.001 – 0.023)
Stent thrombosis	.920	0.002 (-0.034 – 0.038)	.362	0.019 (-0.022 – 0.060)
Ostial	.181	-0.010 (-0.024 – 0.005)	.165	-0.010 (-0.024 – 0.004)
CTO	.002	-0.034 (-0.056 – -0.013)	.036	-0.027 (-0.053 – -0.002)
Stenosis pre procedural (per 10%)	<.001	0.007 (0.005 – 0.009)	.105	0.004 (-0.0009 – 0.009)
Reference diameter pre procedural (mm)	<.001	0.030 (0.023 – 0.037)	.704	0.002 (-0.008 – 0.011)
Length pre procedural (cm)	.900	-0.00002 (-0.004 – 0.003)	.101	0.004 (0.0008 – 0.009)
MLD pre procedural (mm)	<.001	-0.015 (-0.022 – -0.008)	.638	0.004 (-0.014 – 0.023)
Predilatation	<.001	-0.019 (-.027 – -0.011)	.002	-0.012 (-0.020 – -0.005)
Postdilatation	<.001	0.027 (-0.035 – -0.019)	.015	-0.009 (-0.016 – -0.002)
Stenosis post procedural (per 10%)	.077	0.003 (-0.0003 – 0.006)	.029	0.01 (0.0007 – 0.01)
Reference diameter post procedural (mm)	<.001	0.035 (0.027 – 0.042)	.067	-0.022 (-0.045 – 0.002)
Length post procedural (cm)	.312	-0.002 (-0.005 – 0.001)	.086	0.001 (-0.0007 – 0.001)
MLD post procedural (mm)	<.001	0.032 (0.024 – 0.040)	.002	0.039 (0.015 – 0.063)
Number of stents	<.001	-0.012 (-0.018 – -0.006)	.620	-0.002 (-0.012 – 0.007)
Stent length (cm)	<.001	0.019 (0.009 – 0.041)	.286	-0.003 (-0.009 – 0.002)
Stent diameter (mm)	<.001	0.033 (0.025 – 0.042)	.026	0.012 (0.001 – 0.022)

Beta (β) values are indicative of the average increase or decrease of the FFR values in cases of dichotomous variables or the increment per unit increase in cases of continuous variables. 95%CI, 95% confidence interval; CABG, coronary artery bypass graft; CTO, chronic total coronary occlusion; FFR, fractional flow reserve; LAD, left anterior descending coronary artery; MLD, minimum lumen diameter; STEMI, ST-segment elevation myocardial infarction.

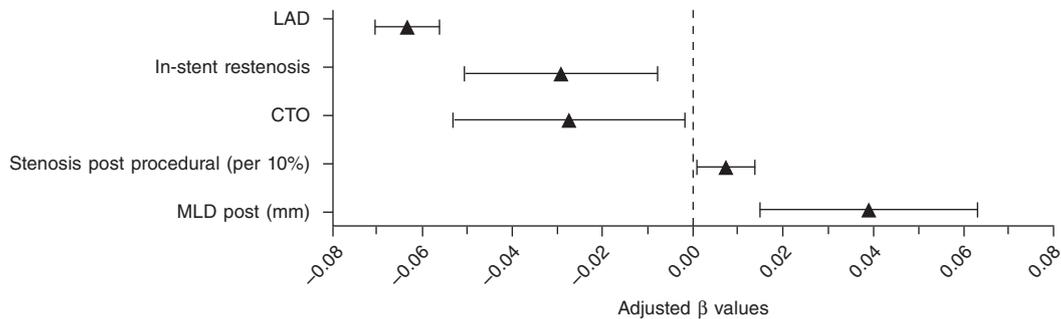


Figure 2. Forest plot of most important predictors of post-PCI FFR. Adjusted beta values with 95% confidence intervals. The figure includes all significant predictors from the multivariate generalized mixed model predicting post-PCI FFR except for categorical variables with beta values < 0.02 . LAD, left anterior descending coronary artery; CTO, chronic total coronary occlusion; MLD, minimum lumen diameter.

seem to increase at the 4-month follow-up. The initially low post-PCI FFR values is thought to be due to the microvascular dysfunction of the recently opened vessel, a phenomenon that improves after several months.²⁷ In-stent restenosis and pre- and postdilatation were associated with lower post-PCI FFR values. A finding that is consistent with former studies that showed that, in general, complex lesions are associated with lower post-PCI FFR values.^{20,21,26,28}

Also, it was interesting to see the impact of clinical presentation on post-PCI FFR values in the study population in which most patients presented with acute coronary syndrome. Contrary to former studies that questioned the validity of invasive hyperemic physiological indices in patients with acute coronary syndrome, we could not confirm the impact of clinical presentation on post-PCI FFR values. However, the identification of a thrombus, that often occurs after a ruptured plaque in patients with acute coronary syndrome, was associated with significantly higher FFR values. Despite the restoration of epicardial flow by the PCI, a relatively large number of patients with STEMI have abnormal myocardial perfusion at the end of the procedure.²⁹ This phenomenon is thought to be related to microvascular obstruction due to distal embolization (reperfusion injury) and tissue inflammation due to myocyte necrosis.^{30,31} The latter may explain the significantly higher post-PCI FFR values reported in patients presenting with thrombus-containing lesions compared to those without such lesions. Conversely, our findings also show that in patients without thrombus-containing lesions the post-PCI FFR may be a valuable diagnostic tool for the identification of patients at a high risk of future adverse cardiac events.

Limitations

This study was conducted with the Navvus microcatheter, a dedicated rapid exchange microcatheter with a mean diameter of 0.022 in that proved its utility in a slight but significant underestimation of the FFR compared to conventional 0.014 in pressure guidewires.³² That is why we cannot directly extrapolate the current findings to wire-based FFR devices.¹⁴ Based on the study protocol, no further action was taken in the presence of low post-PCI FFR values. The Target FFR and FFR REACT studies (NCT03259815 and NTR6711) will provide further information on post-PCI FFR and the potential of further actions to improve post-PCI FFR and clinical outcomes.^{33,34} These studies should also focus on the trade-off of potential benefits and harm when performing additional interventions in order to improve the final FFR values.

CONCLUSIONS

In this substudy of the FFR-SEARCH registry, the largest real-world post-PCI FFR registry conducted to this day, we identified sex, LAD

vessels, postprocedural MLD, and several other independent predictors of postprocedural FFR.

FUNDING

The FFR SEARCH study was conducted with institutional support from ACIST Medical Inc.

AUTHORS' CONTRIBUTION

Conception and design: L.J.C. van Zandvoort, N.M. van Mieghem, and J. Daemen. Data acquisition: L.J.C. van Zandvoort, K. Masdjedi, J. Wilschut, W. Den Dekker, R. Diletti, F. Zijlstra, N.M. van Mieghem, and J. Daemen. Statistical analysis and manuscript writing: L.J.C. van Zandvoort and J. Daemen. Providing critical feedback to the manuscript and approving the final content: L.J.C. van Zandvoort, K. Masdjedi, T. Neleman, M.N. Tovar Forero, J. Wilschut, W. Den Dekker, R. Diletti, F. Zijlstra, N.M. van Mieghem, and J. Daemen.

CONFLICTS OF INTEREST

L.J.C. van Zandvoort received institutional research support from Acist medical Inc. J. Daemen received institutional research support from Pie Medical, ACIST Medical Inc., PulseCath, Medtronic, Boston Scientific, Abbott Vascular, Pie Medical and speaker and consultancy fees from PulseCath, Medtronic, ReCor Medical, ACIST Medical Inc. and Pie Medical. The remaining authors declared no conflicts of interest.

WHAT IS KNOWN ABOUT THE TOPIC?

- FFR has proven to be a useful technique to address coronary physiology and the hemodynamic significance of coronary segments pre- and post-intervention.
- Also, the FFR post-stenting has proven to be a strong and independent predictor of major adverse cardiovascular events at the 2-year follow-up.
- Unfortunately, at present, there is lack of data on independent predictors of post PCI FFR.

WHAT DOES THIS STUDY ADD?

- This study is the largest report to this day on predictors of post-PCI FFR.
- Based on data from the FFR-SEARCH registry, we could identify several patient and procedural predictors of post-PCI FFR.
- The main predictors included sex, LAD vessels, and post-procedural lumen dimensions. These predictors will help us interpret post-PCI FFR values and identify correctly the vessels that are prone to future events.

REFERENCES

1. Topol EJ, Nissen SE. Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. *Circulation.* 1995;92:2333-2342.
2. De Bruyne B, Fearon WF, Pijls NHJ, et al. Fractional flow reserve-guided PCI for stable coronary artery disease. *N Engl J Med.* 2014;1533-4406.
3. Wolfrum M, Fahrni G, de Maria GL, et al. Impact of impaired fractional flow reserve after coronary interventions on outcomes: a systematic review and meta-analysis. *BMC Cardiovasc Disord.* 2016;16:177.
4. Rimac G, Fearon WF, De Bruyne B, et al. Clinical value of post-percutaneous coronary intervention fractional flow reserve value: A systematic review and meta-analysis. *Am Heart J.* 2017;183:1-9.
5. Kasula S, Agarwal SK, Hacıoglu Y, et al. Clinical and prognostic value of poststenting fractional flow reserve in acute coronary syndromes. *Heart.* 2016;102:1988-1994.
6. Sareen N, Baber U, Kezbor S, et al. Clinical and angiographic predictors of haemodynamically significant angiographic lesions: development and validation of a risk score to predict positive fractional flow reserve. *EuroIntervention.* 2017;12:e2228-e2235.
7. Baranaukas A, Peace A, Kibarskis A, et al. FFR result post PCI is suboptimal in long diffuse coronary artery disease. *EuroIntervention.* 2016;12:1473-1480.
8. Crystal GJ, Klein LW. Fractional flow reserve: physiological basis, advantages and limitations, and potential gender differences. *Curr Cardiol Rev.* 2015;11:209-219.
9. Ahmadi A, Leipsic J, Ovrehus KA, et al. Lesion-Specific and Vessel-Related Determinants of Fractional Flow Reserve Beyond Coronary Artery Stenosis. *JACC Cardiovasc Imaging.* 2018;11:521-530.
10. Tebaldi M, Biscaglia S, Fineschi M, et al. Fractional Flow Reserve Evaluation and Chronic Kidney Disease: Analysis From a Multicenter Italian Registry (the FREAK Study). *Catheter Cardiovasc Interv.* 2016;88:555-562.
11. Fineschi M, Guerrieri G, Orphal D, et al. The impact of gender on fractional flow reserve measurements. *EuroIntervention.* 2013;9:360-366.
12. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). *Circulation.* 1988;78:486-502.
13. Diletti R, Van Mieghem NM, Valgimigli M, et al. Rapid exchange ultra-thin microcatheter using fibre-optic sensing technology for measurement of intracoronary fractional flow reserve. *EuroIntervention.* 2015;11:428-432.
14. Menon M, Jaffe W, Watson T, Webster M. Assessment of coronary fractional flow reserve using a monorail pressure catheter: the first-in-human ACCESS-NZ trial. *EuroIntervention.* 2015;11:257-263.
15. van de Hoef TP, Meuwissen M, Escaned J, et al. Fractional flow reserve as a surrogate for inducible myocardial ischaemia. *Nat Rev Cardiol.* 2013;10:439-452.
16. Kim HS, Tonino PA, De Bruyne B, et al. The impact of sex differences on fractional flow reserve-guided percutaneous coronary intervention: a FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) substudy. *JACC Cardiovasc Interv.* 2012;5:1037-1042.
17. Reis SE, Holubkov R, Lee JS, et al. Coronary flow velocity response to adenosine characterizes coronary microvascular function in women with chest pain and no obstructive coronary disease. Results from the pilot phase of the Women's Ischemia Syndrome Evaluation (WISE) study. *J Am Coll Cardiol.* 1999;33:1469-1475.
18. Iqbal MB, Shah N, Khan M, Wallis W. Reduction in myocardial perfusion territory and its effect on the physiological severity of a coronary stenosis. *Circ Cardiovasc Interv.* 2010;3:89-90.
19. Lin FY, Devereux RB, Roman MJ, et al. Cardiac chamber volumes, function, and mass as determined by 64-multidetector row computed tomography: mean values among healthy adults free of hypertension and obesity. *JACC Cardiovasc Imaging.* 2008;1:782-786.
20. Nam CW, Hur SH, Cho YK, et al. Relation of fractional flow reserve after drug-eluting stent implantation to one-year outcomes. *Am J Cardiol.* 2011;107:1763-1767.
21. Doh JH, Nam CW, Koo BK, et al. Clinical Relevance of Poststent Fractional Flow Reserve After Drug-Eluting Stent Implantation. *J Invasive Cardiol.* 2015;27:346-351.
22. Agarwal SK, Kasula S, Hacıoglu Y, Ahmed Z, Uretsky BF, Hakeem A. Utilizing Post-Intervention Fractional Flow Reserve to Optimize Acute Results and the Relationship to Long-Term Outcomes. *JACC Cardiovasc Interv.* 2016;9:1022-1031.
23. Kimura Y, Tanaka N, Okura H, et al. Characterization of real-world patients with low fractional flow reserve immediately after drug-eluting stents implantation. *Cardiovasc Interv Ther.* 2016;31:29-37.
24. Jeremias A, Davies JE, Maehara A, et al. Blinded Physiological Assessment of Residual Ischemia After Successful Angiographic Percutaneous Coronary Intervention: The DEFINE PCI Study. *JACC: Cardiovasc Interv.* 2019;12:1991-2001.
25. van Zandvoort LJC, Masdjedi K, Witberg K, et al. Explanation of Postprocedural Fractional Flow Reserve Below 0.85. *Circ Cardiovasc Interv.* 2019;12:e007030.
26. van Zandvoort LJC, Witberg K, Ligthart J, et al. Explanation of post procedural fractional flow reserve below 0.85: a comprehensive ultrasound analysis of the FFR Search registry. In Cardiovascular Research Technologies (CRT) Conference 2018 March 3-6; Washington DC, United States. 2018.
27. Karamasis GV, Kalogeropoulos AS, Mohd Nazri SR, et al. Serial Fractional Flow Reserve Measurements Post Coronary Chronic Total Occlusion Percutaneous Coronary Intervention. *Circ Cardiovasc Interv.* 2018;11:e006941.
28. Pijls NH, Klauss V, Siebert U, et al. Coronary pressure measurement after stenting predicts adverse events at follow-up: a multicenter registry. *Circulation.* 2002;105:2950-2954.
29. Stone GW, Webb J, Cox DA, et al. Distal microcirculatory protection during percutaneous coronary intervention in acute ST-segment elevation myocardial infarction: a randomized controlled trial. *JAMA.* 2005;293:1063-1072.
30. Shah NR, Al-Lamee R, Davies J. Fractional flow reserve in acute coronary syndromes: A review. *Int J Cardiol Heart Vasc.* 2014;5:20-25.
31. Cuculi F, De Maria GL, Meier P, et al. Impact of microvascular obstruction on the assessment of coronary flow reserve, index of microcirculatory resistance, and fractional flow reserve after ST-segment elevation myocardial infarction. *J Am Coll Cardiol.* 2014;64:1894-904.
32. Pouillot C, Fournier S, Glasenapp J, et al. Pressure wire versus microcatheter for FFR measurement: a head-to-head comparison. *EuroIntervention.* 2018;13:e1850-e1856.
33. van Zandvoort LJC, Masdjedi K, Tovar Forero MN, et al. Fractional flow reserve guided percutaneous coronary intervention optimization directed by high-definition intravascular ultrasound versus standard of care: Rationale and study design of the prospective randomized FFR-REACT trial. *Am Heart J.* 2019;213:66-72.
34. Collison D, McClure JD, Berry C, Oldroyd KG. A randomized controlled trial of a physiology-guided percutaneous coronary intervention optimization strategy: Rationale and design of the TARGET FFR study. *Clin Cardiol.* 2020;43:414-422.



Angiographic and clinical results of the STENTYS Xposition S self-apposing stent. A single-center experience

Ainhoa Pérez Guerrero,* Georgina Fuertes Ferré, Isabel Caballero Jambrina, Juan Sánchez-Rubio, Gabriel Galache Osuna, María Cruz Gracia Ferrer, María Rosario Ortas Nadal, and José Antonio Diarte de Miguel

Servicio de Cardiología, Hospital Universitario Miguel Servet, Zaragoza, Spain

SEE RELATED CONTENT:
<https://doi.org/10.24875/RECICE.M20000191>

ABSTRACT

Introduction and objectives: The STENTYS Xposition S stent (STENTYS S.A, Paris, France) is the only self-apposing sirolimus-eluting stent available in the market. The stent features make it useful to treat challenging lesions with proximal-distal different vessel diameter, ectasia, high thrombus burden, bifurcation lesions including the left main coronary artery or vein grafts. We describe our own experience with the use of this stent and evaluate its efficacy and safety profile.

Methods: We included all consecutive patients treated with the STENTYS Xposition S from January 2018 to October 2019. All coronary lesions were quantified using QCA (quantitative coronary angiography).

Results: A total of 62 lesions in 50 patients were treated with the STENTYS Xposition S. The median age of the patients was 66 years (49-92). The most common clinical presentation was ST-segment elevation acute coronary syndrome in 23 patients (46%). Ectasia and significant vessel diameter variance were the most common scenario in 72.6% of cases and bifurcation in the remaining 27.4% (2 of them in the left main coronary artery). Pre-dilatation was performed in 32 lesions (51.6%) and post-dilatation in 37 (59.7%). Angiographic success was achieved in all patients except for 1. At the median 373-day follow-up (256-439), 1 patient had an acute myocardial infarction 3 months after the percutaneous intervention and 1 patient died due to cardiac failure during admission. There were no cases of definitive stent thrombosis or target lesion revascularization.

Conclusions: The STENTYS Xposition S self-apposing stent showed good angiographic and clinical outcomes in our real-world experience.

Keywords: Self-apposing stent. Coronary lesion. Major adverse cardiovascular events.

Resultados clínicos y angiográficos del *stent* autoexpandible STENTYS Xposition S. Experiencia de un centro

RESUMEN

Introducción y objetivos: El *stent* STENTYS Xposition S (STENTYS S.A., París, Francia) es el único *stent* autoexpandible liberador de sirolimus disponible en el mercado. Sus características hacen que resulte útil en lesiones que presentan gran diferencia del diámetro del vaso proximal-distal, ectasia, alta carga de trombo o que se encuentren en bifurcaciones e injertos venosos. Describimos nuestra experiencia con el uso de este tipo de *stent*, evaluando su seguridad y eficacia.

Métodos: Se incluyeron todos los pacientes consecutivos tratados con STENTYS desde enero de 2018 hasta octubre de 2019. Todas las lesiones coronarias fueron cuantificadas por angiografía coronaria cuantitativa.

Resultados: Se trataron con STENTYS Xposition S 62 lesiones en 50 pacientes. La mediana de edad de los pacientes fue de 66 años (49-92). La clínica de presentación más frecuente fue el síndrome coronario agudo con elevación del segmento ST en 23 pacientes (46%). La ectasia coronaria y la gran diferencia en los diámetros proximal y distal a la lesión fue la indicación más frecuente para el uso de este tipo de *stent*, en el 72,6% de los casos, seguida del intervencionismo sobre bifurcación en el 27,4% de los pacientes (2 de ellos en el tronco coronario izquierdo). Se realizó predilatación en 32 lesiones (51,6%) y posdilatación en 37 (59,7%). Se logró el éxito angiográfico en todos los pacientes excepto en 1. Tras una mediana de seguimiento de 373 días (256-439), 1 paciente presentó infarto agudo de miocardio a los 3 meses y 1 paciente falleció durante el ingreso por insuficiencia cardíaca. No hubo ningún caso de trombosis definitiva del *stent* ni de revascularización de la lesión tratada.

Conclusiones: En nuestra experiencia de la vida real, el *stent* STENTYS Xposition S demostró un buen resultado angiográfico y clínico.

Palabras clave: *Stent* autoexpandible. Lesión coronaria. Eventos cardiovasculares adversos mayores.

* **Corresponding author:** Servicio de Cardiología, Hospital Universitario Miguel Servet, Paseo Isabel la Católica 1-3, 50009 Zaragoza, Spain.
E-mail address: ainhoaperezguerrero@gmail.com (A. Pérez Guerrero).

Received 11 February 2020. Accepted 20 May 2020. Online: 31-07-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Abbreviations

LMCA: left main coronary artery. MACE: major adverse cardiovascular events.

INTRODUCTION

The STENTYS Xposition S (STENTYS S.A., Paris, France) is a sirolimus-eluting self-expanding nitinol stent designed to adapt its size to the vessel diameter and facilitate its complete apposition when exerting chronic strength towards the outside. It has long been confirmed that one of the most important factors of stent thrombosis is the incorrect apposition of the stent.¹ The characteristics of this stent make it especially useful to revascularize acute coronary syndromes (ACS), especially ST-segment elevation acute coronary syndromes with lesions with high thrombotic load. Also, a potential benefit in ectatic coronary vessels and lesions with great proximal and the distal diameter mismatch has been confirmed, bifurcations (left main coronary artery [LMCA] included), and venous grafts.

The objective of this study was to assess the benefit of this stent in the routine clinical practice by analyzing the type of lesions this stent is used with and the immediate angiographic results and at the clinical follow-up.

METHODS

A cohort of consecutive patients treated with the STENTYS Xposition S stent was analyzed from January 2018 through October 2019 in a tertiary hospital where over 1000 percutaneous coronary interventions are performed each year. All coronary lesions were quantified using a quantitative coronary angiography. Lesions in vessels with changes in size (ectasia or proximal-distal diameter mismatch of the lesion), in a bifurcation, in the presence of a high thrombotic load or in a venous graft were analyzed. The interventional strategy to be followed, imaging modalities included, was left to the operator's criterion. The clinical and follow-up data were obtained from the electronic clinical records of the healthcare system of our autonomous community. All events were defined in a standard way according to the Academic Research Consortium-2 (ARC-2) consensus document.² Patients' informed consent was obtained to the interventional procedure and, subsequently, verbal informed consent was given during the follow-up.

The data analysis was conducted using the IBM SPSS 20.0 statistical software package. Continuous variables were expressed as mean \pm standard deviation or median with interquartile range depending on whether they followed a normal distribution or not, respectively. Qualitative variables were expressed as relative percentage. The cumulative incidence of events at the follow-up was estimated.

RESULTS

From January 2018 through September 2019, 1692 percutaneous coronary interventions with stent implantation were performed. The STENTYS Xposition S stent was used in 50 patients (62 lesions). The patients' median age was 66 years [49-92]. Eighty-eight per cent of the patients were males. Table 1 shows the clinical characteristic of patients and coronary lesions. The most common clinical presentation was ST-segment elevation acute coronary syndrome in 23 patients (46%) followed by non-ST-segment elevation acute

Table 1. Clinical characteristics of patients and angiographic characteristics of the lesions

Patients (N)	50
Age (years)	66.6 (49-92)
Males	44 (88%)
Arterial hypertension	33 (66%)
Body mass index (kg/m ²)	27.9 \pm 4.9
Dyslipidemia	32 (64%)
Diabetes mellitus	12 (24%)
Smoking	27 (54%)
Family history of ischemic heart disease	3 (6%)
Peripheral vasculopathy	3 (6%)
Atrial fibrillation	6 (12%)
Chronic pulmonary disease	6 (12%)
Kidney disease	6 (12%)
Stable angina pectoris	5 (10%)
NSTEMACS	22 (44%)
STEMACS	23 (46%)
Lesions (N)	62
Lesion length (mm)	14.56 \pm 3.64
Reference diameter (mm)	4.1 \pm 0.8
Percent stenosis. QCA (%)	70.08 \pm 17
Location of the lesion	
Left main coronary artery	3 (4.8)
Left anterior descending coronary artery	11 (17.7)
Left circumflex artery	15 (24.2)
Right coronary artery	33 (53.2)
Classification of the lesion	
A	0
B1	24 (38.8)
B2	19 (30.6)
C	19 (30.6)
Indication for STENTYS	
Ectasia. Proximal-distal diameter mismatch	45 (72.6)
Bifurcation	17 (27.4)
Provisional stenting technique	15 (88.2)
Double stent technique	2 (11.8)

NSTEMACS, non-ST-segment elevation acute coronary syndrome; QCA, quantitative coronary angiography; STEACS, ST-segment elevation acute coronary syndrome. Kidney damage: glomerular filtration rate < 60 mL/min/1.73 m². Data are expressed as N (%) or mean \pm standard deviation.

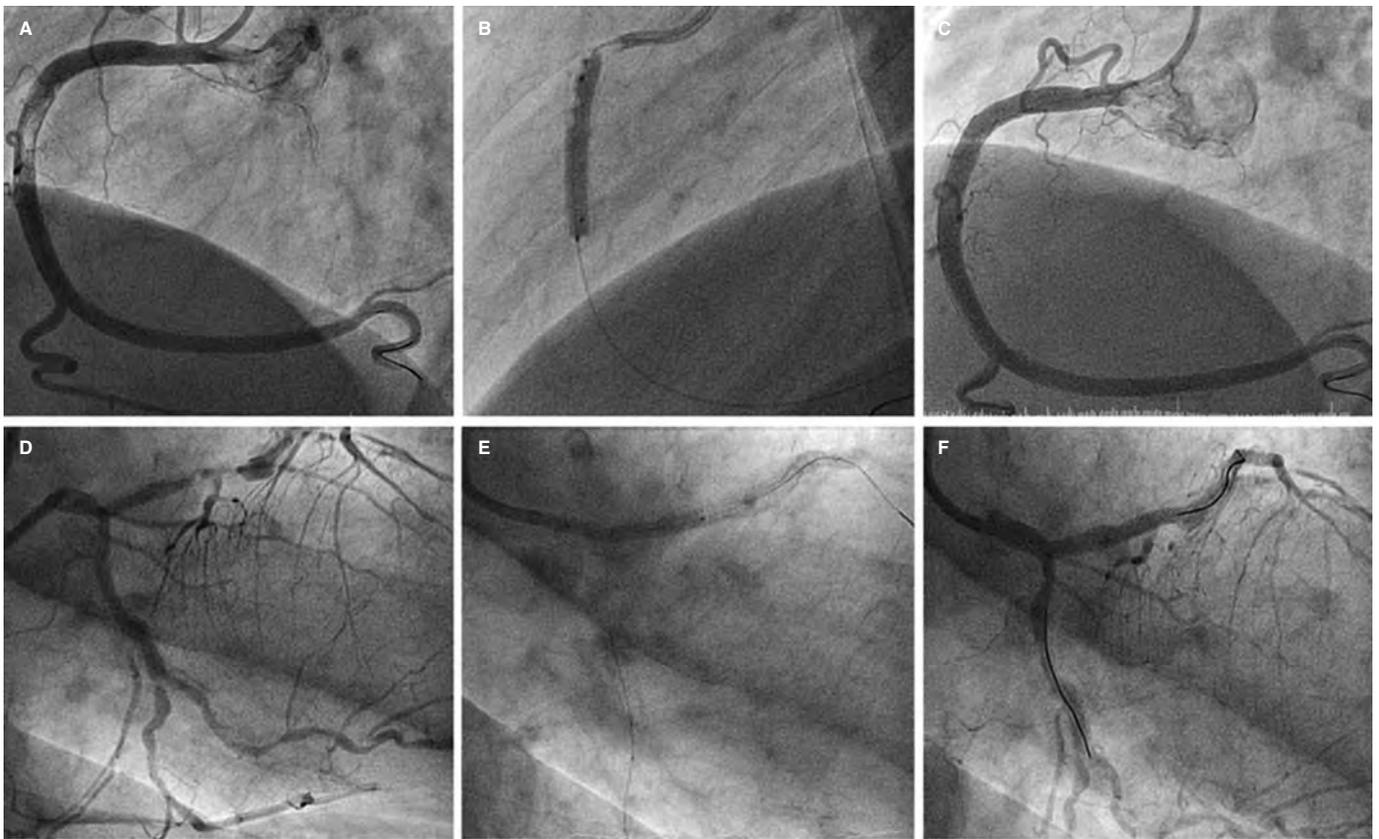


Figure 1. A: lesion with significant thrombotic load in the mid right coronary artery, which remains after thrombus aspiration. B: 3.5-4.5 mm × 27 mm Xposition S direct stent implantation. C: final angiographic result. D: significant stenosis in distal left main coronary artery. E: 3-3.5 mm × 27 mm Xposition S stent implantation from the proximal left main coronary artery to the left anterior descending coronary artery. F: angiographic result after postdilatation.

coronary syndrome in 22 patients (44%), and stable angina in 5 patients (10%). According to the classification established by the American College of Cardiology/American Heart Association the most common type of lesion was B1 lesion (38.7%). The right coronary artery was the most frequently treated vessel in 33 patients (53.2%).

Ectasia and great proximal-distal diameter mismatch at the lesion were the main indication for the use of this stent, in 72.6% of the lesions, with a mean vessel reference diameter of $4.1 \text{ mm} \pm 0.8 \text{ mm}$. A certain size was required to use this type of stent. The percutaneous coronary intervention on a bifurcation was the second most common indication, in 27.4% of the patients (2 of them on the LMCA). The most common type of bifurcation according to the Medina classification was 1-1-0, in 9 cases (52.9%). The secondary branch was damaged in 17% of the patients. The provisional stenting technique was the most widely used in 15 cases (88.2% of bifurcations) re-crossing to the secondary branch in 9 of them (60%). The dilatation of the secondary branch only occurred in 7 patients and only in the other 2 stents were implanted: one in a 0-1-1 bifurcation according to the Medina classification (minicrash technique) and the other in a 1-1-1 bifurcation according to this classification (TAP technique [T-and protrusion technique]). In both cases the STENTYS Xposition S stent was implanted in the main vessel and a non-self-apposing stent in the secondary branch (figure 1).

A high thrombotic load (Thrombolysis in Myocardial Infarction flow grade 4-5) was seen in 8 lesions. All of them in ectatic coronary vessels or with proximal-distal caliber mismatch. No case of venous graft treated with STENTYS was reported.

Predilatation occurred in 32 lesions (51.6%) and postdilatation in 37 (59.7%). The criterion used for postdilatation was angiography guided visual underexpansion. Intravascular ultrasound was performed in 15 patients (30%) before the implant. It was also used in 2 patients to optimize the percutaneous coronary intervention given the persistent stent underexpansion seen on the angiography. In both cases the minimum lumen area was $> 5.5 \text{ mm}^2$ with stent expansion $> 80\%$ and lack of incomplete apposition (defined as a strut separation of $> 0.4 \text{ mm}$ axial and 1 mm longitudinal) (figure 2). The optical coherence tomography was performed in a patient with ST-segment elevation acute coronary syndrome before and after the implant. It revealed a high thrombotic load with lack of immediate stent malapposition.

Angiographic success was achieved (with the stent properly implanted, a residual lesion $\leq 10\%$, and Thrombolysis in Myocardial Infarction flow grade 3) in all patients but 1, in whom stent implantation failed in a severely calcified LMCA lesion. In this case, predilatation was first attempted using a conventional balloon and then a cutting balloon on the LMCA severe distal lesion. A 3.3-4.5 mm × 22 mm STENTYS Xposition S stent was implanted with stent loss during retrieval, which remained braced to the guide catheter. Afterwards, a balloon-expandable drug-eluting stent was successfully implanted. The un-crimped stent was retrieved by crossing a guidewire from the femoral access through the stent distal struts. It was finally captured with a snare.

The median score obtained in the PRECISE-DAPT risk calculator (Predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy) was 16.5 (7-25), and the median score obtained in the DAPT index (Dual

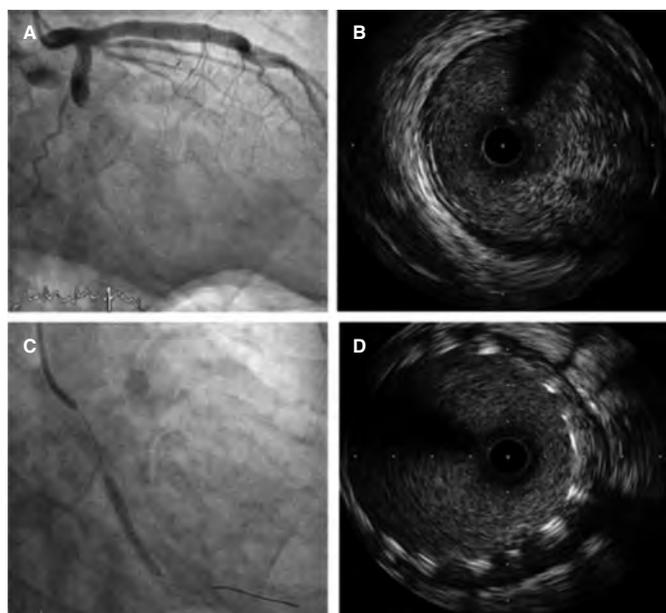


Figure 2. **A:** acute thrombotic occlusion in left circumflex artery with Thrombolysis in Myocardial Infarction flow grade 0. **B:** the intravascular ultrasound shows a great deal of thrombus in the lesions despite thrombus aspiration. **C:** implantation of 2 3.5-4.5 mm × 27 mm Xposition S overlapping stents. **D:** the intravascular ultrasound performed after stent implantation confirms the good angiographic results and lack of stent malapposition.

antiplatelet therapy) was 1.15 (−2-4). Ticagrelor was the most commonly used P2Y₁₂ inhibitor (58.1%). A 12-month course of dual antiplatelet therapy was prescribed in 48 patients (96%).

After a median follow-up of 373 days (256-439), 1 patient had an acute myocardial infarction 3 months after the intervention. However, the coronary angiography did not reveal coronary artery disease progression but confirmed the good results of the previous intervention. An 84-year-old woman died at admission due to heart failure. Three patients died of non-cardiac causes: 1 due to septic shock at admission, the other patient died 6 months after the percutaneous coronary intervention due to high-grade lymphoma, and the third one 4 months after the percutaneous coronary intervention due to lung cancer. No cases of definitive stent thrombosis or revascularization of the treated lesion were reported. No bleeding was seen either at the follow-up.

DISCUSSION

This type of stent is not widely used in our setting and we believe 2 are the reasons why. The first one is the need for a learning curve to know how to handle this implant. In former iterations of the device, the delivery system had some technical limitations like the jumping phenomenon that could occur right when the sheath was being released due to the elastic properties of nitinol. Unlike its predecessor (STENTYS sirolimus DES), the stent of the new STENTYS Xposition S system, is mounted over a semicompliant balloon and covered by a 0.0032 in-thick sheath. The reason for balloon inflation is not to dilate the stent, but to rupture the external sheath from the distal to the proximal border to allow a proper vessel-wall stent apposition. This has reduced the complexity of the release mechanism.³ However, we should remember that after the implant, the retrieval of both the balloon and the device sheath should be conducted with care by separating the guide catheter from the ostium to avoid deep intubation. The other reason that may explain why

this stent is still not widely used can be the augmented profile of the device and its rigidity, which both reduce its navigational and crossing capabilities compared to balloon-expandable stents.

Due to the characteristics of the stent and the experience gained using it, the clinical settings where it can be useful are: ectatic vessel, since the stent reaches 6.5 mm of diameter with the device L size; proximal and distal diameter mismatch due to its adaptive capabilities to the vessel caliber; lesions with high thrombotic load, since this stent self-expanding capabilities facilitate its expansion until it reaches the vessel wall if thrombus reabsorption occurs, which avoids late stent malapposition; and bifurcations with ostial damage and 30° to 70° angles. The stent z-shaped mesh and the presence of small interconnectors facilitate re-crossing the lateral branch and disconnecting the struts without having to use the final kissing balloon technique. Thanks to its self-expanding capabilities, the unconnected struts cover the lateral branch ostium making the double stent technique unnecessary on many occasions.

In the studies published on former iterations of the device, the self-expanding stent proved superior to the balloon-expandable stent regarding better apposition. The randomized APOSSITION II clinical trial,⁴ conducted among patients with acute myocardial infarction, showed a lower rate of stent malapposition (defined as > 5% of struts per patient as seen on the optical coherence tomography) 3 days after the primary percutaneous coronary intervention. The APOSSITION IV clinical trial,⁵ also conducted among patients with acute myocardial infarction, showed a significantly lower percentage of stent malapposition at the 4-month follow-up in patients treated with self-expanding stents compared to patients treated with balloon-expandable stents (0.07% vs 1.16%; *P* = .002). However, no inter-group differences were found at the 9-month follow-up (0.43% vs 0.28%; *P* = .55) or in the rate of major adverse cardiovascular events (MACE). The clinical repercussions of this improvement in the early apposition of the stent has not been studied thoroughly. The APOSSITION III trial⁶ showed that the use of STENTYS BMS in the percutaneous coronary intervention setting was associated with acceptable cardiovascular results at the 2-year follow-up, an overall rate of MACE of 11.2%, and a rate of stent thrombosis of 3.3%. We should mention that this study revealed a significant reduction of adverse events after the systematic implementation of a standard protocol (predilatation, implantation, postdilatation). The data available support the hypothesis of the need for mild postdilatation to avoid early complications probably because the stent does not have enough radial strength to achieve a proper expansion in rigid often calcified lesions, especially when predilatation is not fully effective. Therefore, postdilatation would avoid the incomplete expansion of the stent, which may increase the risk of stent thrombosis.⁷

Our study with the STENTYS Xposition S stent reached angiographic success in 98.4% of the cases, although we should remember that, from the anatomical point of view, they were not complex lesions (only 30% were type C lesion). Stent implantation failed in 1 severely calcified LMCA lesion; it is precisely in this type of lesions where its use is ill-advised, especially if predilatation is not effective.⁸

Regarding its use in bifurcations the studies published to this day have also discussed a former iteration of this device with good results. In the observational, multicenter, and prospective OPEN II trial,⁹ the rate of MACE at the 12-month follow-up was 13% (10.1% at 6 months). This rate of events was basically due to the need for revascularization of the treated lesion, while the rate of stent thrombosis at the 12-month follow-up was 1%. We should also mention that the kissing balloon technique was only used in 21.7% of the patients. Also, there were no significant differences in the rate of MACE between patients in whom the kissing balloon technique was used and those in whom it was not used.⁹

To this day, the only study published on the new STENTYS Xposition S model is the TRUNC, a prospective and multicenter study that assessed the efficacy and safety profile of this type of stent in the LMCA. Angiographic success was achieved in 96.6% of the patients and the overall rate of MACE was 8.3% at the 12-month follow-up, basically due to revascularization of the lesion treated in 5.4%.¹⁰ Here we should mention the preliminary results reported by the SIZING (Worldwide every-day practice registry assessing the Xposition S self-apposing stent in challenging lesions with vessel diameter variance) and WIN (World-wide registry to assess the STENTYS Xposition S for revascularization of coronary arteries in routine clinical practice) registries. Both registries confirm the safety and efficacy profile of the current iteration of the stent in the routine clinical practice.

Limitations

Our study has several limitations. Because of its retrospective, single-center nature and the limited number of cases involved, we cannot draw definitive conclusions on the device safety and efficacy profile. No intracoronary imaging modality was performed systematically to guide the implant, which may have been useful, especially the optical coherence tomography. However, we believe that this study is relevant due to the scarce evidence available on the last iteration of this stent.

CONCLUSIONS

In our series of lesions located in ectatic vessels or with proximal-distal diameter mismatch and in bifurcations, the STENTYS Xposition S stent is a good therapeutic alternative that achieves good immediate angiographic results and good mid-term clinical results.

FUNDING

No funding to declare.

AUTHORS' CONTRIBUTIONS

Data collection: A. Pérez Guerrero, I. Caballero Jambrina. Data analysis: A. Pérez Guerrero, G. Fuertes Ferré, I. Caballero Jambrina, G. Galache Osuna, M.C. Gracia Ferrer. Analysis and interpretation of data: A. Pérez Guerrero, G. Fuertes Ferré, J. Sánchez-Rubio, G. Galache Osuna, M.C. Gracia Ferrer. Critical review of manuscript: J.A. Diarte de Miguel, M.R. Ortas Nadal.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- Balloon expandable stents can have limitation in certain scenarios like in the revascularization of lesions with significant proximal-distal diameter mismatch, high

thrombotic loads, and situations of bifurcations or in venous grafts. In these situations, the STENTYS Xposition S self-expanding stent can be especially useful.

WHAT DOES THIS STUDY ADD?

- This type of stent is not widely used in our specialty. We described the experience of our own center with the STENTYS Xposition S stent. Despite the greater difficulty when trying to advance it and the complexity involved in its delivery, the rate of successful implantation was high. We should not forget that this type of stent is recommended in non-complex or non-calcified anatomical lesions. In general, predilatation is recommended to prepare the lesion and postdilatation to secure the proper expansion of the stent since the stent lacks the necessary radial strength. In our series of patients, the STENTYS Xposition S stent was safe and with a low rate of adverse cardiovascular adverse events at the 1-year follow-up.

REFERENCES

1. Cook S, Eshtehardi P, Kalesan B, et al. Impact of incomplete stent apposition on long-term clinical outcome after drug-eluting stent implantation. *Eur Heart J.* 2012;33:1334-1343.
2. Garcia-Garcia HM, McFadden EP, Farb A, et al. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. *Circulation.* 2018;137:2635-2650.
3. Lu H, IJsselmuiden AJ, Grundeken MJ, et al. First-in-man evaluation of the novel balloon delivery system STENTYS Xposition S for the self-apposing coronary artery stent: impact on longitudinal geographic miss during stenting. *EuroIntervention.* 2016;11:1341-1345.
4. Van Geuns R-J, Tamburino C, Fajadet J, et al. Self-expanding versus balloon-expandable stents in acute myocardial infarction: Results from the APPOSITION II study. Self-expanding stents in ST-segment elevation myocardial infarction. *J Am Coll Cardiol Interv.* 2012;5:1209-1219.
5. Van Geuns RJ, Yetgin T, La Manna A, et al. STENTYS self-apposing sirolimus-eluting stent in ST-segment elevation myocardial infarction: results from the randomised APPOSITION IV trial. *EuroIntervention.* 2016;11:1267-1274.
6. Koch KT, Grundeken MJ, Vos NS, et al. One-year clinical outcomes of the STENTYS Self-Apposing(R) coronary stent in patients presenting with ST-segment elevation myocardial infarction: results from the APPOSITION III registry. *EuroIntervention.* 2015;11:264-271.
7. Sato T, Kameyama T, Noto T, Nozawa T, Inoue H. Impact of preinterventional plaque composition and eccentricity on late-acquired incomplete stent apposition after sirolimus-eluting stent implantation: an intravascular ultrasound radiofrequency analysis. *Coron Artery Dis.* 2012;23:432-437.
8. Verheye S, Ramcharitar S, Grube E, et al. Six-month clinical and angiographic results of the STENTYS R self-apposing stent in bifurcation lesions. *EuroIntervention.* 2011;7:580-587.
9. Naber CK, Pyxaras SA, Nef H, et al. Final results of a self-apposing paclitaxel-eluting stent for the percutaneous treatment of de novo lesions in native bifurcated coronary arteries study. *EuroIntervention.* 2016;12: 356-358.
10. Tamburino C, Briguori C, Jessurun GA, et al. TCT-329 prospective evaluation of drug eluting selfapposing stent for the treatment of unprotected left main coronary artery disease: 1-year results of the TRUNC study. *J Am Coll Cardiol.* 2018;72:134-135.



Percutaneous and surgical aortic valve replacement. Impact of volume and type of center on results

Iván J. Núñez-Gil,^{a,*} Javier Elola,^b María García-Márquez,^b José L. Bernal,^{b,c} Cristina Fernández-Pérez,^{b,d} Andrés Íñiguez,^e Luis Nombela-Franco,^a Pilar Jiménez-Quevedo,^a Javier Escaned,^a Carlos Macaya,^a and Antonio Fernández-Ortiz^a

^a Servicio de Cardiología, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

^b Fundación Instituto para la Mejora de la Asistencia Sanitaria (IMAS), Madrid, Spain

^c Servicio de Control de Gestión, Hospital Universitario 12 de Octubre, Instituto de Investigación I+12, Madrid, Spain

^d Servicio de Medicina Preventiva y Estadística, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain

^e Servicio de Cardiología, Hospital Álvaro Cunqueiro, Vigo, Pontevedra, Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000198>

ABSTRACT

Introduction and objectives: To analyze if there is an association between certain structural variables of the treating centres (availability of cardiac surgery and an intensive care unit [CICU] led by cardiologists) and the volume of procedures performed that may be impacting the results of surgical (SAVR) or transcatheter (TAVI) aortic valve treatment.

Methods: Retrospective and observational study of all patients discharged from hospitals from the Spanish National Health System who underwent a SAVR or a TAVI procedure. The source of the data was the administrative minimum basic data set. The outcome variables analyzed were in-hospital mortality, length of stay (both of them risk-adjusted), and presence of complications. As structural variables for the centers studied we used the availability of cardiac surgeries and CICU.

Results: A total of 2055 TAVI and 15 146 SAVR episodes were identified. The adjustment models for in-hospital mortality showed good discrimination (AUC for the SAVR and TAVI model: 0.84; 95%CI, 0.82-0.85) and calibration ($P < .001$). The model median odds ratio was 1.73, indicative of a high inter-hospital variability. High-volume hospitals, with cardiac surgery services, and CICU-capable centers had the lowest risk-adjusted mortality rate in both procedures.

Conclusions: A consistent association is observed between the structural characteristics of the treating centers and the results of aortic valve management both surgical and transcatheter. Also, the availability of a CICU could be a relevant factor in the outcomes of these procedures.

Keywords: TAVI. Volume. Results. Aortic stenosis. Surgery.

Reemplazo valvular aórtico percutáneo y quirúrgico. Influencia del volumen y del tipo de centro tratante en los resultados

RESUMEN

Introducción y objetivos: Analizar la asociación entre algunas variables estructurales de los centros tratantes (disponibilidad de cirugía cardíaca y de unidad de cuidados intensivos cardiológicos [UCIC]), así como su volumen de procedimientos, con los resultados del reemplazo quirúrgico de válvula aórtica (RQVA) o transcatéter (TAVI).

Métodos: Estudio observacional retrospectivo de todos los pacientes dados de alta en los hospitales del Sistema Nacional de Salud español a quienes se realizó un procedimiento RQVA o TAVI en los años 2014 y 2015. La fuente de los datos fue el Conjunto Mínimo Básico de Datos. Las variables de resultados analizadas fueron la mortalidad intrahospitalaria, la duración de la estancia (ambas ajustadas por el riesgo) y la presencia de complicaciones. La disponibilidad de cirugía cardíaca y la disponibilidad de UCIC se utilizaron como variables estructurales de los centros.

* **Corresponding author:** Unidad de Cardiología Intervencionista, Hospital Clínico San Carlos, IdISSC, Prof. Martín Lagos s/n, 28040 Madrid, Spain.
E-mail address: ibnsky@yahoo.es (I.J. Núñez-Gil).

Received 5 May 2020. Accepted 24 June 2020. Online: 02-10-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Resultados: Se analizaron 2.055 TAVI y 15.146 RQVA. Los modelos de ajuste para la mortalidad intrahospitalaria mostraron una buena discriminación (área bajo la curva ROC para el modelo conjunto de TAVI y RQVA: 0,84; IC95%, 0,82-0,85) y calibración ($p < 0,001$). La *odds ratio* mediana del modelo fue de 1,73, lo que señala una elevada variabilidad interhospitalaria. Los hospitales con mayor volumen de actividad, con servicio de cirugía cardíaca y dotados de UCIC muestran menor mortalidad ajustada al riesgo en ambos procedimientos.

Conclusiones: Se observa una asociación consistente entre las características estructurales de los centros tratantes y los resultados del reemplazo valvular aórtico, tanto quirúrgico como transcáteter. Además, la disponibilidad de UCIC podría ser un factor relevante en los resultados de dichos procedimientos.

Palabras clave: TAVI. Volumen. Resultados. Estenosis aórtica. Cirugía.

Abbreviations

RA-SMR: risk-adjusted standardized mortality ratio. **RA-LOS:** risk-adjusted length of stay ratio. **MBD:** minimum basic dataset. **SAVR:** surgical aortic valve replacement. **TAVI:** transcatheter aortic valve implantation.

INTRODUCTION

Severe aortic stenosis is a common disease in our setting and has high morbidity and mortality rate. Its basic treatment is valve replacement.¹ Over the last 2 decades, transcatheter aortic valve implantation (TAVI) has joined the traditional surgical aortic valve replacement (SAVR).²

Data are clear on the association between results and certain characteristics of the centers. The fact that has been most described in the medical literature is that, regarding mortality and complications, better results are obtained in those centers that reach the activity threshold (per center and per operator) for certain processes and procedures,³⁻⁷ including coronary artery bypass graft (CABG)^{5,8} and primary angioplasty.⁹⁻¹¹ Regarding TAVI, the association between volume and results has been reported in hospitals in the United States.¹²⁻¹⁴ In Germany, this association is less obvious.¹⁵ In Spain, the association between volume and results has also been reported for CABG.¹⁶

There are fewer studies that analyze the structural characteristics of the centers and their association with the characteristics of the healthcare systems of every country and the results obtained. In Spain, Bertomeu et al.¹⁷ found a lower mortality rate in patients with acute myocardial infarction (AMI) in high-volume centers with higher complexity. Worner et al.¹⁸ described a lower mortality rate in the management of AMI in hospitals with cardiac surgery and intensive care unit (CICU) capabilities. Rodríguez-Padial et al.¹⁹ found better results in the management of AMI in hospitals serving large communities. The association between CICU availability and better results has also been reported in our setting for the management of cardiogenic shock due to ST-segment elevation myocardial infarction.²⁰

Our objective was to analyze the structural variables of the treating centers (availability of CICU), the volume of procedures performed and their association with results obtained after aortic valve replacement (whether through TAVI or SAVR).

METHODS

Population and sources of data

This is an observational and retrospective study of all the patients discharged from the hospitals of the Spanish National Healthcare

System who underwent a SAVR or a TAVI procedure. The source of data was the minimum basic dataset (MBD) of the Spanish National Healthcare System of 2014 and 2015 (the only years available with a specific code for TAVI in the MBD). The clinical results of the patients transferred were assigned to the centers from which they were eventually discharged. Whenever the same episode was treated through TAVI and SAVR, it was considered as a TAVI treated episode and SAVR as a TAVI related complication. The main result variables were in-hospital mortality, length of the hospital stay, and in-hospital complications. The codes used for the complications seen are shown on [table 1 of the supplementary data](#).

Hospital structural variables

To analyze the possible correlation between the hospital structural variables and the results of aortic valve implantation both the volume of procedures performed and the cardiovascular resources available were studied. Hospitals were classified based on the availability of cardiology related resources and according to the RECALCAR criteria²¹ ([table 2 of the supplementary data](#)). Regarding this study, to analyze the inter-hospital differences, only those with cath lab capabilities without (type 3) and with cardiac surgery (type 4) were included. The availability of CICU based on a survey previously conducted by the Spanish Society of Cardiology was also included.²² The characteristics to consider the presence of a CICU were: a) a comprehensive capacity to manage patients in critical condition including invasive mechanical ventilation, and b) the administrative adhesion of the CICU to the cardiology unit.

Statistical analysis

The risk adjustment models were specified based on the Centers for Medicare and Medicaid Services (CMS) methodology. Regarding CABG, the variables included in the 30-day mortality model were considered as independent variables.²³ Also, certain variables anticipated by the Society of Thoracic Surgeons score for aortic valve replacement—and that can be identified in the MBD²⁴—were included too. Finally, the CMS model was adjusted to the data structure of the MBD after gathering secondary diagnoses based on clinical categories.²⁵ The multilevel logistics regression models were also adjusted.^{26,27} Only statistically significant comorbidities and odds ratio (OR) > 1.0 were considered for the adjustment model.

Based on specified models the risk-adjusted standardized mortality ratio (RA-SMR) was estimated.²⁸ To adjust the length of the hospital stay, the Poisson regression model was used including the year of hospital discharge, the sex of the patient, and the degree of severity of groups related by refined diagnosis as risk factors. The expected length of the hospital stay was obtained from the individual predictions of the adjusted model. Also, the risk-adjusted length of stay ratio (RA-LOSR) was estimated as the coefficient between the length of the stay observed and the length of the stay expected.

To distinguish between high and low-volume hospitals (based on the number of episodes treated), a group clustering algorithm was used. To that end, the mathematical model used was developed with two thirds of the database and validated with the remaining third. The algorithm ranked as high-volume centers for TAVI those that performed ≥ 46 procedures, and as high-volume centers for SAVR those that performed ≥ 240 procedures during the study 2 year-period (2014-2015).

Quantitative variables were expressed as means \pm standard deviations and the qualitative ones as frequencies and percentages. The correlation among the quantitative variables was analyzed using Pearson correlation coefficient. For comparison purposes, the Student *t* test for 2 samples and the analysis of variance (ANOVA) were used with correction of the level of significance using the Bonferroni method for ≥ 3 groups. Comparisons among the different categorical variables were conducted using the chi-square test or Fisher's exact test.

All comparisons were bilateral, and differences were considered statistically significant with *P* values $< .05$. Statistical analyses were conducted using the STATA 13 and SPSS v21.0 software package.

RESULTS

A total of 2055 TAVIs and 15146 SAVRs were performed. Back in 2014 a total of 812 TAVIs were performed in 47 centers and in 2015 the number went up to 1243 in 53 centers.

The differences seen in the profile of the patients who underwent TAVI and SAVR are shown on [table 1](#) and [table 2](#), respectively, based on the type of hospital where procedures were performed. No statistically significant differences regarding age and sex were seen in patients who underwent TAVI in any of the 4 groups. Still, comorbidity was significantly higher (higher Charlson index and higher incidence of heart failure) in patients treated in type 3 non-CICU hospitals.

Regarding patients who underwent SAVR, by definition in type 4 hospitals, no statistically significant differences were seen regarding age, sex or presence of comorbidities among patients treated with and without CICU except for a higher prevalence of cardiogenic shock and previous percutaneous coronary interventions in non-CICU hospitals (2.0% vs 1.3%, *P* $< .001$; and 4.9% vs 3.9%, *P* = .004, respectively) ([table 2](#)).

The in-hospital mortality adjustment model for surgical aortic valve replacement showed good discrimination capabilities (area under the ROC curve, 0.84; 95% confidence interval [95%CI], 0.82-0.85) and calibration (*P* $< .001$). The model median odds ratio was 1.73, indicative of a high inter-hospital variability.

The SAVR specific in-hospital mortality adjustment model also showed excellent discrimination and calibration capabilities too (area under the ROC curve, 0.84; 95%CI, 0.83-0.84; calibration, *P* $< .001$) that were slightly lower for the TAVI specific adjustment model (area under the ROC curve, 0.79; 95%CI, 0.74-0.84; calibration, *P* $< .001$).

Characteristics of the treating center and TAVI results

Type 4 hospitals had a significantly lower RA-SMR compared to type 3 hospitals (4.04 ± 0.98 vs 4.47 ± 0.79). No statistically significant differences were seen on the RA-LOSR (0.99 ± 0.81 vs 1.07 ± 0.81 ; *P* = .278). The presence of a CICU was associated with a slightly lower, but still statistically significant, RA-SMR (4.03 ± 0.87 vs 4.1 ± 1.07 ; *P* $< .001$). The correlation between CICU and a lower RA-SMR was also found in type 4 (4.03 ± 0.88 vs 4.05 ± 1.08 ; *P* $< .001$) and type 3 hospitals (4.09 ± 0.06 vs 4.59 ± 0.87 ; *P* $< .001$) ([table 3](#)).

CICU capable type 4 hospitals had a higher incidence of postoperative shock (1.8% vs 0.6%; *P* = .017), the same incidence of sepsis (0.8% vs 0.8%; *P* $< .819$), and a lower RA-SMR (4.03 ± 0.88 vs 4.05 ± 1.08 ; *P* $< .001$) compared to non-CICU hospitals.

Regarding the volume of procedures performed by the hospitals, the median of TAVI per year was 11 [2-36] for low-volume centers and 33 [9-67] for high-volume hospitals. The RA-SMR was lower in high-volume hospitals (3.95 ± 1.08 vs 4.26 ± 0.72 ; *P* $< .001$) ([table 4](#) and [figure 1](#)). The mean adjusted stay did not show any differences between CICU capable and non-CICU hospitals (1.00 ± 0.85 vs 0.98 ± 0.77 ; *P* = .581). In general, regarding the crude complication rates, TAVI did not show any statistically significant differences between high and low-volume hospitals ([table 4](#)).

Characteristics of the treating center and SAVR results

The presence of a CICU turned out to be a protective factor for in-hospital mortality in these patients (OR, 0.79; 95%CI, 0.67-0.93; *P* = .005). However, the different RA-SMRs seen among various centers with and without CICU capabilities did not show statistically significant differences (5.91 ± 1.49 with CICU vs 5.94 ± 1.72 without it; *P* = .335) ([figure 1](#)). The same thing happened with the RA-LOSR. CICU capable type 4 hospitals had a higher incidence of postoperative shock (2.2% vs 1.3%; *P* = .024) but a lower incidence of sepsis (1.1% vs 2.3%; *P* $< .001$) ([table 5](#)).

In relation to the volume of procedures performed, the RA-SMR was lower in high-volume hospitals (5.89 ± 1.54 vs 6.27 ± 2.02 ; *P* $< .001$) ([table 6](#)) without any statistically significant differences with respect to the RA-LOSR (0.99 ± 0.73 vs 1.06 ± 0.75 ; *P* = .463). No statistically significant differences were seen between high and low-volume hospitals in the crude complication rates ([table 6](#)).

Association between TAVI and SAVR results

In type 4 hospitals, no statistically significant linear correlations were found between the RA-SMRs of TAVI and those of SAVR (*r* = 0.21; *P* = .14). Similarly, the SAVR high-volume variable had a non-statistically significant protective effect when it was introduced in the risk-adjustment model of TAVI related in-hospital mortality (OR, 0.73; 95%CI, 0.33-1.62). The 17 hospitals (1134 episodes identified) that shared the TAVI and SAVR high-volume feature had a TAVI related RA-SMR that was significantly lower compared to centers with the TAVI and SAVR low-volume feature (4 ± 1.1 vs 4.5 ± 0.7 ; *P* $< .001$). A single center (80 episodes) with a high-volume of TAVI and a low-volume of SAVR had the lowest TAVI related RA-SMR of all (2.8 ± 0.3 ; *P* $< .001$ with respect to a high-volume of TAVI and SAVR performed).

DISCUSSION

This study findings that included real-world data in our country, show a consistent correlation between the hospital structural characteristics and the results obtained in aortic valve replacement

Table 1. Differences in the profile of patients and in the results of transcatheter aortic valve implantation based on the structural characteristics of each center (2014-2015)

	Type 3 hospitals		Type 4 hospitals		P
	Non-CICU	CICU	Non-CICU	CICU	
Number of episodes	85	25	865	1064	
Age	81.3 ± 5.9	82.4 ± 2.5	80.6 ± 6.9	80.8 ± 6.8	.408
Sex	54.1	44	52.1	50.4	.705
Charlson index	7.6 ± 1.5	7.2 ± 1.8	7.1 ± 1.6	7.3 ± 1.7	.022
Cardiogenic shock	1.2	0.0	0.8	1.1	.854
Previous percutaneous transluminal coronary angioplasty	12.9	24.0	20.6	15.7	.02
Infectious endocarditis	0.0	0.0	0.1	0.2	.952
CABG in the episode	0.0	0.0	0.5	0.3	.836
Percutaneous transluminal coronary angioplasty in the episode	2.4	0.0	3.7	5.4	.155
Previous CABG in the episode	3.5	8.0	9.1	7.9	.311
Cancer, metastatic cancer, and acute leukemia (CC8_14)	3.5	4.0	3.2	5.0	.293
Protein-calorie malnutrition (CC21)	0.0	0.0	0.5	0.3	.836
Morbid obesity: other endocrine/metabolic/nutritional disorders (CC22_25_26)	50.6	64.0	55.1	48.1	.011
Vascular or circulatory disease (CC27_32)	5.9	0.0	3.1	5.1	.103
Other gastrointestinal disorders (CC38)	16.5	8.0	10.6	11.3	.404
Dementia or other specific cerebral disorders (CC51_53)	1.2	0.0	1.4	2.4	.307
Hemiparesis, paraplegia, paralysis, functional disability (CC70_74_103_104_189_190)	0.0	0.0	1.2	2.0	.27
Congestive heart failure (CC85)	43.5	44.0	28.8	32.0	.014
Acute myocardial infarction (CC86)	1.2	0.0	0.7	0.9	.878
Unstable angina and other acute ischemic heart diseases (CC87)	0.0	0.0	0.9	0.6	.634
Angina; acute myocardial infarction (CC88)	3.5	12.0	2.4	2.7	.036
Hypertension (CC95)	43.5	56.0	58.6	51.9	.005
Stroke (CC99_100)	2.4	0.0	1.3	0.8	.492
Vascular or circulatory disease (CC106_109)	17.6	28.0	18.6	21.6	.267
Chronic obstructive pulmonary disease (CC111)	9.4	24.0	13.4	12.7	.277
Pneumonia (CC114_116)	1.2	0.0	1.2	2.3	.259
Kidney dialysis (CC134)	2.4	0.0	0.3	0.8	.139
Kidney damage (CC135_140)	36.5	24.0	23.9	27.8	.04
Pressure ulcers or chronic skin ulcer (CC157_160)	1.2	4.0	0.5	0.3	.031
Chronic skin ulcer except for pressure ulcers (CC161)	0.0	0.0	0.6	0.0	.078
Diabetes mellitus or diabetic complications except for proliferative retinopathy (CC17_19_123)	34.1	32.0	34.7	32.9	.868

CABG, coronary artery bypass graft; CC, Condition Categories;²⁵ CICU, cardiac surgery and intensive care unit.

Note: 16 episodes could not be identified into any of the 4 groups of hospitals.

Data are expressed as no. (%) or mean ± standard deviation.

procedures, both surgical and transcatheter (figure 1). High-volume hospitals with cardiac surgery and intensive care units (CICU) have lower risk-adjusted mortality rates in both procedures.

In relation to the association between volume and results, our study also shows TAVI results that are consistent to those described

by the medical literature,¹⁰⁻¹⁴ with mortality rates that are similar to those seen in other countries in the study period (2014-2015) and higher to those published for 2015-2017.¹⁴ In Spain, the mortality rate differences seen after adjusting for high and low-volume centers are lower to the ones reported, which may be explained because, actually in those years in Spain, low-volume

Table 2. Differences in the profile of patients and in the results of surgical aortic valve replacement based on the structural characteristics of each center (2014-2015)

	Hospitales tipo 4		P
	Non-CICU	CICU	
Number of episodes	6456	7523	
Age	69.3 ± 11.2	69.6 ± 11.3	.053
Sex	41.7	41.8	.823
Charlson index	6.5 ± 1.8	6.5 ± 1.9	.885
Cardiogenic shock	2.0	1.3	.001
Previous percutaneous transluminal coronary angioplasty	4.9	3.9	.004
Infectious endocarditis	1.5	1.4	.507
CABG in the episode	18.9	18.9	.894
Percutaneous transluminal coronary angioplasty in the episode	0.5	0.8	.116
Previous CABG in the episode	2.4	3.5	< .001
Cancer, metastatic cancer, and acute leukemia (CC8_14)	2.0	2.6	.023
Protein-calorie malnutrition (CC21)	0.6	0.2	< .001
Morbid obesity: other endocrine/metabolic/nutritional disorders (CC22_25_26)	49.7	49.5	.789
Vascular or circulatory disease (CC27_32)	4.1	3.7	.209
Other gastrointestinal disorders (CC38)	7.0	8.2	.006
Dementia or other specific cerebral disorders (CC51_53)	0.8	0.8	.666
Hemiparesis, paraplegia, paralysis, functional disability (CC70_74_103_104_189_190)	1.7	1.7	.737
Congestive heart failure (CC85)	19.2	24.1	< .001
Acute myocardial infarction (CC86)	1.4	1.4	.670
Unstable angina and other acute ischemic heart diseases (CC87)	1.7	1.6	.528
Angina; acute myocardial infarction (CC88)	1.2	1.4	.242
Hypertension (CC95)	55.6	53.5	.015
Stroke (CC99_100)	1.7	2.0	.140
Vascular or circulatory disease (CC106_109)	19.7	21.1	.034
Chronic obstructive pulmonary disease (CC111)	7.7	7.7	.893
Pneumonia (CC114_116)	1.9	2.1	.309
Kidney dialysis (CC134)	0.3	0.4	.857
Kidney damage (CC135_140)	18.9	18.5	.576
Pressure ulcers or chronic skin ulcer (CC157_160)	0.8	0.5	.058
Chronic skin ulcer except for pressure ulcers (CC161)	0.2	0.2	.707
Diabetes mellitus or diabetic complications except for proliferative retinopathy (CC17_19_123)	25.3	23.3	.007

CABG, coronary artery bypass graft; CC, Condition Categories;²⁵ CICU, cardiac surgery and intensive care unit.

Note: 1167 episodes could not be identified in any of the 2 groups of hospitals.

Data are expressed as no. (%) or mean ± standard deviation. Only statistically significant factors with OR > 1 are shown.

centers were being compared to very low-volume centers. Therefore, 52 out of the 53 center that performed TAVIs in Spain from 2014 through 2015 were within the range of the 2 lower quartiles (5-54 procedures per year), per volume of procedures performed, in the study conducted by Vemulapalli et al.¹⁴. Only 7 of those centers were above the range of the lower tercile in the study conducted by Kaier et al.¹⁵.

These data should be interpreted in the context of the learning curve of this technique in our country.²⁹

The correlation between a higher volume and a lower RA-SMR was also found for SAVR. Again in this case, low-volume centers were being compared since only 12 and 10 out of the 42 centers, in 2014 and 2015 respectively, performed > 200 SAVRs, and over 70% of

Table 3. Differences in the results of transcatheter aortic valve implantation based on the characteristics each center (2014-2015)

	Type 3 hospitals		Type 4 hospitals		P
	Non-CICU	CICU	Non-CICU	CICU	
Acute myocardial infarction	1.2	0.0	0.7	0.9	.878
Implantation of permanent pacemaker	17.6	16.0	13.2	15.0	.536
Postoperative stroke	1.2	0.0	1.0	0.6	.624
Prosthetic heart valve complications	3.53	0.00	1.85	4.32	.002
Postoperative shock	0.00	0.00	0.58	1.79	.017
Postoperative kidney damage	1.2	0.0	2.5	2.4	.743
Hemorrhage or hematoma complicating the procedure	16.5	32.0	10.5	13.7	.003
Accidental puncture or laceration during the procedure	3.5	0.0	3.2	4.0	.600
Postoperative infection	1.2	0.0	0.6	1.7	.145
Sepsis	0.0	0.0	0.8	0.8	.819
Vascular surgery during admission	2.4	4.0	5.0	5.7	.542
RA-LOSR	1.10 ± 0.87	0.97 ± 0.47	0.98 ± 0.77	1.00 ± 0.85	.581
RA-SMR	4.59 ± 0.87	4.09 ± 0.06	4.05 ± 1.08	4.03 ± 0.88	< .001

CICU, cardiac surgery and intensive care unit; RA-LOSR, risk-adjusted length of stay ratio; RA-SMR, risk-adjusted standardized mortality ratio. Data are expressed as no. (%) or mean ± standard deviation.

Table 4. Differences in the results of transcatheter aortic valve implantation based on the volume of cases of each center (2014-2015)

	Low-volume centers	High-volume centers	P
Acute myocardial infarction	0.63	0.95	.311
Implantation of permanent pacemaker	14.21	14.36	.489
Postoperative stroke	0.91	0.71	.402
Prosthetic heart valve complications	2.92	4.86	.366
Postoperative shock	1.46	1.33	.172
Postoperative kidney damage	2.54	2.29	.412
Hemorrhage or hematoma complicating the procedure	13.60	12.15	.188
Accidental puncture or laceration during the procedure	2.72	4.18	.054
Postoperative infection	1.30	1.10	.424
Sepsis	1.17	0.55	.105
Vascular surgery during admission	4.15	5.92	.049
RA-LOSR	0.992 ± 0.655	1.008 ± 0.787	.237
RA-SMR	4.26 ± 0.72	3.95 ± 1.08	< .001

RA-LOSR, risk-adjusted length of stay ratio; RA-SMR, risk-adjusted standardized mortality ratio.

Data are expressed as no. (%) or mean ± standard deviation.

the centers were within the 2 lower quartiles of SAVR volume according to the study conducted by Hirji et al.³⁰.

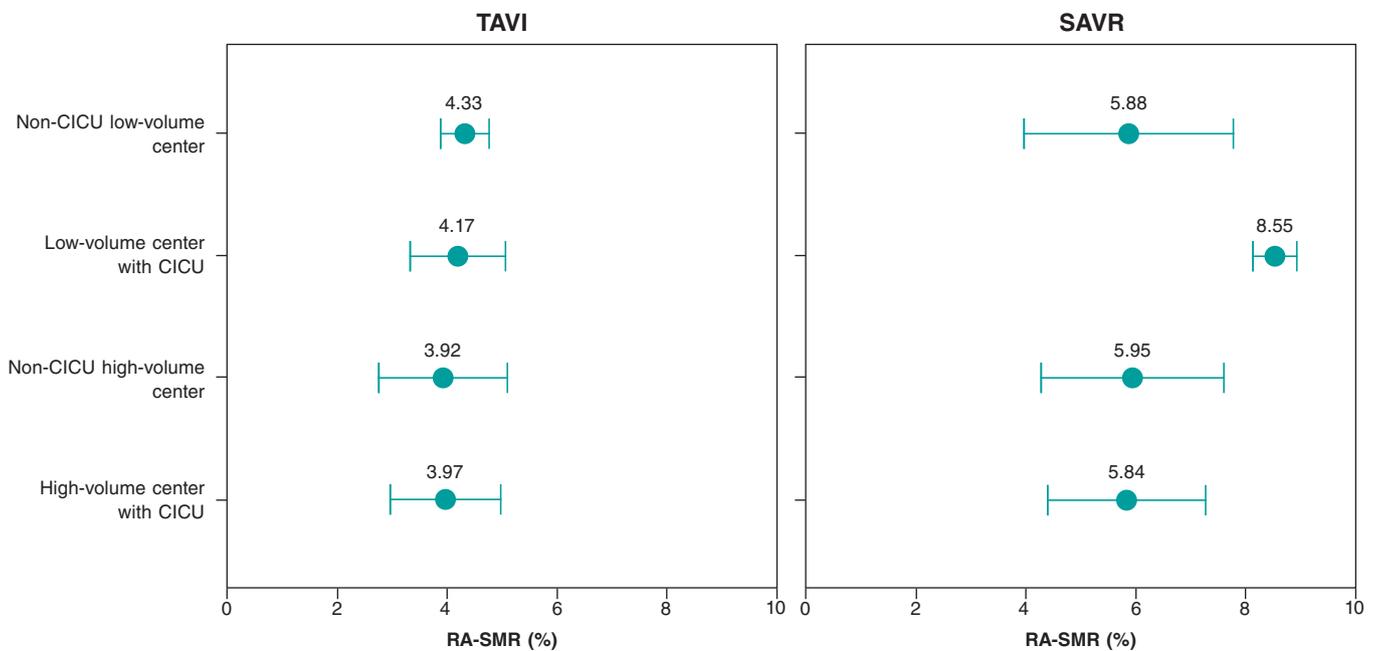
In this study, TAVI and SAVR high-volume centers had a lower TAVI-adjusted mortality rate compared to low-volume centers for

both procedures, which is consistent with the findings reported by Mao et al.³¹. However, the only hospital identified as a high-volume center for TAVI and a low-volume center for SAVR had excellent TAVI results; since it was a single center with limited number of cases (4% of all TAVIs performed), this finding, suggestive that specific experience is more relevant than global experience in aortic valve replacement procedures, should be studied in the future. However, this is reasonable because it shows that here experience accumulates per processes or specific dedicated teams rather than centers in general.

Since no references were found in the medical literature, the newest finding of this study was the association between the presence of a CICU and the lower mortality rate reported for both techniques. This correlation is even more solid and clinically significant for TAVI rather than SAVR, which seems somehow intuitive, since patients treated with SAVR are often referred to general intensive care units.

The association between CICU availability and optimal results in the management of cardiogenic shock in the AMI setting²⁰ had been described by the Spanish National Healthcare System. However, this association had not been reported in surgical procedures. Medical literature describes a virtuous relation between the volume of SAVRs performed and TAVI results, which is probably associated with the greater experience of the heart team.^{29,31} The presence of a CICU can be a variable that includes both the cardiologists' greater experience and higher participation in the management of patients in critical cardiac condition and the experience of the hospital, cardiology unit, and cardiac surgery unit. In both cases, the CICU contributes to a better management of patients treated with interventional procedures (TAVI and SAVR) across the entire healthcare process.

Therefore, the results described may be important to plan healthcare and allocate resources such as teaching and training in the 2 aforementioned procedures.



	High-volume		Low-volume		High-volume		Low-volume	
	Non-CICU	CICU	Non-CICU	CICU	Non-CICU	CICU	Non-CICU	CICU
Center =	7	11	12	12	13	22	6	1
N =	525	742	340	322	5255	7319	1200	204

Figure 1. In-hospital mortality adjusted comparison for transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR). Note that, regarding SAVR, in low-volume centers with CICU only 1 center was excluded. CICU, cardiac surgery and intensive care unit; RA-LOSR, risk-adjusted length of stay ratio; RA-SMR, risk-adjusted standardized mortality ratio.

Table 5. Differences in the results of surgical aortic valve replacement based on the characteristics of each center (2014-2015)

	Type 4 hospitals		P
	Non-CICU	CICU	
Acute myocardial infarction	1.4	1.4	.67
Implantation of permanent pacemaker	4.0	4.5	.138
Postoperative stroke	1.1	1.3	.305
Prosthetic heart valve complications	2.5	1.1	.729
Postoperative shock	1.3	2.2	.024
Postoperative kidney damage	6.9	6.1	.038
Hemorrhage or hematoma complicating the procedure	6.2	6.3	.767
Accidental puncture or laceration during the procedure	1.0	0.8	.095
Postoperative infection	1.8	2.2	.132
Sepsis	2.3	1.1	< .001
Vascular surgery during admission	2.7	3.1	.166
RA-LOSR	1.00 ± 0.68	0.99 ± 0.67	.770
RA-SMR	5.91 ± 1.49	5.94 ± 1.72	.335

CICU, cardiac surgery and intensive care unit; RA-LOSR, risk-adjusted length of stay ratio; RA-SMR, risk-adjusted standardized mortality ratio. Data are expressed as no. (%) or mean ± standard deviation.

Table 6. Differences in the results of surgical aortic valve replacement based on the volume of cases of each center (2014-2015)

	Low-volume centers	High-volume centers	P
Acute myocardial infarction	1.81	1.37	.066
Implantation of permanent pacemaker	3.75	4.32	.117
Postoperative stroke	0.93	1.22	.117
Prosthetic heart valve complications	1.54	1.14	.072
Postoperative shock	2.26	2.44	.320
Postoperative kidney damage	6.63	6.67	.462
Hemorrhage or hematoma complicating the procedure	5.95	6.35	.279
Accidental puncture or laceration during the procedure	0.82	0.88	.445
Postoperative infection	1.57	2.04	.112
Sepsis	1.46	1.69	.269
Vascular surgery during admission	2.22	2.93	.055
RA-LOSR	1.06 ± 0.75	0.99 ± 0.73	.463
RA-SMR	6.27 ± 2.02	5.89 ± 1.54	< .001

CICU, cardiac surgery and intensive care unit; RA-LOSR, risk-adjusted length of stay ratio; RA-SMR, risk-adjusted standardized mortality ratio. Data are expressed as no. (%) or mean ± standard deviation.

Limitations

This study is a retrospective analysis of administrative data. However, even with its inherent limitations, the validity of its design has been compared to clinical registries.^{26,32} Such reliability allows us to compare the results of multiple hospitals³³ and has been used specifically to analyze TAVI results.^{11-13,29,30} However, we should mention that data from the MBD should be interpreted with caution because they were not audited. Finally, this study shows the early experience with TAVI, probably still within the learning curve of this technique in the centers studied, which is why findings should be compared to more recent and larger series.

CONCLUSIONS

There is a correlation between the structural characteristics of the treating centers and the results obtained in aortic valve replacement, both surgical and endovascular, with great heterogeneity among the various centers. Large volume hospitals with cardiac surgery units and CICU capabilities have a lower risk-adjusted mortality rate in both procedures.

FUNDING

This study has been funded by an unconditional grant from the Interhospital Foundation for Cardiovascular Research.

AUTHORS' CONTRIBUTIONS

I. J. Núñez-Gil: conceptualization, drafting of the manuscript and analysis; J. Elola and M. García-Márquez: conceptualization, data collection and analysis, drafting and critical review of the manuscript; J. L. Bernal and C. Fernández: data collection and analysis and critical review of the manuscript; A. Íñiguez, L. Nombela Franco, P. Jiménez-Quevedo, J. Escaned and C. Macaya: elaboration and critical review of the manuscript; and A. Fernández-Ortiz: conceptualization, data analysis, preparation and critical review of the manuscript.

CONFLICTS OF INTEREST

None reported.

ACKNOWLEDGEMENTS

We wish to thank the Health Information Institute of the Spanish National Healthcare System at the Spanish Ministry of Health, Consumer Affairs and Social Welfare for partially disclosing the MBD database.

WHAT IS KNOWN ABOUT THE TOPIC?

- Symptomatic severe aortic stenosis is a common cause of morbidity and mortality in our country. The treatment recommended here is aortic valve replacement.
- In numerous medical and surgical procedures, the volume of procedures performed by the treating hospital has proven to play a significant role in the results obtained.

- This correlation between volume and results has been specifically reported for TAVI. In Spain, it has been reported for AMI, cardiogenic shock, and coronary revascularization surgery, among others.

WHAT DOES THIS STUDY ADD?

- This article analyses real-world data in our country from over 17000 patients who received a prosthetic aortic valve through SAVR or TAVI.
- The findings show an important heterogeneity and a consistent correlation between the structural characteristics of the treating centers and the results obtained in aortic valve replacement both through SAVR and TAVI.
- Large-volume centers with cardiac surgery units and CICU capabilities run by cardiologists have lower risk-adjusted mortality rates in both procedures.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000154>.

REFERENCES

- Alkhouli M, Alqahtani F, Ziada KM, Aljohani S, Holmes DR, Mathew V. Contemporary trends in the management of aortic stenosis in the USA. *Eur Heart J.* 2020;41:921-928.
- Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38:2739-2791.
- Luft HS, Hunt SS. Evaluating individual hospital quality through outcome statistics. *JAMA.* 1986;255:2780-2784.
- Thiemann DR, Coresh J, Oetgen WJ, Powe NR. The association between hospital volume and survival after acute myocardial infarction in elderly patients. *N Engl J Med.* 1999;340:1640-1648.
- Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med.* 2002;346:1128-1137.
- Gandjour A, Bannenberg A, Lauterbach KW. Threshold volumes associated with higher survival in health care: a systematic review. *Med Care.* 2003;41:1129-1141.
- Ross JS, Normand ST, Wang Y, et al. Hospital Volume and 30-Day Mortality for Three Common Medical Conditions. *N Engl J Med.* 2010;362:1110-1118.
- Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med.* 1979;301:1364-1369.
- Canto JG, Every NR, Magid DJ, et al. The volume of primary angioplasty procedures and survival after acute myocardial infarction. *N Engl J Med.* 2000;342:1573-1580.
- Vakili BA, Kaplan R, Brown DL. Volume-Outcome Relation for Physicians and Hospitals Performing Angioplasty for Acute Myocardial Infarction in New York State. *Circulation.* 2001;104:2171-2176.
- Srinivas VS, Hailpern SM, Koss E, Monrad ES, Alderman MH. Effect of Physician Volume on the Relationship Between Hospital Volume and Mortality During Primary Angioplasty. *J Am Coll Cardiol.* 2009;53: 574-579.
- Kim LK, Minutello RM, Feldman DN, et al. Association between transcatheter aortic valve implantation volume and outcomes in the United States. *Am J Cardiol.* 2015;116:1910-1915.
- Badheka AO, Patel NJ, Panaich SS, et al. Effect of hospital volume on outcomes of transcatheter aortic valve implantation. *Am J Cardiol.* 2015; 116:587-594.
- Vemulapalli S, Carroll JD, Mack MJ, et al. Procedural Volume and Outcomes for Transcatheter Aortic-Valve Replacement. *N Engl J Med.* 2019;380: 2541-2550.

15. Kaier K, Oettinger V, Reinecke H, et al. Volume–outcome relationship in transcatheter aortic valve implantations in Germany 2008–2014: a secondary data analysis of electronic health records. *BMJ Open.* 2018;8:e020204.
16. Goicolea Ruigómez FJ, Elola J, Durante-López A, Fernández-Pérez C, Bernal JL, Macaya C. Cirugía de revascularización aortocoronaria en España. Influencia del volumen de procedimientos en los resultados. *Rev Esp Cardiol.* 2020;73:488-494.
17. Bertomeu V, Cequier A, Bernal JL, et al. Mortalidad intrahospitalaria por infarto agudo de miocardio. Relevancia del tipo de hospital y la atención dispensada. Estudio RECALCAR. *Rev Esp Cardiol.* 2013;66:935-942.
18. Worner F, San Román A, Sánchez PL, Viana A, González-Juanatey JR. Atención a los pacientes con enfermedades cardíacas agudas y críticas. Posición de la Sociedad Española de Cardiología. *Rev Esp Cardiol.* 2015;69:239-242.
19. Rodríguez-Padial L, Elola FJ, Fernández-Pérez C, et al. Patterns of inpatient care for acute myocardial infarction and 30-day, 3-month and 1-year cardiac readmission rates in Spain. *Int J Cardiol.* 2017;230:14-20.
20. Sánchez-Salado JC, Burgos V, Ariza-Solé A, et al. Trends in cardiogenic shock management and prognostic impact of type of treating center. *Rev Esp Cardiol.* 2020;73:546-553.
21. Íñiguez Romo A, Bertomeu Martínez V, Rodríguez Padial L, et al. The RECALCAR project. Healthcare in the cardiology units of the Spanish National Health System, 2011 to 2014. *Rev Esp Cardiol.* 2017;70:567-575.
22. Worner F, San Román A, Sánchez PL, Viana Tejedor A, González-Juanatey JR. The healthcare of patients with acute and critical heart disease. Position of the Spanish Society of Cardiology. *Rev Esp Cardiol.* 2016;69:239-242.
23. Procedure-Specific Measure Updates and Specifications Report Hospital-Level 30-Day Risk-Standardized Mortality Measure Isolated Coronary Artery Bypass Graft (CABG) Surgery – Version 4.0. Yale New Haven Health Services Corporation/Center for Outcomes Research & Evaluation (YNHHC/CORE). *Centers for Medicare & Medicaid Services (CMS).* 2017.
24. Society of Thoracic Surgeons'. Online STS Adult Cardiac Surgery Risk Calculator. Available online: <http://riskcalc.sts.org/stswebriskcalc/#/>. Consultado 20 Dic 2019.
25. Pope GC, Ellis RP, Ash AS, et al. Principal inpatient diagnostic cost group model for Medicare risk adjustment. *Health Care Financ Rev.* 2000;21: 93-118.
26. Sharon-Lise T, Normand SLT, Glickman ME, Gatsonis CA. Statistical methods for profiling providers of medical care: issues and applications. *J Am Stat Assoc.* 1997;92:803-814.
27. Goldstein H, Spiegelhalter DJ. League tables and their limitations: statistical aspects of institutional performance. *J Royal Stat Soc.* 1996;159:385-443.
28. Shahian DM, Normand SL, Torchiana DF, et al. Cardiac surgery report cards: comprehensive review and statistical critique. *Ann Thorac Surg.* 2001;72:2155-2168.
29. Lunardi M, Pesarini G, Zivelonghi C, et al. Clinical outcomes of transcatheter aortic valve implantation: from learning curve to proficiency. *Open Heart.* 2016;3:e000420.
30. Hirji SA, McCarthy E, Kim D, et al. Relationship Between Hospital Surgical Aortic Valve Replacement Volume and Transcatheter Aortic Valve Replacement Outcomes. *JACC Cardiovasc Interv.* 2020;13:335-343.
31. Mao J, Redberg RF, Carroll JD, et al. Association Between Hospital Surgical Aortic Valve Replacement Volume and Transcatheter Aortic Valve Replacement Outcomes. *JAMA Cardiol.* 2018;3:1070-1078.
32. Bernal JL, Barrabés JA, Íñiguez A, et al. Clinical and administrative data on the research of acute coronary syndrome in Spain: minimum basic data set validity. *Rev Esp Cardiol.* 2018;72:56-62.
33. Krumholz HM, Wang Y, Mattera JA, et al. An administrative claims model suitable for profiling hospital performance based on 30 day mortality rates among patients with an acute myocardial infarction. *Circulation.* 2006;113: 1683-1692.



A decade of left atrial appendage closure: from procedural data to long-term clinical benefit

Rafael J. Ruiz-Salmerón,^{a,*} María Ronquillo-Japón,^a Carlos Robles-Pérez,^a Manuel Iglesias-Blanco,^a Carlos Rubio-Iglesias,^a Rafael García de la Borbolla,^a César Carrascosa-Rosillo,^a Sergio Rodríguez de Leiras,^a Manuel Vizcaíno-Arellano,^a Irene Méndez-Santos,^a and Juan Polo-Padillo^b

^a Servicio Endovascular, Hospital Virgen Macarena, Seville, Spain

^b Departamento de Medicina Preventiva y Salud Pública, Facultad de Medicina, Seville, Spain

ABSTRACT

Introduction and objectives: A better positioning of left atrial appendage closure (LAAC) requires assessment of its clinical benefits to reduce thromboembolic and bleeding events in a real-world population.

Methods: Single-center retrospective study of our consecutive LAAC activity for 9 years. Both the device success and procedural success were registered as well as the reduction of the expected rates of thromboembolic and major bleeding events.

Results: A total of 260 LAAC procedures were performed in a population with nonvalvular atrial fibrillation with CHA₂DS₂-VASc and HAS-BLED scores of 4.3 ± 1.6 and 3.7 ± 1.2 , respectively. Procedural success was 98.8%, and the rate of serious adverse events within the first 7 days was 2.3%. At a median follow-up of 2.5 ± 1.9 years and an estimated population of 637.9 patients-year, the thromboembolic event rate was 1.4 per 100 patients-year (75.5% risk reduction) and the rate of major bleeding was 3.0 per 100 patients-year (58.5% risk reduction), which was significantly lower than anticipated. The thromboembolic and major bleeding events per 100 patients-year showed a lower tendency for patients with very long follow-up (over 4 years) compared to the remaining of the population (0.7 vs 2.0 with $P = .17$, and 1.7 vs 4.0 with $P = .09$, respectively).

Conclusions: In our population, the LAAC showed high procedural success and a low rate of periprocedural adverse events. LAAC induced a significant reduction in the rate of predicted thromboembolic and hemorrhagic events, and this reduction was maintained even at very long follow-up.

Keywords: Percutaneous closure. Arterial embolism. Cerebral ischemia.

Una década de cierre percutáneo de la orejuela izquierda: desde el procedimiento hasta el beneficio a largo plazo

RESUMEN

Introducción y objetivos: Conocer el beneficio clínico del cierre percutáneo de la orejuela izquierda (OI) en nuestro medio; en concreto, la reducción de eventos tromboembólicos y hemorrágicos, que permitiría un mejor posicionamiento de esta intervención.

Métodos: Estudio retrospectivo que recoge la actividad del cierre de OI en un centro durante 9 años. Se registraron la tasa de éxito del dispositivo y del procedimiento, así como las tasas de eventos tromboembólicos y de hemorragia mayor.

Resultados: Se evaluaron 260 procedimientos de cierre de OI en una población con fibrilación auricular no valvular y puntuación en las escalas CHA₂DS₂-VASc de $4,3 \pm 1,6$ y HAS-BLED de $3,7 \pm 1,2$. El éxito del procedimiento fue del 98,8%, y la tasa de eventos adversos graves en los primeros 7 días fue del 2,3%. Con un seguimiento medio de $2,5 \pm 1,9$ años y una población de 637,9 pacientes-año, la tasa de eventos tromboembólicos fue de 1,4 por 100 pacientes-año (75,5% de reducción del riesgo) y la de hemorragia mayor fue de 3,0 por 100 pacientes-año (58,5% de reducción del riesgo), ambas significativamente menores que las predichas. Las tasas de eventos por 100 pacientes-año en los pacientes con seguimiento muy largo (más de 4 años) mostraron tendencia a ser menores que en el resto de la población (0,7 frente a 2,0, con $p = 0,17$, para evento tromboembólico, y 1,7 frente a 4,0, con $p = 0,09$, para hemorragia mayor).

* **Corresponding author:** Servicio Endovascular, Hospital Virgen Macarena, Avda. Doctor Fedriani 3, 41009 Seville, Spain.
E-mail address: rjruizsalmeron@yahoo.es (R.J. Ruiz-Salmerón).

Received 19 August 2020. Accepted 30 October 2020. Online: 02-02-2021.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Conclusiones: En nuestra población, el cierre de la OI mostró un elevado éxito del procedimiento y una baja tasa de eventos inmediatos. El cierre de la OI indujo una significativa reducción en la tasa prevista de eventos tromboembólicos y hemorrágicos, y dicha reducción se mantuvo a muy largo plazo.

Palabras clave: Cierre percutáneo. Embolia arterial. Isquemia cerebral.

INTRODUCTION

Percutaneous left atrial appendage closure (LAAC) has been extensively studied in clinical trials. Despite the excellent results of efficacy and safety regarding the LAAC from randomized clinical trials,¹ these studies are limited by their design, which is still not applicable to our routine clinical practice. Maybe this is the reason why in our setting, the LAAC program is still far from reaching its full potential.² Without detriment to the current level and grade of clinical recommendation for the LAAC,³ the medical community will only gain confidence in this procedure when further studies are presented assessing its performance in our routine clinical practice.

The LAAC is a solid structural procedure that in Spain is only second to transcatheter aortic valve implantation (TAVI).⁴ The experience gained with the LAAC has moved the focus of attention from the early aspects of success and safety towards other issues still not properly addressed such the performance of LAAC reducing long-term cardiovascular events or its lingering benefits over time.

To this day, there are very few papers gathering the long-term experience gained with the LAAC with a median follow-up of 2.5 years.^{1,5-9} It is only from this long-term perspective that we will understand the value of a procedure largely based on the prophylaxis of the thromboembolic complications occurred during the patient's life.

The objective of this study was to present our own experience in the follow-up of the population treated with LAAC from the beginning of this program to assess its overall performance and, especially, the reduction of long and very long-term thromboembolic and bleeding events.

METHODS

Our study is a retrospective analysis of the LAAC activity developed consecutively in a teaching hospital from March 2011 through February 2020. This procedure was indicated by different large volume hospital units including the internal medicine, neurology, and cardiology units. Our unit has included the LAAC as a strategic program within our structural heart procedures.

Left atrial appendage closure: the procedure and the device implanted

All procedures were performed in an identical working setting (facilities and personnel). However, 3 different modalities were used: on the one hand, general anesthesia and conscious sedation, both with transesophageal ultrasound guidance, and a third modality with fluoroscopy guidance only while the patient remained awake.

Although at the beginning of our experience only general anesthesia was used, 2.5 years later the possibility of conscious sedation administered by our personnel started to become a reality; the criterion to choose between general anesthesia or conscious sedation was logistical due to the discretionary participation of the anesthesiology unit in structural heart procedures. In both modalities, the type of probe used for the transesophageal ultrasound was the exact same one.

The protocol of conscious sedation consisted of sedoanalgesia through the IV administration of 50 mg of pethidine followed by a bolus of 0.5 mg/kg of propofol with slow infusion in 3 min. with continuous monitoring of saturation and hemodynamics. After the introduction of the transesophageal probe several boluses of 10 mg of IV propofol were administered on demand based on the patient's discomfort or rejection.

The procedure guided by fluoroscopy only was spared for cases with absolute or relative contraindication for transesophageal ultrasound use (in our unit we do not have intracavitary ultrasound) and for patients considered very frail for anesthetic induction; however, it became a reality 4 years after we started our experience. In these patients, a coronary computed tomography angiography was recommended to assess the left atrial appendage and discard the presence of an inner thrombus; in any case, an angiography was performed via transseptal access through a pigtail catheter from the left atrial appendage ostium without selective cannulation to discard the presence of thrombus. After catheterizing the left atrial appendage, a 180° rotational acquisition was performed through the injection of contrast at a flow rate of 8 mL/s with a total of 48 mL; by doing this a 3D image of the left atrial appendage was obtained (software i-Pilot, Siemens, Germany) that fused with the real fluoroscopy.

The 2 most popular devices in the market today were used: the WATCHMAN device in its WATCHMAN 2.5 and WATCHMAN Flex versions; Boston Scientific, United States) and the AMPLATZER ACP/Amulet device (Abbott, United States); the LAMBRE device (Lifetech Scientific, China) was implanted anecdotically. The selection of one or the other did not follow any clinical or anatomical criteria and the alternate use of both devices was well-balanced. Only in fluoroscopy-guided procedures the AMPLATZER Amulet device was preferential since its delivery criteria are basically fluoroscopic.

Performance of left atrial appendage closure and follow-up

The definitions were based on the Munich consensus document regarding the LAAC.¹⁰ Successful LAACs were defined as successful devices (successful implantation of the first device selected) and successful procedures (uneventful final successful implantation within the first 24 hours). The device was released after confirming the suitability of ultrasound and fluoroscopic parameters. In cases performed under fluoroscopy guidance, position and stability were

assessed over the fusion imaging as well as the lack of uncovered lobes in the angiography.

Regarding treatment after the implant, there was no pre-specified criterion and the patient's bleeding risk was adjusted. All patients were assessed using a thoracic ultrasound within the first 24 hours prior to hospital discharge. Adherence to the transesophageal ultrasound control 1.5 months after the procedure was very irregular.

Follow-up was conducted back in February 2020 by reviewing the Andalusian (Diraya) electronic health record system. The appearance and dates of the following events were registered: death and causes, ischemic stroke/systemic embolism, major bleeding (inacpacitating and major hemorrhages), and medical therapy at the follow-up. The futility of the LAAC was defined as mortality rate due to non-cardiac causes reported within the first year.

The performance of the LAAC at the follow-up was assessed using the risk reduction rate of thromboembolic (ischemic stroke/systemic embolism) or bleeding events (major bleeding) while taking into account the risk estimates from the CHA₂DS₂-VASc¹¹ and HASBLED scores,¹² respectively.

A 4-year follow-up limit has been established to start taking about «very long evolution» since this was the follow-up period of the Protect AF clinical trial¹ that confirmed the superiority regarding mortality of LAAC over anticoagulation.

Statistical analysis

The estimates were obtained using IBM SPSS v26.0 and Epidat 4.2 statistical software. Initially, a descriptive analysis of data was conducted by generating means and standard deviations of numerical variables, and frequency and percentage distributions of qualitative variables.

The comparison between the demographic and clinical quantitative variables was conducted using the ANOVA test after verifying the hypotheses of normality using the Shapiro-Wilks test; when significant differences were seen, multiple comparisons were conducted using the Bonferroni correction.

The comparison among the different qualitative variables was conducted using contingency tables and the chi-square test.

The comparison between event incidence rates was conducted using the Rothman index score and 95% confidence intervals (95%CI) were estimated using Rosner's method.

Finally, Kaplan-Meier curves were generated and then compared using the log rank test.

RESULTS

Population

The population studied included 260 patients with nonvalvular atrial fibrillation aged between 42 and 92 years old. The clinical characteristics of the population are shown on [table 1](#).

The most common indication for LAAC was the absolute contraindication for anticoagulant therapy due to hemorrhagic events in 229 cases (88.1%) or high-risk (2 patients with brain tumors and 1 patient with an aortic dissection; 1.1%). In 28 patients (10.8%) indication was due to the inability to take oral anticoagulants due to different bleeding risks: in 13 due to rejection to anticoagulant

Table 1. Clinical characteristics of the population

Age (years)	74.8 ± 8.1
Males	160 (61.5%)
Risk factors	
Arterial hypertension	238 (91.5%)
Diabetes (types 1 and 2)	118 (45.4%)
Smoking	93 (35.8%)
Dyslipidemia	130 (50%)
Kidney disease	64 (24.6%)
Ischemic heart disease	89 (34.2%)
Previous stroke	
Ischemic stroke	38 (14.6%)
Hemorrhagic stroke	57 (21.9%)
CHA ₂ DS ₂ -VASc	4.3 ± 1.6
CHA ₂ DS ₂ -VASc ≥ 4	176 (67.7%)
HAS-BLED	3.7 ± 1.2
HAS-BLED ≥ 3	222 (85.4%)

Data are expressed as no. (%) or median ± standard deviation.

therapy, in 6 due to previous psychiatric history that did not recommend it, in 3 due to higher risk of falling, in 3 due to poor control of the international normalized ratio, and in other 3 due to cardioembolic stroke yet despite the proper anticoagulant therapy.

When the LAAC was indicated, therapy was mostly anticoagulation (68.8% of the patients): vitamin K antagonists (83 cases, 31.9%), direct anticoagulants (71 cases, 27.3%) or dual therapy (anticoagulation and single antiplatelet therapy, 25 cases, 9.6%). Regarding patients who were not on anticoagulant therapy prior to the LAAC, 48 of them (18.5%) were on antiplatelet therapy and 33 (12.7%) did not use any antiplatelet/anticoagulant drugs.

While follow-up was being conducted (February 2020 or prior to the patient's death), our population was being treated with absence of antiplatelet/anticoagulant therapy (51 patients, 19.9%), single antiplatelet therapy with acetylsalicylic acid (135 patients, 52.5%), single antiplatelet therapy with clopidogrel (51 patients, 19.9%), dual antiplatelet therapy (14 patients, 5.4%) or anticoagulation (6 patients, 3%) ([figure 1](#)).

Procedural characteristics

Procedures were performed mostly under general anesthesia and monitored under transesophageal ultrasound guidance (59.6%). Conscious sedation, also monitored under transesophageal ultrasound guidance, was performed in 27.3% of all procedures. Only 13.1% of all procedures were performed under fluoroscopy guidance only.

The most commonly used device was the WATCHMAN (142 patients, 54.6%) followed by the AMPLATZER ACP/Amulet (116 patients, 44.6%), and occasionally the LAMBRE (2 patients, 0.8%). Given the extension of the follow-up period, 2 models of the WATCHMAN (generation 2.5 in 125 patients and WATCHMAN

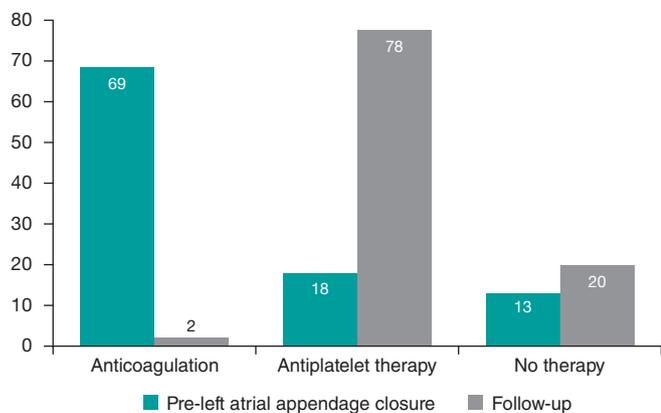


Figure 1. Evolution of antithrombotic therapy prior to the left atrial appendage closure (LAAC) until the final follow-up (%).

Flex in 17 patients) and 2 models of the AMPLATZER device (ACP in 16 patients and Amulet in 100 patients) were used.

The device success rate was 98.5% (failed in 4 patients). Failed cases were due to the device not meeting the sealing criteria for the left atrial appendage so it had to be recaptured; after choosing a different device (different size, and in 1 case, also a different model), the procedure ended satisfactorily.

Procedural success was 98.8%; 1 oropharyngeal hemorrhage due to traumatic intubation and 2 tamponades were the reason for the lack of success. Tamponades (0.77%) were due, in the first case, to a perforation of the left atrial appendage in the recapture maneuver of the WATCHMAN device; the second case, after 24 hours, was due to the perforation of the left pulmonary artery possibly eroded by the LAmbre device. These 2 patients had a good clinical progression, the first one after pericardiocentesis and the second one after surgery with pericardial patch interposition between the pulmonary artery and the left atrial appendage. No deaths, strokes, or systemic embolisms were reported during the procedure or within the first 24 hours.

The number of serious adverse events reported within the first week was 6 (2.3%) as shown on table 2.

The comparative analysis between the results of the first 50 LAACs and the remaining ones give us a glimpse of the existence of a learning curve that can be seen in the procedural variables that assess the operator’s technical skills (significant reduction of fluoroscopy time and radiation dose from the first 50 procedures): 13.6 ± 5.5 min vs 18.7 ± 18.2 min and 18 413 µGym ± 11 622 µGym vs 24 798 µGym ± 18 802 µGym,² respectively with P values = .03). However, no differences were found in the procedural success rate (98% for the first 50 cases and 99% for the remaining ones).

The procedural characteristics of the left atrial appendage closure are shown on table 3.

Follow-up and events

With a median follow-up of 2.5 years ± 1.9 years (median, 1.4 years; 95%CI, 1.1 to 1.9 years) our series included 637.9 patients-year.

A total of 58 deaths were reported at the follow-up (22.3% of the sample, 9.1% patients-year). Half of them were due to cardiac causes (4.6% patients-year). A total of 6 deaths were due to

Table 2. Serious adverse events within the first 7 days after the implant

Day	Event	Description	Death
Procedure	Hemorrhage	Traumatic intubation for general anesthesia	No
Procedure	Tamponade	Pericardiocentesis	No
1 day	Tamponade	Perforation of pulmonary artery Surgery	No
4 days	Bronchial aspiration	Bronchial aspiration while eating	Yes
4 days	Hemorrhage	Upper gastrointestinal bleeding	Yes
6 days	Hemorrhage	Upper gastrointestinal bleeding	No

Table 3. Procedural characteristics

<i>Procedural modality</i>	
General anesthesia	155 (59.6%)
Conscious sedation	71 (27.3%)
Fluoroscopy	34 (13.1%)
<i>Device</i>	
ACP-Amulet	116 (44.6%)
WATCHMAN	142 (54.6%)
LAmbre	2 (0.8%)
<i>Device size (mm)</i>	25.2 ± 3.4
<i>Fluoroscopy time (min)</i>	14.6 ± 9.7
<i>Radiation (µGym2)</i>	19 636 ± 13 488
<i>Device success</i>	98.5%
<i>Procedural success</i>	98.8%

Data are expressed as no. (%) or median ± standard deviation.

noncardiac causes within the first year, which means that LAAC futility rate was 2.3%.

Events such as ischemic strokes/systemic embolisms were reported in 9 patients (1.4% patients-year, 95%CI. 0.6-2.7); compared to the estimated risk of 5.7% patients-year, the reduction of relative risk was 75.2% (P < .001). A total of 19 major hemorrhages were reported (3.0% patients-year. 95%CI. 1.8-4.7), which is a 58.5% reduction of relative risk compared to the estimated risk of 7.2% patients-year (P < .001)

The assessment of the protective capacity of LAAC to avoid long-term thromboembolic phenomena and major hemorrhages is very relevant. Events were compared in patients with follow-ups of up to 4 years (N = 206; 346.7 patients-year) and in patients beyond this 4-year follow-up mark (N = 54; 291.3 patients-year). It was confirmed that, over time, protection against thromboembolic and hemorrhagic events still remains, and there is even a decreasing tendency: annual rate per 100 patients-year for ischemic stroke/embolism of 2.0 vs 0.7 (P = 0.17) and for major hemorrhages of

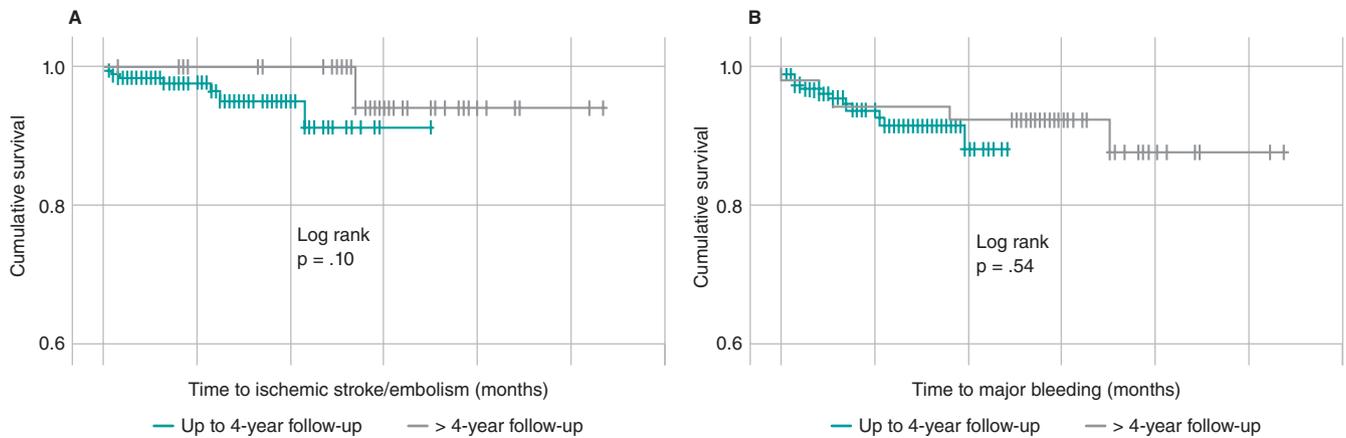


Figure 2. Thromboembolic event-free (A) and major bleeding-free (B) survival curves of patients with ≤ 4 year (green) and > 4 -year follow-up (gray). The curve comparison does not show any significant differences for either one of the events.

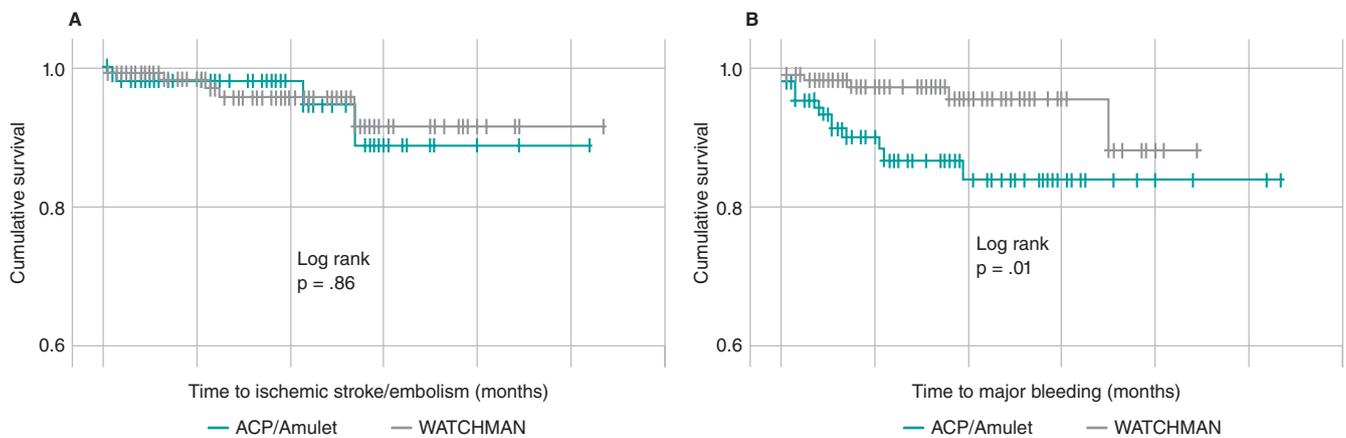


Figure 3. Thromboembolic event-free (A) and major bleeding-free (B) survival curves of patients with the AMPLATZER (green) and the WATCHMAN device (gray). No differences were seen in the devices used for thromboembolic events, but there were differences regarding major bleeding with a higher event-free survival rate in patients treated with the WATCHMAN device.

4.0 vs 1.7 ($P = .09$) in patients with up to 4-year follow-ups and longer follow-ups, respectively. The comparison of event-free survival rates for thromboembolism and major bleeding between the different populations based on the duration of the follow-up did not show any significant results (log rank with $P = .10$ for thromboembolisms and $P = .54$ for hemorrhages) (figure 2).

Follow-up based on the type of device implanted

A comparative analysis of the event-free survival rate in patients treated with the WATCHMAN and AMPLATZER devices found no significant differences between the 2 regarding their protective capabilities against ischemic strokes/systemic embolisms (log rank $P = .86$); however, the WATCHMAN showed a major hemorrhage-free cumulative incidence rate superior to the AMPLATZER device (log rank $P = .01$) (figure 3).

DISCUSSION

This real-world single-center registry shows our experience performing left atrial appendage closure in 260 consecutive patients with nonvalvular atrial fibrillation over the last 9 years. Results have been exposed in an attempt to answer the following questions:

what were the results of LAAC in our population? what is the actual performance of LAAC reducing thromboembolic or hemorrhagic events compared to the estimated risk rates? and finally, is this this event reduction maintained at the follow-up?

The clinical characteristics of our population are consistent with those of the LAAC target population in the routine clinical practice. Thus, our population showed clinical characteristics of thromboembolic risk that were similar to those published in large registries: the CHA_2DS_2 -VASc score of 4.3 was intermediate between the AMPLATZER Amulet registry¹³ with a CHA_2DS_2 -VASc score of 4.2 and the NCDR registry¹⁴ with a CHA_2DS_2 -VASc score of 4.6. Regarding the risk of bleeding, in our population the mean HAS-BLED score was 3.8, slightly higher compared to the numbers already published, and situated between the EWOLUTION registry with a HAS-BLED score of 2.3^{15,16} and the AMPLATZER Amulet registry with a HAS-BLED score of 3.3.¹³

This high risk of bleeding of our population may be explained by the fact that the indication for LAAC for almost 90% of the patients was a past medical history of bleeding (mostly gastrointestinal followed by cerebral); for the remaining 10%, the indication for LAAC was the «inability to take oral anticoagulants due to different risks of bleedings»,¹⁰ that is, by a number of reasons that forced the patient (5% of the population) or the doctor to make the decision

of choosing mechanical local therapy over the anticoagulant therapy. Although in our case the volume of elective decisions regarding the LAAC is far from the volume reported in the German registry LAARGE,¹⁷ where patient selection was essential to propose the indication in a fourth of the population, a reflection can be made on to what extent information brought to the patient is decisive to generalize this therapy.

The LAAC is a procedure with high device and procedural success rates in most of the series already published. In our series the device success rate in the implant was 98.5%; 1.5% of failed procedures were due to an erroneous selection of the size of the device. However, the left atrial appendages of all the patients from the series were eventually sealed, which contrasts with up to 7% of the procedures cancelled due to inaccessible left atrial appendage anatomies;¹⁴ this may have to do with our capacity to approach this procedure using different modalities (general anesthesia, conscious sedation, and fluoroscopy without ultrasound guidance) and different types of occluder devices (yet the device had to be changed for a different one only in 1 patient in order to finish the procedure). Our procedural success rate was 98.8%, which is higher compared to the rate reported in other registries with similar populations regarding their baseline clinical characteristics.¹⁴ Regarding procedural safety, our adverse event rate within the first 7 days after the procedure was 2.3%, which is consistent with the rate reported by large registries.¹³⁻¹⁶ Overall, this speaks of the progressive decline seen in the rate of adverse events reported during the early stage after the procedure.

In the consecutive analysis of procedural results like the left atrial appendage closure, right from the beginning of our experience and until today, the presence of a learning curve may be anticipated. However, beyond procedural variables like the radiation duration and dose, no differences were reported regarding the procedural success rate between the early period and the rest of the experience. Standardizing procedures and training the operators may be the reasons of the high success rate reported in left atrial appendage closure despite the poor early experience reported.¹⁸

Our registry, with a median follow-up of 2.5 years and a fifth of the patients with follow-up periods > 4 years allows us to assess the efficacy of the LAAC with a certain perspective. In the first place, mortality rate is surprisingly high since 22.3% of the patients included died at the follow-up. This is an annual mortality rate of 9.1%, 3 times higher compared to the 4-year follow-up of the Protect AF,¹ but it is nearly identical as other registries with a similar risk population compared to ours.⁹ The highest mortality risk seen at the follow-up has been associated with factors such as age, male sex, history of stroke or intracranial hemorrhage, low ejection fraction, and chronic kidney disease;^{8,9} in any case, this high mortality rate seen at the follow-up shows how frail this diseased population really is, which would justify an interesting debate on the futility of the LAAC in some patients¹⁹ (2.3% in our series).

The primary endpoint of LAAC is to reduce the risk of cardiac embolism in a population with nonanticoagulated atrial fibrillation. In our case, the annual rate of ischemic stroke and embolism was 1.4%, which was a significant reduction of the relative risk of 75%, which is consistent with the best data reported in the medical literature.²⁰ Regarding major bleeding, in a population with an estimated rate of bleeding > 7%, our rate was 3.0%, that is, half the rate reported by other authors.⁹

To this day, very few studies have been conducted on the long-term efficacy profile of the left atrial appendage closure. In the Ibérico II registry,⁸ the rate of thromboembolic events remained low while the rate of major bleeding was lower compared to the early rates

at the 2-year follow-up. In our population, the analysis of patients with very long clinical courses (implantation times > 4 years) revealed that the efficacy of the LAAC still remains. Also, that thromboembolic and bleeding events showed a tendency towards a lower incidence rate compared to the earliest stage.

Limitations

This study has some limitations. In the first place, no systematic antithrombotic pattern was followed after implantation. Instead, it was left to the operator's discretion, which may have impacted the short-term bleeding rate. On the other hand, no systematic imaging follow-up was arranged 45 days to 3 months after implantation, which means that an important piece of information was lost: the rate of thrombosis associated with the device, lack of residual sealing...

CONCLUSIONS

In our setting, left atrial appendage closure is an effective therapy for patients with nonvalvular atrial fibrillation and coagulation issues. It significantly reduces the rates of thromboembolic and hemorrhagic events that remain consistent in the very long term.

FUNDING

No funding related for this work.

AUTHORS' CONTRIBUTION

R.J. Ruiz-Salmerón: author of the manuscript; M. Ronquillo-Japón, C. Robles-Pérez, M. Iglesias-Blanco, C. Rubio-Iglesias, R. García de la Borbolla, C. Carrascosa-Rosillo, S. Rodríguez de Leiras, M. Vizcaíno-Arellano, and I. Méndez-Santos: critical review and J. Polo-Padillo: statistical analysis.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THE TOPIC?

- It is estimated that only 5% of the patients with nonvalvular atrial fibrillation and inability to use oral anticoagulant therapy have benefited from the left atrial appendage closure. The evidence from randomized clinical trials is based on a population that is not similar to the one considered eligible for LAAC in the real world, which is a limitation. Relevant real-world registries do not have long-term follow-ups either.

WHAT DOES THIS STUDY ADD?

- Our study provides data on the performance of the left atrial appendage closure in our routine clinical practice on procedural success and performance reducing thromboembolic and major bleeding events, which, overall, is significant compared to the estimated rates and also remains consistent over the very long-term.

REFERENCES

- Reddy VY, Sievert H, Halperin J, et al. Percutaneous Left Atrial Appendage Closure vs Warfarin for Atrial Fibrillation: A Randomized Clinical Trial. *JAMA.* 2014;312:1988-1998.
- Fukutomi M, De Backer O, Søndergaard L. Indications, current adoption and future perspectives for percutaneous left atrial appendage closure. *EuroIntervention.* 2019;14:1707-1709.
- Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2021;42:373-498.
- Ojeda S, Romaguera R, Cruz-González I, Moreno R. Registro Español de Hemodinámica y Cardiología Intervencionista. XXIX Informe Oficial de la Sección de Hemodinámica y Cardiología Intervencionista de la Sociedad Española de Cardiología (1990-2019). *Rev Esp Cardiol.* 2020;73:927-936.
- Wiebe J, Franke J, Lehn K, et al. Percutaneous Left Atrial Appendage Closure With the Watchman Device: Long-Term Results Up to 5 Years. *J Am Coll Cardiol Interv.* 2015;8:1915-1921.
- Betts TR, Leo M, Panikker S, et al. Percutaneous left atrial appendage occlusion using different technologies in the United Kingdom: A multicenter registry. *Catheter Cardiovasc Interv.* 2017;89:484-492.
- Korsholm K, Nielsen KM, Jensen JM, Jensen HK, Andersen G, Nielsen-Kudsk JE. Transcatheter left atrial appendage occlusion in patients with atrial fibrillation and a high bleeding risk using aspirin alone for post-implant antithrombotic therapy. *EuroIntervention.* 2017;12:2075-2082.
- López-Mínguez JR, Nogales-Asensio JM, Infante De Oliveira E, et al. Reducción de eventos a largo plazo tras el cierre de la orejuela izquierda. Resultados del Registro Ibérico II. *Rev Esp Cardiol.* 2019;72:449-551.
- Regueiro A, Cruz-Gonzalez I, Bethencourt A, et al. Long-term outcomes following percutaneous left atrial appendage closure in patients with atrial fibrillation and contraindications to anticoagulation. *J Interv Card Electrophysiol.* 2018;52:53-59.
- Tzikas A, Holmes DR, Gafoor S, et al. Percutaneous left atrial appendage occlusion: the Munich consensus document on definitions, endpoints and data collection requirements for clinical studies. *EuroIntervention.* 2016;12:103-111.
- Lip GY, Nieuwlaet R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest.* 2010;137:263-272.
- Pisters R, Lane DA, Nieuwlaet R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: The Euro Heart Survey. *Chest.* 2010;138:1093-1100.
- Landmesser U, Schmidt B, Nielsen-Kudsk JE, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. *EuroIntervention.* 2017;13:867-876.
- Freeman JV, Varosy P, Price MJ, et al. The NCDR left atrial appendage occlusion registry. *J Am Coll Cardiol.* 2020;75:1503-1518.
- Boersma LV, Schmidt B, Betts TR, et al. EWOLUTION investigators. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. *Eur Heart J.* 2016;37:2465-2474.
- Boersma LV, Ince H, Kische S, et al. Efficacy and safety of left atrial appendage closure with WATCHMAN in patients with or without contraindication to oral anticoagulation: 1-year follow-up outcome data of the EWOLUTION trial. *Heart Rhythm.* 2017;14:1302-1308.
- Fastner C, Nienaber CA, Park JW, et al. Impact of left atrial appendage morphology on indication and procedural outcome after interventional occlusion: results from the prospective multicenter German LAARGE registry. *EuroIntervention.* 2018;14:151-157.
- Sawant AC, Seibolt K, Sridhara S, et al. Operator experience and outcomes after transcatheter left atrial appendage occlusion with the Watchman device. *Cardiovasc Revasc Med.* 2020;21:467-472.
- Asmarats L, Rodés-Cabau J. Resultados a largo plazo tras el cierre de la orejuela izquierda: ampliando la perspectiva en la prevención no farmacológica del ictus en pacientes con fibrilación auricular. *Rev Esp Cardiol.* 2019;72:440-442.
- Glikson M, Wolff R, Hindricks G, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion – an update. *EuroIntervention.* 2020;15:1133-1180.

Percutaneous treatment of pulmonary valve and arteries for the management of congenital heart disease

Federico Gutiérrez-Larraya Aguado,* César Abelleira Pardeiro, and Enrique José Balbacid Domingo

Servicio de Cardiología Infantil, Hospital Universitario La Paz, Madrid, Spain



ABSTRACT

Brief review of current indications, materials, techniques, complications, results, and controversies around percutaneous procedures for the management of pulmonary valve and arterial branches disease. This article gives the interventional cardiologist a perspective on the material currently available.

Keywords: Valvuloplasty. Angioplasty. Percutaneous valve.

Tratamiento percutáneo de la válvula pulmonar y las arterias pulmonares en cardiopatías congénitas

RESUMEN

Se presentan las indicaciones actuales, el material, las técnicas, las complicaciones, los resultados y las controversias de los procedimientos percutáneos que permiten abordar la patología valvular y de las ramas pulmonares. El presente artículo ofrece una perspectiva del material actualmente disponible de forma clara para el cardiólogo intervencionista.

Palabras clave: Valvuloplastia. Angioplastia. Válvulas percutáneas.

Abbreviations

CHD: congenital heart disease. **CPC:** cavopulmonary connection. **PB:** pulmonary branches. **PR:** pulmonary regurgitation. **PS:** pulmonary stenosis. **PVA:** pulmonary valve atresia. **RV:** right ventricle. **RVOT:** right ventricular outflow tract.

PULMONARY VALVE STENOSIS

The origin of pulmonary valve stenosis (PVS) is almost exclusively congenital. It amounts to 7% to 10% of all congenital heart diseases (CHD). Although it is often an isolated defect, it can be associated with other congenital malformations.

Acquired stenosis is extremely rare and is associated with carcinoid syndrome or rheumatic fever. An emergent form is the stenosis of surgical bioprosthesis or valved conduits.

PVS can coexist with infundibular or supra-ventricular pulmonary stenosis, the latter often associated with Noonan, Williams or Alagille syndromes as well as with congenital rubella.

Clinical presentation is varied and goes from critical stenosis or pulmonary valve atresia (PVA) in the newborn baby to mild stenosis that can go untreated.

Although its presentation in the adult life is often asymptomatic, in cases of severe stenosis, exertional dyspnea, ventricular dysfunction, arrhythmias or sudden death have been reported. In this group, it can have a native presentation after previous surgery or valvuloplasty.

Etiology

PVS can have 3 anatomopathological presentations¹ (figure 1):

* **Corresponding author:** Servicio de Cardiología Infantil, Hospital Infantil La Paz, P.º de la Castellana 261, 20846 Madrid, Spain.
E-mail address: flarraya@yahoo.es (F. Gutiérrez-Larraya Aguado).

Received 16 October 2020. Accepted 4 December 2020. Online: 16-03-2021.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

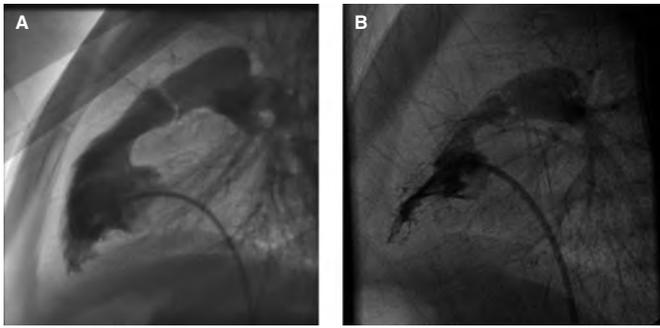


Figure 1. A: Valve stenosis due to dysplastic valve (left). B: Typical valve stenosis.

- *Typical PVS.* It is the most common: a typical tricommissural valve with mild thickening of the leaflets and commissural fusion. The valve annulus is normally developed, and post-stenotic dilatation often occurs. Valve opening is typically dome-shaped with a central stenotic orifice. It rarely presents calcification.
- *PVS due to dysplastic valve.* It represents almost 20% of all cases of PVS, although it is common in Noonan syndrome. Valve leaflets are thickened and myxomatous with limited opening and scarce commissural fusion. It can be associated with annular hypoplasia and even with proximal pulmonary trunk.
- *PVS associated with other CHD* such as interatrial communication, interventricular communication, transposition of great arteries, double outlet right ventricle (RV) or tetralogy of Fallot. The valve is often bicuspid or even unicuspid. It can be associated with infundibular or pulmonary supra-ventricular stenosis and annular hypoplasia.

Pulmonary valvuloplasty

Since 1982, percutaneous pulmonary valvuloplasty has been the technique of choice to treat pulmonary valve stenosis in newborn babies until adult life. The goal here is to overextend and tear the leaflets at commissural raphe level.

This technique is often curative and has a low rate of restenosis at the follow-up. It can often be treated with a second procedure.

The degree of immediate residual pulmonary regurgitation (PR) does not usually go from severe to mild; instead, it can progress with the passing of time. Despite of this, the need for valve replacement is not usually the case.

Indications

The natural history of pulmonary valve stenosis is associated with the degree of obstruction. Although the Doppler-derived mean pressure gradient is most reliably associated with the peak-to-peak hemodynamic gradient, the international guidelines²⁻³ establish the degree of obstruction based on the instantaneous Doppler-derived peak pressure gradient:

- *Mild stenosis* (instantaneous Doppler-derived peak pressure gradient < 36 mmHg or peak velocity < 3 m/sec). The course of the disease is often benign and it can be compatible with living a normal life. In the adult patient, evaluations every 5 years are advised.

Table 1. Treatment indications in pulmonary valve stenosis

<i>Critical stenosis of the newborn baby</i>
<i>Severe pulmonary valve stenosis (Doppler-derived peak pressure gradient > 60 mmHg or Doppler-derived mean pressure gradient > 40 mmHg) in asymptomatic patient</i>
<i>Moderate pulmonary valve stenosis (instantaneous Doppler-derived peak pressure gradient > 50 mmHg or Doppler-derived mean pressure gradient > 30 mmHg) in symptomatic patient</i>
<i>Surgery will be indicated in association with:</i>
Moderate or severe pulmonary regurgitation.
Subvalvular or supra-ventricular stenosis.
Severe tricuspid regurgitation.
Symptomatic dilatation of pulmonary artery due to extrinsic compression of nearby structures.
Need for surgical correction of other associated anomalies or arrhythmia surgery (the Maze technique).
<i>Percutaneous valvuloplasty can be the first option in case of dysplastic valves compared to surgery. Still, the rate of success can be lower.</i>

- *Moderate stenosis* (instantaneous Doppler-derived peak pressure gradient of 36 mmHg to 64 mmHg or peak velocity of 3-4 m/sec). Although often asymptomatic, the limited RV cardiac output can give rise to the appearance of exertional dyspnea or fatigue; 20% of cases can progress towards a greater degree of obstruction. Evaluations every 2 years are advised.
- *Severe stenosis* (instantaneous Doppler-derived peak pressure gradient > 64 mmHg, peak velocity > 4 m/sec or Doppler mean pressure gradient > 40 mmHg). It is associated with the presence of symptoms, RV dysfunction or cyanosis. Treatment is always indicated here.

The indications for the management of pulmonary valve stenosis are shown on [table 1](#).^{4,5}

Technique and material

The percutaneous pulmonary valvuloplasty technique has been reported extensively¹ and it can be performed under conscious sedation, local anesthesia or even general anesthesia in the pediatric patient. A total of 100 IU/Kg of sodium heparin are administered up to a maximum of 5000 IU. Transthoracic or transesophageal echocardiography are not often used here.

Femoral vein access is the most common of all, although other alternative accesses can also be used such as the jugular vein or the transhepatic access. In cases of large pulmonary valve annulus, 2 simultaneous venous accesses may be necessary to perform the double balloon technique. Arterial access is optional.

After the baseline registry of pressures, a right ventriculography will be performed preferably in the lateral and posterolateral projections with a 30° cranial inclination. The measurements of the pulmonary annulus are taken during systole at valve-leaflet junction level.

After crossing the pulmonary valve with a catheter, the exchange guidewire will be in position to provide the distal pulmonary artery with high support (preferably the inferior lobar artery). Different types of balloon catheter can be used and early diameters 1.2-1.25

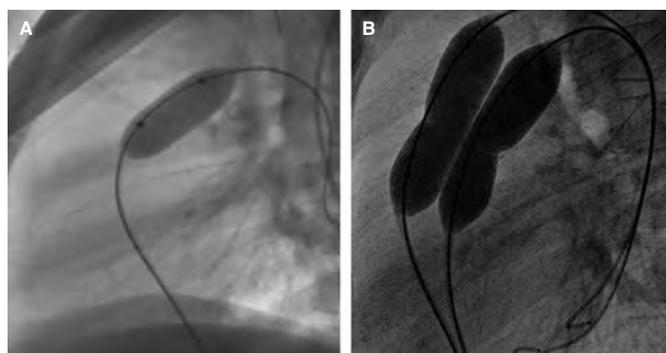


Figure 2. A: Balloon pulmonary valvuloplasty. B: Double balloon pulmonary valvuloplasty.

times larger compared to the pulmonary annulus diameter are advised (figure 2A). If the hemodynamic gradient remains > 30 mm Hg and in the absence of significant PR, it is recommended to repeat the procedure with a new balloon catheter until reaching a 1.4 ratio. The 1.5 ratio should be respected except for cases of dysplastic valves. The recommended length of the balloon is 20 mm in newborns and infants, 30 mm in pediatric patients, and 40 mm in adults.

In case of large valve annulus, the double balloon technique can be used (figure 2B); in this case, both balloons should have the same length. The effective diameter of the combined 2 balloon catheters⁶ is shown on table 2, and can be estimated as follows:

$$\text{Effective diameter} = 0.82 (\text{diameter 1} + \text{diameter 2})$$

No significant differences have been reported in terms of effectiveness between the percutaneous pulmonary valvuloplasty with single or double balloon.

Results and follow-up

The rate of immediate procedural success is close to 90% with a very low mortality rate (0.24%) and scarce major complications

(0.35%). In the dysplastic pulmonary valve, the rate of success is even lower.¹ Surgery can be spared as a second option in this type of valvular anatomy.

The rate of restenosis seen at the follow-up is 21% in the historic series and between 8% and 10% in the most recent clinical trials.⁷⁻⁹ Risk factors are the presence of dysplastic valve, residual hemodynamic gradient ≥ 30 mmHg, and use of a balloon-to-annulus ratio < 1.2 .

In the absence of severe-to-mild PR, repeating the percutaneous valvuloplasty is the selection of choice except for the management of valve dysplasia where surgery can be indicated.

At the follow-up, PR was present in 40% to 90% of the patients with an increase seen at the follow-up. Risk factors are a higher degree of early stenosis, younger age at the moment of the valvuloplasty, and a greater balloon-to-annulus ratio.

Despite this, valve replacement is rarely indicated with indications that will be based on the presence of symptoms like ventricular volumes and RV function parameters is rare. Studies suggest that the same indication parameters as in the corrected TOF with residual PR could be used.¹⁰

Special situations

Pulmonary valve atresia

PVA is a complex CHD characterized by the complete obstruction of pulmonary flow and observed within the first days of life following the ductus arteriosus physiological closure; it is incompatible with life if left to its natural progression.

The basic anatomical marker is valve atresia, often membranous, with fused leaflets and valve annulus hypodevelopment. Other lesions are often associated with this main anomaly, among them, the variable RV and tricuspid valve hypodevelopment and coronary circulation anomalies. Both the pulmonary trunk and arteries often appear normal.

The management of these patients includes early stabilization by keeping the temporal maintenance of ductal patency with

Table 2. Effective diameter using the double balloon technique

Diameter	6 mm	7 mm	8 mm	10 mm	12 mm	14 mm	15 mm	16 mm	18 mm	20 mm	22 mm	24 mm
6 mm	9.0											
7 mm	10.7	11.5										
8 mm	11.5	12.3	13.1									
10 mm	13.3	14.0	14.8	16.4								
12 mm	15.1	15.8	16.5	18.0	19.6							
14 mm	16.9	17.6	18.3	19.7	21.3	22.9						
15 mm	17.8	18.5	19.2	20.6	22.1	23.7	24.5					
16 mm	18.7	19.4	20.1	21.5	23.0	24.6	25.4	26.2				
18 mm	20.6	21.2	21.9	23.3	24.7	26.3	27.0	27.8	29.5			
20 mm	22.5	23.1	23.7	25.1	26.5	28.0	28.8	29.5	31.1	32.7		
22 mm	24.4	25.0	25.6	26.9	28.3	29.7	30.5	31.2	32.8	34.4	36.0	
24 mm	26.3	26.9	27.5	28.8	30.1	31.5	32.2	33.0	34.5	36.1	37.7	39.3

prostaglandin E1 infusion. The ultimate therapeutic approach will depend on the severity of the associated lesions. The early opening of the valve is indicated in patients with the most favorable prognosis in terms of sufficiently developed RV and tricuspid valve and lack of RV-dependent coronary circulation.

This technique is often performed via percutaneous access^{11,12} (videos 1-8 of the supplementary data) by accessing the RV and the right ventricular outflow tract (RVOT) or mammary artery via venous access and inserting a right coronary curved (JR) catheter under the imperforate valve plane. Once its correct position has been secured it is advanced through a system of microcatheter and radiofrequency guidewire, with which the valve plane is pierced. Afterwards, a sequential valvuloplasty with balloon catheter will be performed.

Although after this procedure, antegrade flow is established from the RV, this flow is rarely enough to keep an adequate level of arterial oxygen saturation due to different factors: persistent RVOT obstruction at valvular/infundibular level, restrictive behavior of the RV, and tricuspid valve hypodevelopment. All of it conditions an insufficient pulmonary flow through the natural pathway and a significant right-to-left interatrial shunt with the corresponding desaturation. For this reason, an accessory source of pulmonary flow is often required that should remain beyond the neonatal period.

Over the last few years, a new alternative has been implanting a coronary stent into the ductus arteriosus. This can be performed during the same procedure or during a second procedure via venous antegrade or arterial retrograde access. The goal here is to implant a 3 mm to 4 mm coronary stent in such a way that ductal length is fully covered, thus avoiding stent protrusion into the aortic or pulmonary borders.

This technique facilitates keeping enough pulmonary flow and arterial oxygen saturation until the RV is properly developed. Ductal stent usually closes spontaneously by endoluminal proliferation within the first year of life. In some cases, a new in-stent stent implantation may be required at the follow-up.

Fetal pulmonary valvuloplasty

Fetal pulmonary valvuloplasty is a rare technique applicable to fetuses with prenatal diagnosis of critical pulmonary valve stenosis or PVA and risk of progression towards RV hypoplasia. It is often performed between the 21st and 28th weeks of pregnancy. The goal here is to promote a better intrauterine development of right heart structures, thus favoring biventricular physiology after birth.

Through simultaneous ultrasound guidance and after achieving a proper fetal position, a transuterine, fetal transthoracic, and cardiac puncture is performed by accessing the RVOT with a 22-G Chiva needle. The pulmonary valve is then punctured with the needle in case of atresia and a 0.014 inch coronary guidewire is distally placed. Mounted over this guidewire and inside the needle, a very low-profile coronary balloon catheter is advanced and valve dilatation is performed.

Regarding results, this is a complex technique that requires multidisciplinary experience and collaboration. One of the difficulties is achieving the right needle orientation since the size of the RV cavity is so small and its geometry so complex. There is a high rate of complications including fetal arrhythmias, pericardial effusion or even fetal death.

A recent international multicenter clinical trial¹³ documented this procedure in 58 fetuses and reported a 55% rate of complications

including 7 deaths. Compared to the disease progression of patients treated with a similar cohort of treatment-naïve fetuses, a greater tendency towards biventricular physiology was confirmed after birth in the first group (87% vs 43%). Despite this, to this date, no criteria have been established with indications for this technique. Therefore risks, the group experience, and the possible benefits should all be assessed in each particular case.

PERCUTANEOUS PULMONARY VALVES

Many CHD require RVOT reconstruction using a patch, a bioprosthesis or a conduit between the RV and the pulmonary artery. In the tetralogy of Fallot, 90% of the patients who undergo surgery during childhood will reach the adult age and a significant number of them will develop regurgitation or PS following the annulus section or use of conduits. When and how to treat these conditions is still controversial since there is no expert consensus, and the American, Canadian, and European guidelines⁵ establish general rules with suboptimal levels of evidence. Also, each particular case shows characteristics unforeseen by the algorithms proposed.

Surgeons use different materials to solve these dysfunctions: allografts, porcine pericardium based heart valves—with and without support—, mechanical valves, and valved (hand-made) and non-valved conduits. Over the last 2 decades, percutaneous coronary interventions have broken into our setting pushed by the development of bioprosthesis mounted on stents; still, we don't know when to treat asymptomatic patients: precocity in replacement is associated with faster deterioration and more procedures being performed—each one with its own risk—while late procedures may no longer stop or revert the deterioration of ventricular function and volumes.

The morphology of a dysfunctional RVOT is very complex, determines the therapeutic approach (the "pyramid" morphology is not very compatible with self-expanding valves), and behaves dynamically. Echocardiography is not enough here. Instead, the computed tomography scan is required to see the coronary anatomy. Also, the cardiac magnetic resonance imaging (that cannot be performed in all cases due to problems with clips, pacemakers or heart valves causing interferences) facilitates the assessment of volumes and function, and the visualization of such dynamic behavior. Currently, the RV function is more important than the RV size both to indicate the implant and to make follow-up assessments. The coronary anatomy does not always show the behavior during and after implantation. As a matter of fact, the different RVOT measure changes during implantation don't cause linear changes in coronary arteries, which is why coronary angiography still plays an essential role. The length of self-expanding valves is significantly greater compared to balloon-expandable (and surgical) valves, which is why the total distance in the area left for implantation becomes crucial. We have known for years that the pulmonary and the aortic valves don't share the same architecture and work differently. Also, that the same heart valves operate differently in the aortic and pulmonary positions (actually, they may even not close effectively).¹⁴

Indications and historical perspective

The indications for percutaneous pulmonary valves included in the European⁵ and American¹⁵ guidelines are similar to surgical replacement. In symptomatic patients the indication is well established. Asymptomatic patients, instead, require ECG data (absolute prolonged QRS interval duration > 180 or progression), hemodynamic data (like a correlation of pressures between the RV and the left ventricle > 0.7), and Doppler-derived peak and mean pressure

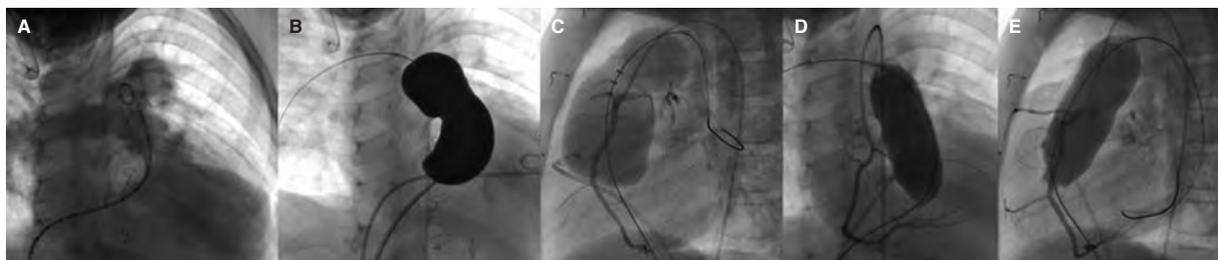


Figure 3. Angiography examples. **A:** in pulmonary trunk, individualized, in right anterior oblique projection at 20° + cranial at 40°. **B:** with balloon catheter for interatrial communication measurement and morphologic assessment, in the same projection. **C:** in lateral projection showing how over-dilatation occludes the left anterior descending coronary artery that originates from the right coronary artery. **D:** selective coronary angiography with a balloon of the same diameter as the implantable valve diameter, without coronary obstruction, the same projection as in A. **E:** with the same balloon as in D, in lateral projection.

gradients > 50 and > 30, respectively. But, above all, magnetic resonance imaging data in cases of significant pulmonary regurgitation (regurgitation fraction > 30%): right ventricular end-diastolic volumes > 160 mL/m², double right end-diastolic volume compared to the left one, end-diastolic volume > 80 mL/m², and RV ejection fraction < 0.40-0.45 (or negative progression).

The first heart valve ever implanted percutaneously was the Bonhoeffer pulmonary valve back in 2000. It was based on the idea of suturing a bovine jugular vein with the valve in a vascular stent. The valve was given the name Melody (Medtronic Inc, United States) and obtained the CE marking and the Canadian marking in 2006 and the United States Food and Drug Administration marking back in 2010. It is indicated for elderly patients with dysfunctional surgical conduits. Its off-label use has increased and it is used in patients of up to 20 kg of weight and in native RVOTs,¹⁶ with technical modifications (previous stent implantation in the implant area) to minimize some of the most common complications reported (stent fracture), but with precautions due to the significant numbers of infectious endocarditis reported (a problem shared with the surgical bovine heart valve Contegra (Medtronic, United States). The limitation of valve sizes available (18 mm, 20 mm, and 22 mm) is also a problem because many patients with regurgitation have large-caliber pulmonary trunks, which has led to imaginative solutions for extended uses.

In 2008 The Edwards SAPIEN heart valve (Edwards Lifesciences LLC, United States) for aortic positioning started being used in the right position thanks to the COMPASSION clinical trial that proved it safe and effective for conduits with moderate or severe pulmonary regurgitation with or without stenosis.¹⁷ Its sizes are larger (23, mm 26 mm, and 29 mm), it does not fracture, and the incidence rate of infectious endocarditis is lower (although, on this regard, the literature available is not that "solid"). In 2016 the Edwards SAPIEN XT heart valve was approved by the European and American regulatory agencies for use in children and adults with regurgitation or PS; the current SAPIEN 3 heart valve is approved for the aortic position only, but numerous off-label implants have been reported in the pulmonary position.

The procedure requires a meticulous prior preparation. An arterial access and 2 venous accesses, preferably femoral, are required. It can also be implanted via jugular vein access. The angiographic study (figure 3) serves 2 purposes: a) study the anatomy and sizes of the "trunk" or conduit and pulmonary branches (PB) for which different projections are needed (the RV outflow tract is better seen on the right anterior oblique projection at 20° + cranial at 20° and in the lateral position; still, changes need to be made in this particular case), and inject contrast agents both in the trunk and in the RV while the trunk is occluded with a balloon catheter; and b) study the anatomical relations of proximity since the adjacent

structures can be compressed (the ascending aorta or the coronary arteries). To that end, while the balloon catheter remains inflated in the pulmonary artery, an aortogram or coronary angiography or both is performed. A 34 mm or 35 mm very compliant cutting balloon for interatrial communication can be used. However, at times, the balloon compliance exceeds the target diameter of the implant causing coronary or aortic compression. When this happens, other balloons of identical diameter to the target implant will be required. In the presence of a calcified conduit, the approach should be gradual given the risk of rupture. If the Melody valve is used, a previous stent should always be implanted—covered if the conduit is calcified—which is not required in the remaining heart valves.

There is no consensus as to whether the entire procedure should be performed in 1 or 2 stages leaving the first stage to anatomical/physiological study and stent implantation.

Pulmonary prosthetic valves available

There are 2 large groups of heart valves available, balloon-expandable valves and self-expanding valves. The former have been around a little longer, are approved by regulatory agencies, over 10 000 of them have already been implanted worldwide, have greater radial strength, allow a better control of the diameter to reach, shorten when dilated, and are extremely demanding from the technical point of view. Self-expanding valves are more modern, are in the pipeline in several clinical trials still pending approval, reach larger diameters, and are longer; still, there can be problems in the pulmonary trunk distal portion as they don't shorten, there is no control over their diameter (they reach their nominal value), and no re-dilatations are possible. Figure 4 shows the heart valves currently available for pulmonary use.

The Melody TPV valve

The Melody TPV valve (Medtronic Inc, United States)¹⁸ is a balloon-expandable valve. It is built from a bovine jugular vein with an 18 mm native valve sutured to a platinum-iridium CP stent (NuMED, Canada). The overall length of the entire system is 28 mm and shortens in relation to the final diameter. It can expand from 16 mm to 22 mm in diameter (it probably also works up to 24 mm). Valve crimping is manual and it is delivered and released using Medtronic Ensemble patented system—a version of the double balloon angioplasty BIB (NuMED Inc., United States)—with a 22-Fr profile in its distal portion and a 16-Fr profile in its proximal portion, of 100 mm in length; it is advanced through a high-support guidewire allocated in a pulmonary branch (preferably the left one).

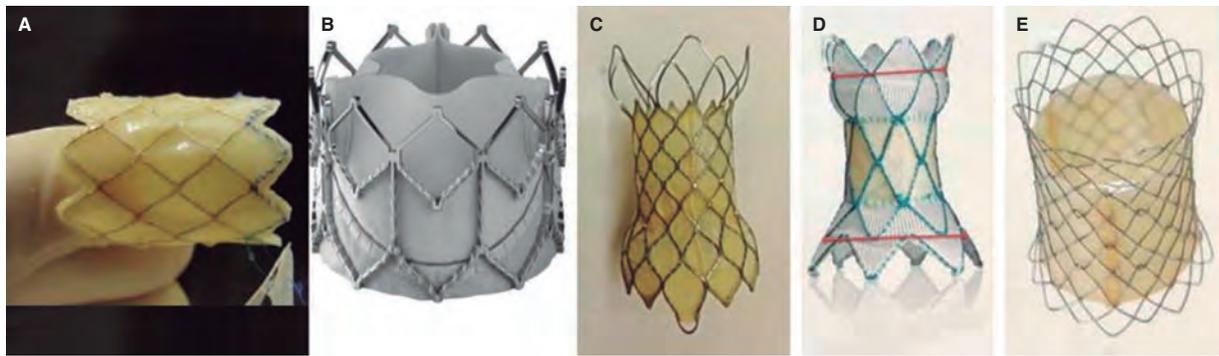


Figure 4. Percutaneous pulmonary valves. **A:** Melody valve (Medtronic, United States). **B:** Edwards XT valve (Edwards Lifesciences LLC, United States). **C:** Venus valve (Venus MedTech, China). **D:** Harmony valve (Medtronic, United States). **E:** Pulsta valve (Taewoong Medical, South Korea).

The Edwards SAPIEN valve

The Edwards SAPIEN valve (Edwards Lifesciences LLC, United States)¹⁸ is a balloon-expandable valve with porcine pericardium leaflets mounted on a cobalt chromium stent. Its height is smaller compared to the Melody valve. The SAPIEN XT THV model has been approved for the pulmonary position and is built in 23 mm (height of 14.3 mm), 26 mm (height of 17.2 mm), and 29 mm (height of 19.1 mm). Valve crimping is performed with a specific device, proximal to the position of the balloon, “mounted” on it, and once in the inferior vena cava, delivered and released using Novaflex patented system (Edwards Lifesciences, United States) with 18-Fr, 19-Fr or 20-Fr profiles depending on the valve diameter. It is very rigid and not easy to advance or retrieve especially with a previous stent already implanted, which can end up damaging the tricuspid valve. The SAPIEN 3 THV model is built of the same diameters (in heights of 18 mm, 20 mm, and 22.5 mm) but it is an evolution whose internal covered portion is fairly shorter (9.3 mm, 10.2 mm and 11.6 mm). It has an outer protection of polyethylene terephthalate to minimize the possibility of leaks. Its stent has different geometries in the proximal and distal portions so that it shortens even more in its proximal border. It is delivered through the “deflectable” Edwards Commander Delivery System of 14-Fr for the 23 mm and 26 mm valves, and 16-Fr for the 29 mm valve with a patented introducer sheath (Edwards eSheath). It has been reported that through greater volume inflations compared to the nominal volume, the SAPIEN 3 valve can reach 30 mm.

The Venus P-valve

The Venus P-valve (Venus MedTech, China) is designed for native tracts. It is a self-expanding, trileaflet valve of porcine pericardium with a 30 mm in length nitinol stent covered by porcine pericardium—except for its distal portion—that dilates in both borders (1 cm in each border), with radiopaque marks to facilitate its location; the diameter of the valve is that of the nondilated portion (18 mm to 34 mm). Delivery system is MedTech patented with a 20-to-22-Fr distal caliber, a 16-Fr proximal caliber, and a 22-to-24-Fr introducer sheath. Valve crimping is manual by submerging it in a cold saline solution.¹⁹

Two clinical trials have been conducted to achieve the CE marking, one in China and the other one in Europe. Both have been completed and are in the data evaluation stage with inclusion criteria similar to those of the remaining valves.

The Harmony mTPV 25 valve

The Harmony mTPV 25 valve (Medtronic, United States) is a self-expanding nitinol structure with a polyester covering and

a porcine pericardium valve stitched in the middle. Its conceptual design is vast: the first clinical trials started in the United States in 2013, but, to this date, the valve is still under constant modification (Harmony TPV 22, Harmony TPV 25, and modified Harmony TPV 25). It is available for research purposes only.

The PULSTA valve

The PULSTA valve²⁰ (Taewoong Medical, South Korea) is designed for native tracts. It is a nitinol, trileaflet, self-expanding valve of porcine pericardium also covered with porcine pericardium except for its proximal and distal (major) portions. It has radiopaque marks to outline the area covered. Numbering corresponds to the narrowest area—commisure level—from 18 mm to 32 mm. A larger diameter (1 mm to 2 mm) compared to the pulmonary trunk is selected; the dome-shaped area measures 4 mm more compared to the narrow area. It is built in 2 different lengths: 33 mm and 38 mm. The delivery system caliber is 18-Fr for up to 28 mm and 20-Fr for larger sizes. Its radial strength is lower compared to that of the Melody or SAPIEN valves, That is why it is not the heart valve of choice for stenotic conduits.

Currently, most implants have been performed in Asia, but since December 2019 there is an ongoing clinical trial being conducted in Europe, in which Spain participates. The inclusion criteria are similar to those of any other valve.

Complications and limitations

The complications and limitations of the heart valves described above are:

- Compressions: in approximately 5% of the patients there is risk of coronary compression during the procedure. Large heart valves can distort the aortic root with regurgitation.
- Ruptures: of the conduit, especially if calcified, during predilatation requiring immediate implantation of a covered stent; navigating heart valves is not easy and requires high-support guidewires capable of perforating the PB; during advance and retrieval maneuvers, the tricuspid valve can be damaged causing regurgitation.

Still, mortality rate during the procedure is around 1.4%.²¹

Fractures were a common thing at the follow-up (12.4%) with the old Melody implants without previous stent implantation and when the risk factors were young age, greater pre- and postprocedural

residual gradient, smaller conduit size, proximity to sternum, and presence of recoil after delivery.²² The second most common complication is infectious endocarditis (4.9%), mostly with the Melody, with a higher incidence rate compared to surgical cases. Several hypotheses have been proposed to explain this: damage to the valve during the assembly, no strict observance of sterility measures, previous endocarditis, unsatisfactory hemodynamic results, poor dental hygiene, piercings, tattoos, etc.²³

Data from registries²⁴ and multicenter clinical trials on the mid-term evolution of the Melody heart valve and further reinterventions of the valve.²⁵ During a > 5-year follow-up period it is expected that in up to 14.4% to 15% of the cases some procedure will be performed, mostly due to fractures. There is a great variety of indications among the different centers. Actually, in up to 65% of all procedures a valve-in-valve procedure has been performed. This confirms that infectious endocarditis is still the Achilles heel of the Melody valve with a 2.4% incidence rate per patients-year. There are no data available on other types of valves.

PERCUTANEOUS TREATMENT OF PULMONARY BRANCHES

The percutaneous management of PB stenosis has become widely used after the arrival of new materials and technologies. Currently, it is the first option because surgical outcomes are poor. PB stenosis can be congenital, associated with syndromes (Williams-Beuren, Alagille, etc.) or connatal infections like rubella or be part of complex CHD like tetralogy of Fallot, pulmonary atresia or pulmonary artery sling. However, stenosis is the evolutionary or residual result of surgery in these same and other CHD as in the aftermath of the Jatene arterial switch procedure (the Lecompte maneuver) or when it is necessary to place a conduit between the RV and the PB. Percutaneous treatment improves cardiac output and alleviates pressure to the RV, re-balances the distribution of flow to both lungs, improves functional class, exercise capacity (VO_2 and VE/VCO_2), and eventually the prognosis of patients with univentricular and biventricular physiology. The following are considered criteria for hemodynamic repercussions: gradient ≥ 20 mmHg, angiographic stenosis $\geq 50\%$, RV or pulmonary artery pressure $\geq 60\%$ of systemic blood pressure (biventricular) or asymmetry ($\geq 30\%$) in pulmonary reperfusion as seen on the magnetic resonance imaging or the scintigraphy. This flow asymmetry can stop unilateral non-significant stenosis from translating into pressure gradients since we are dealing with a parallel flow.²⁶

Generalities

Balloon angioplasty

Balloon angioplasty is spared for patients with low body weight when the anatomy is not suitable for stent implantation or when the segments will be involved in future surgeries. Immediate restenosis, of up to 50%, due to recoil or extrinsic compression is more common compared to stents. It is a safe procedure with a < 1% rate of major complications. Taking the hilar diameter as the vessel reference, balloons whose critical diameter is 3 times larger compared to the diameter of stenosis are selected without exceeding the double of the reference diameter (figure 5). To be effective the notch needs to go away, and a controlled intimal-medial tear needs to occur for eccentric remodeling, which means that results may not be immediate. The procedure is considered successful with lumen increases $\geq 50\%$ of the minimum diameter, reductions $\geq 20\%$ of RV or systemic pressure or flow increases $\geq 20\%$ towards the target lung.²⁷ Using the latest noncompliant high-pressure balloons and microtome or cutting balloons improves the results of angioplasties that do not respond to conventional balloons or that are

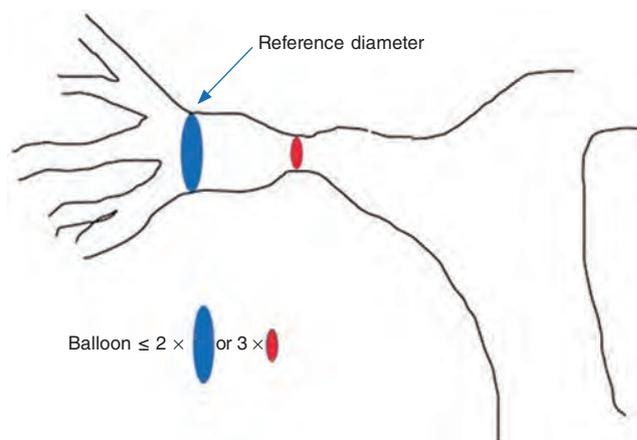


Figure 5. Reference diameters in the percutaneous treatment of pulmonary branches.

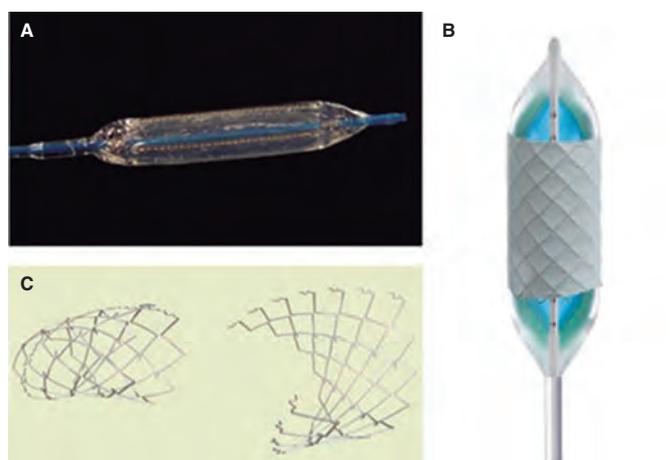


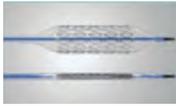
Figure 6. A: Cutting balloon. B: BIB balloon with mounted covered CP stent. C: BeGrow stent.

especially resistant like those of lobar branches in patients with genetic syndromes. Common cutting balloons are 8 mm in diameter and they need to be placed in the target area through a sheath to avoid damaging the tricuspid or pulmonary valve when advanced or retrieved (figure 6).

Stent angioplasty

Stent angioplasty, described by Mullins in the 1980s, provides structural support and avoids immediate restenosis due to recoil or folding. Its mid- and long-term results are superior to conventional angioplasty. Better profiles and semi-open or open cell designs that allow re-dilatation have made this technique available for younger and thinner patients. However, this has come at the expense of successive re-dilatations needed to adapt to the size of the vessel due to growth or to dilate the origin of jailed branches. Several studies prove that these successive re-dilatations are safe and effective. Closed-cell stents are more stable in the manual crimping and they usually have greater radial strength. They normally navigate on the balloon inside a sheath towards the stenosis to avoid damaging the right valves, stent migration so they can be repositioned before implantation.²⁸ The profile of this sheath is proportional to the diameter of the balloon on which it is mounted. Same sized premounted balloons have a better profile; some models do not even require the

Table 3. Stents currently used in pulmonary branches

Uncovered			Covered	
Premounted	Formula		BeGraft aortic	
	Valeo		Atrium iCAST	
Not premounted	AndraStent XL y XXL		CP Covered	
	CP stent			
	Palmaz Génesis		Optimus Covered	

AndraStent (Andamed, Germany): cobalt chromium; semi-open cell design; XL of 8-25 mm and XXL of 10 mm to 32 mm.
 Atrium (Maquet, Germany): stainless steel; open cell design; 5 mm to 10 mm; approved for the management of tracheobronchial stenosis.
 Formula (Cook Medical, United States): stainless steel; open cell design that can be redilated twice its size without shortening; 5 mm to 10 mm; 6-Fr-to-7-Fr.
 Valeo (Bard, United States): stainless steel; semi-open cell design that can be redilated twice its size without shortening; 5 mm to 10 mm; 6-Fr-to-7-Fr.
 CP stent (NuMED, United Kingdom): iridium-platinum + gold hinges; 12 mm to 24 mm; exponential shortening with the diameter.
 Optimus (Andratec, Germany): cobalt chromium; semi-open cell design; fewer shortening compared to the CP stent.
 BeGraft (Bentley, Germany): flexible; 12 mm to 24 mm; less proportional shortening compared to the CP stent.
 Palmaz Genesis (Cordis, United States): stainless steel; closed-open cell design; 3 mm to 18 mm.

use of long introducers for implantation purposes. One of the most commonly used balloons is the BIB double balloon, currently 8 mm to 30 mm in diameter. It consists of 2 concentric balloons where the inflation of the internal one allows us to predict how the stent will behave in the stenosis facilitating sequential expansion, and repositioning if necessary (figure 6). Considering a normal Nakata index of 250 mm²/m² to 300 mm²/m², an adult patient of 2 m² of body surface will need a stent capable of reaching an ideal diameter of 18 mm to 20 mm in each branch. Self-expanding stents improve the profile because they don't need a balloon for implantation purposes and are not re-dilatable. To this date, they have been approved for other locations like the biliary route or the femoropopliteal axis.²⁹

In general, bare-metal stents are implanted leaving the covered ones for cases where it is necessary to repair the damaged vessel wall or regulate flow using a diabolo-shaped configuration towards one branch or the other or else through a systemic-pulmonary artery shunt (table 3).

New technologies

Some of these new technologies are:

- Drug-eluting balloons: noncompliant balloons with an antiproliferative substance covering like rapamycin analogues or placlitaxel approved to treat peripheral arterial stenosis, but particularly useful to treat in-stent restenosis due intimal proliferation.³⁰
- Bioresorbable stents: they avoid further re-dilatations in growing patients. They can be built with organic polymers or

corrodible metal alloys like iron or magnesium. Some studies show inflammatory responses in the vessel wall and doubts surrounding significant restenosis. Still pending approval by the United States Food and Drug Administration, the Pediatric Bioresorbable Stent (480 Biomedical Stent Inc., United States) is the design in the most advanced clinical trial stages so far and has been specifically designed to treat PB stenosis in pediatric CHD.

- Breakable stents: cells with hinges programmed to break with a balloon like the BeGrow (Bentley, Germany) or ready for resorption like the Growth Stent (QualiMeD, Germany) consisting of 2 halves joined by biodegradable sutures that disappear within 5 months, thus facilitating blood vessel growth (figure 6).

Complications

Percutaneous procedures on pulmonary branches are associated with moderate (angioplasty) or high (stent) risk. They are often performed under general anesthesia, with unfractionated heparin at 100 IU/Kg (to a maximum of 5000 IU) and with an activated clotting time ≥ 250 seconds. The most common complications and risk factors are shown on table 4; and they are more common when the procedure is an emergency procedure and when the patient is of a younger age reaching 38% in newborn babies. As a general rule, the support guidewire should be placed in the inferior lobar branch and further guidewires should not be used. Once removed, advancing the sheath again through the recently dilated segment is also ill-advised. Tears or dissections are more common in the traditional balloon, typically without any clinical repercussions. When there are repercussions,

Table 4. Complications and most common risk factors

Complications	Risk factors
Vascular damage	Overdilatation, too rigid guidewire, surgical patches, recent surgery
Thrombosis	Cavopulmonary connection, cyanosis, small branches, short activated clotting time, no antiplatelet therapy
Stent embolization	Low weight, disproportion, bifurcation, malapposition, emergency, manual crimping
Reperfusion edema	Chronic cyanosis, older age
Mismatch	Early implantation, non-dilatable design
Restenosis	Short overlapping, genetic syndrome, cavopulmonary connection, bifurcation, residual waist, oversizing, external compression, self-expanding stent

anticoagulation reversal is required by re-inflating the balloon in the leak area, implanting a stent or through surgery. In-stent restenosis is often due to intimal proliferation but also to stent fractures that cause it to lose its structural integrity or due to extrinsic compression. It is less common with semi-open cell designs and with the greater flexibility of self-expanding stents. There are no clear recommendations on antithrombotic treatment after implantation. Endothelialization occurs 6 months after implantation and, although thrombosis is rare, the routine clinical practice is using antiplatelet therapy during that time.³¹

Specific situations

Bifurcations

There are 2 technical options to repair these stenoses without compromising the contralateral branch flow:

- Through the simultaneous implantation of 2 stents, each one mounted on its own guidewire and sheath. Both stents should be of the same size and both balloons should be inflated simultaneously and progressively ([figure 1A of the supplementary data](#)).
- By implanting a long open-cell stent from one of the branches towards the pulmonary trunk to later recross towards the contralateral branch with a different guidewire and then implant a second shorter stent ([figure 1B of the supplementary data](#)). This technique is useful when we only have 1 venous access or when the implantation of a pulmonary valve with pre-stenting is intended.

Cavopulmonary connection

In the fragile Fontan-type univentricular physiology—a pumpless non-pulsatile pulmonary circuit—the criteria upon which the indication is based are in a lower threshold compared to biventricular physiology. Also, almost any degrees of angiographic stenosis or hemodynamic gradient are significant since they can significantly increase central venous pressure and large asymmetries in flow distribution towards both lungs. Securing the most symmetrical flow distribution possible to both lungs is key to avoiding the formation of arteriovenous fistulas. That is why it may be necessary to reduce the flow of a fistula previously created or towards 1 of the branches through a diabolo-shaped covered stent ([figure 2 of the supplementary data](#)). These procedures are complex because of

the access routes (femoral, jugular, transhepatic), because patients have been operated on many times, have a higher risk of thrombosis (polyglobulia, non-pulsatile slow flow), sometimes they even have recent surgical beds, are young patients, etc. The PB angioplasty is the most commonly performed procedure—only second to the extracardiac conduit angioplasty—in an extensive modern cohort of patients with total cavopulmonary connection (CPC) both after superior CPC and after completing the inferior CPC ([figure 3 of the supplementary data](#)). Stenosis most often occurs in the left PB (the right PB proximal segment originally) due to its longer course, compression of the neighboring ascending aorta, and the presence of lower flow in the stage between the pulsatile Glenn and the total CPC.³²

The final size of PB and therefore their flow is directly associated with the long-term success of this physiology and with the patient's functional class. However, it is often necessary to perform periodic invasive reassessments of the state of the stents previously implanted to adjust them to growth. This is because non-invasive methods may not be sensitive enough. After stent implantation, the clinical practice guidelines published by the American Heart Association recommend anticoagulant therapy for 3 to 6 months.

Postoperative state

The repair of certain CHD is associated with a risk of residual or evolutionary PB stenosis. With the Lecompte maneuver, associated with the arterial switch for the repair of the d-transposition of great arteries, PB stenosis occurs early in up to 28% of patients. On the other hand, pulmonary supravulvular stenosis is the leading cause of reintervention during childhood. Percutaneous treatment is technically challenging because we are dealing with small patients with sometimes recent sutures, in bifurcation, and a compromised space with the SVC and the ascending aorta. ([figures 4 and 5 of the supplementary data](#)). For that reason, traditional balloon angioplasty may be the only effective option in less than half of the cases.³³

Other CHD with common residual PB stenosis after surgery are the tetralogy of Fallot, truncus arteriosus, the pulmonary artery sling, etc. and all those that require having to place a conduit between the RV and the PB like the Ross, Rastelli, Yasui, Sano procedures, etc.

The current technological advances made in imaging techniques, materials, and devices has revolutionized the possibilities regarding the percutaneous management of pulmonary trunk, valve, and PB lesions. That is why the indications published in the clinical practice guidelines are being changed.

FUNDING

No funding.

AUTHORS' CONTRIBUTION

F. Gutiérrez-Larraya Aguado, coordination and final draft revision; C. Abelleira Pardeiro and E.J. Balbacid Domingo partial drafts and provision of figures.

CONFLICTS OF INTEREST

None reported.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000196>.

REFERENCES

- Rao PS. Percutaneous Balloon Pulmonary Valvuloplasty: State of the Art. *Catheter Cardiovasc Interv.* 2007;69:747-763.
- Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. American Society of Echocardiography, European Association of Echocardiography. *J Am Soc Echocardiogr.* 2009;22:1.
- Silvilairat S, Cabalka AK, Cetta F, et al. Echocardiographic assessment of isolated pulmonary valve stenosis: which outpatient Doppler gradient has the most clinical validity. *J Am Soc Echocardiogr.* 2005;18:1137.
- Warnes CA, Williams RG, Bashore, et al. TMACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2008;118:e714.
- Baumgartner H, De Backer J, Babu-Narayan S, et al. 2020 ESC Guidelines for the management of adult congenital heart disease (ACHD). *Eur Heart J.* 2021;42:563-645.
- Narang R, Das G, Dev V, et al. Effect of the balloon-annulus ratio on the intermediate and follow-up results of pulmonary balloon valvuloplasty. *Cardiology.* 1997;88:271-276.
- McCord BW. Independent predictors of long-term results after balloon pulmonary valvuloplasty. Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) Registry Investigators. *Circulation.* 1994;89:1751-1759.
- Voet A, Rega F, Van de Bruaene A, et al. Long-term outcome after treatment of isolated pulmonary valve stenosis. *Int J Cardiol.* 2012;156:11-15.
- Devanagondi R, Peck D, Sagi J, et al. Long-Term Outcomes of Balloon Valvuloplasty for Isolated Pulmonary Valve Stenosis. *Pediatr Cardiol.* 2017;38:247-254.
- Ruckdeschel E, Kim YY. Pulmonary valve stenosis in the adult patient: pathophysiology, diagnosis and management. *Heart.* 2019;105:414-422.
- Petit CJ, Glatz AC, Qureshi AM, et al. Outcomes After Decompression of the Right Ventricle in Infants With Pulmonary Atresia With Intact Ventricular Septum Are Associated With Degree of Tricuspid Regurgitation: Results From the Congenital Catheterization Research Collaborative. *Circ Cardiovasc Interv.* 2017;10:e004428.
- Morgan GJ, Narayan SA, Goreczny S, et al. A low threshold for neonatal intervention yields a high rate of biventricular outcomes in pulmonary atresia with intact ventricular septum. *Cardiol Young.* 2020;30:649-655.
- Hogan WJ, Grinenco S, Armstrong A, et al. Fetal Cardiac Intervention for Pulmonary Atresia with Intact Ventricular Septum: International Fetal Cardiac Intervention Registry. *Fetal Diagn Ther.* 2020;47:731-739.
- Pragt H, van Melle JP, Verkerke GJ, Mariani MA, Elbels T. Pulmonary versus aortic pressure behavior of a bovine pericardial valve. *J Thorac Cardiovasc Surg.* 2020;159:1051-1059.e1.
- Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation.* 2019;139:e637-697.
- Boshoff DE, Cools BL, Heying R, et al. Off label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label? *Catheter Cardiovasc Interv.* 2013;81:987-995.
- Kenny D, Rhodes J, Fleming G, et al. 3-Year outcomes of the Edwards SAPIEN Transcatheter heart valve for conduit failure in the pulmonary position from the COMPASSION multicenter clinical trial. *J Am Coll Cardiol Interv.* 2018;11:1920-1929.
- Fleming GA, Hill KD, Green AS, et al. Percutaneous pulmonary valve replacement. *Prog Ped Cardiol.* 2012;33:143-150.
- Cao QL, Kenny D, Zhou D, et al. Early clinical experience with a novel self-expanding percutaneous stent-valve in the native right ventricular outflow tract. *Catheter Cardiovasc Interv.* 2014;84:1131-1137.
- Kim GB, Song MK, Bae EJ, et al. Successful feasibility human trial of a new self-expandable percutaneous pulmonary valve (Pulsta valve) implantation using knitted nitinol wire backbone and trileaflet α -gal-free porcine pericardial valve in the native right ventricular outflow tract. *Circulation Cardiovasc Interv.* 2018;11:e006494.
- Virk SA, Liou K, Chandrakumar D, Gupta S, Cao C. Percutaneous pulmonary valve implantation: a systematic review of clinical outcomes. *Int J Cardiol.* 2015;201:487-489.
- Ansari MM, Cardoso R, Garcia D, et al. Percutaneous pulmonary valve implantation: present status and evolving future. *J Am Coll Cardiol.* 2015;66:2246-2255.
- Sharma A, Cote AT, Hosking MCK, et al. A systematic review of infective endocarditis in patients with bovine jugular vein valves compared with other valve types. *J Am Coll Cardiol Interv.* 2017;10:1449-1458.
- Nordmeyer J, Ewert P, Gewillig M, et al. Acute and midterm outcomes of the postapproval MELODY registry: a multicenter registry of transcatheter pulmonary valve implantation. *Eur Heart J.* 2019;40:2255-2264.
- Shahanavaz S, Berger F, Jones TJ, et al. Outcomes of transcatheter reintervention for dysfunction of a previously implanted transcatheter pulmonary valve. *J Am Coll Cardiol.* 2020;13:1529-1540.
- Feltes TF, Bacha E, Beekman RH, et al. Indications for Cardiac Catheterization and Intervention in Pediatric Cardiac Disease: A scientific Statement from the American Heart Association. *Circulation.* 2011;123:2607-2652.
- Patel AB, Ratnayaka K, Bergersen L. A review: Percutaneous pulmonary artery stenosis therapy: state-of-the-art and look to the future. *Cardiol Young.* 2019;29:93-99.
- Hiremath G, Qureshi AM, Prieto L, et al. Balloon Angioplasty and Stenting for Unilateral Branch Pulmonary Artery Stenosis Improve Exertional Performance. *JACC Cardiovasc Interv.* 2019;12:289-297.
- Zablah JE, Morgan GJ. Pulmonary Artery Stenting. *Interv Cardiol Clin.* 2019;8:33-46.
- Cohen JL, Glickstein JS, Crystal MA. Drug-Coated Balloon Angioplasty: A novel treatment for pulmonary artery in-stent stenosis in a patient with Williams syndrome. *Pediatr Cardiol.* 2017;38:1716-1721.
- Giglia TM, Massicotte MP, Tweddell JS, et al. Prevention and treatment of thrombosis in pediatric and congenital heart disease: a scientific statement from the American Heart Association. *Circulation.* 2013;128:2622-2703.
- Franco Díez E, Balbacid Domingo E, Arreo del Val V, et al. Percutaneous Interventions in Fontan Circulation. *Int J Cardiol Heart Vasc.* 2015;8:138-146.
- Nakanishi T, Matsumoto Y, Seguchi M, et al. Balloon Angioplasty for Postoperative Pulmonary Artery Stenosis in Transposition of the Great Arteries. *J Am Coll Cardiol.* 1993;22:859-866.



Debate: Percutaneous left atrial appendage closure. The clinical cardiology perspective

A debate: Cierre percutáneo de la orejuela izquierda. Perspectiva desde la clínica

Juan Cosín-Sales^{a,b,*}

^a Servicio de Cardiología, Hospital Arnau de Vilanova, Valencia, Spain

^b Facultad de Medicina, Universidad CEU Cardenal Herrera, Valencia, Spain



SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000200>

QUESTION: Briefly, what is the evidence behind the percutaneous left atrial appendage closure (LAAC) regarding oral anticoagulation (OA)? Is there any evidence on direct-acting oral anticoagulants (DAOAs)?

ANSWER: The main clinical evidence published on this regard comes from 3 randomized clinical trials (2 vs anti-vitamin K and 1 vs DAOAs), registries, and case series. The PROTECT AF clinical trial¹ included 707 patients with atrial fibrillation (AF) and CHADS₂ scores ≥ 1 who were randomized on a 2:1 ratio to receive the Watchman device (Boston Scientific, United States) or warfarin. The composite endpoint (stroke, cardiovascular death, and systemic embolism) was less prevalent in patients with the Watchman device [relative risk [RR], 0.62; 95% confidence interval [95%CI], 0.35-1.25]; however, adverse events were more common in the device group (RR, 1.69; 95%CI, 1.01-3.19) mainly due to periprocedural complications. These increased adverse events triggered a second clinical trial, the PREVAIL,² that included 407 patients with CHADS ≥ 2 randomized on a 2:1 ratio to receive the Watchman device or warfarin. The primary efficacy endpoint at the 18-month follow-up (stroke, systemic embolism or cardiovascular or inexplicable death) occurred less often than expected in the warfarin group and the non-inferiority target was not achieved. However, the secondary efficacy endpoint (stroke or systemic embolism 7 days after implantation) was achieved; also, adverse events were less common compared to those of the PROTECT AF trial.

Data from the PROTECT AF¹ and PREVAIL² clinical trials were combined in a meta-analysis³ that concluded that the Watchman device was not inferior to anti-vitamin K therapy for the composite endpoint of stroke, cardiovascular death, and systemic embolism. We should mention that patients with the Watchman device had lower chances of bleeding including hemorrhagic strokes. Nonetheless, there was a statistically insignificant higher rate of ischemic stroke and systemic embolism in the Watchman group.

The controversial aspect of these 2 clinical trials is that they only included patients with an indication for OA. However, in the routine clinical practice, the LAAC is used in patients contraindicated to OA.

The third and last clinical trial is the PRAGUE-17⁴ that compared the LAAC to DAOAs. It included 402 patients with AF (CHA₂DS₂-VASc: 4.7 \pm 1.5) and a past medical history of major bleeding or cardioembolic

event while on DAOAs or with a CHA₂DS₂-VASc ≥ 3 and HAS-BLED > 2. Apixaban was the most commonly used DAOA (95.5%). The median follow-up was 19.9 months. No statistically significant differences were found in the annual rates of the primary endpoint (stroke, transient ischemic attack, systemic embolism, cardiovascular death, clinically relevant or major bleeding or procedural complications) that were 10.99% with the LAAC and 13.42% with DAOAs (sub-hazard ratio, 0.84; 95%CI, 0.53-1.31 for non-inferiority). A total of 9 patients (4.5%) experienced major complications due to device implantation.

Regarding real-world registries, the NCDR LAAO⁵ is a large registry designed to assess the utility, safety, and effectiveness of LAAC percutaneous devices in the clinical practice. It includes 38 158 procedures performed in the United States. The mean score in the CHADS-VASC scale was 4.6 \pm 1.5, and in the HAS-BLED scale, 3.0 \pm 1.1. In-hospital major adverse events occurred in 2.16% of the patients; the most common complications were pericardial effusion that required intervention (1.39%), and major bleeding (1.25%), while strokes (0.17%) and death (0.19%) were rare.

Q.: Which are the current indications for the LAAC? Should the clinical guidelines most recently published be changed somehow?

A.: The most common indications in the routine clinical practice are high bleeding risk and contraindications to DAOAs (eg, dialysis), but as I said, the LAAC has not been studied in clinical trials with the proper statistical power in these subgroups

The recent guidelines published by the European Society of Cardiology (ESC)⁶ give the LAAC a class IIb recommendation and a B level of evidence for the prevention of strokes in patients with AF and contraindications to long-term anticoagulant therapy (eg, intracranial hemorrhage without reversible cause). The clinical guidelines published by the American Heart Association, American College of Cardiology, and the Heart Rhythm Society (AHA/ACC/HRS)⁷ also give it a class IIb recommendations as a therapeutic option for patients with an indication for oral anticoagulation, but with a high risk of bleeding, poor compliance or tolerance to anticoagulant therapy. In both guidelines, recommendations are limited. The consensus document published by the European Heart Rhythm Association (EHRA)⁸ regarding the LAAC makes an extensive review including the largest possible number of indications:

* Corresponding author: Servicio de Cardiología, Hospital Arnau de Vilanova, San Clemente 12, 46015 Valencia, Spain.

E-mail address: jcosinsales@gmail.com [J. Cosin-Sales].

Online: 24-02-2021.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

- 1) Patients with contraindications to OA due to:
 - a) High risk of potentially life-threatening or incapacitating hemorrhage or due to untreatable causes like intracranial/intraspinal bleeding (eg, diffuse amyloid angiopathy or untreatable vascular malformation) or severe gastrointestinal (eg, diffuse angiodysplasia) pulmonary or urogenital bleeding that cannot be corrected.
 - b) Serious adverse events with anti-vitamin K therapy or contraindications to DAOAs.
- 2) Patients who don't follow their anticoagulant therapy properly. This indication is controversial, and we should always inform the patient that his main treatment is anticoagulation while trying to solve the problem associated with poor compliance.
- 3) Some specific subgroups:
 - a) Ineffective OA: stroke in a patient properly anticoagulated.
 - b) After pulmonary vein ablation with left atrial appendage electrical isolation due to the high embolic risk involved after this procedure.
 - c) Combination of pulmonary vein ablation and LAAC within the same procedure.
 - d) «Primary» prevention: in patients with interatrial communication treated with percutaneous closure during the same procedure even before the patient develops AF.

Q.: Which is the common practice at your center?

A.: The most common indications are patients with AF on hemodialysis who, we already know, are poor candidates to anti-vitamin K therapy and have contraindications to DAOAs. Also, patients with very high risk of bleeding without treatable cause, especially digestive or due to other causes (eg, Rendu-Osler-Weber disease) and always after trying to solve it with a DAOA.

Q.: How valuable are imaging modalities in the selection of patients and procedural guidance?

A.: The use of imaging modalities is essential if we wish to perform successful procedures. Before the intervention, the anatomy of the left atrial appendage should be studied to see if it is eligible for closure. Also, the right material should be chosen and the presence of thrombi in the left atrium and left atrial appendage should be discarded. In general, this preprocedural assessment is performed with a transesophageal echocardiography, yet the computed tomography scan has been gaining traction.

During the procedure, x-ray images and transesophageal echocardiography are the common imaging modalities to use. When available, intracardiac echocardiography can also be used.

Between 6 and 24 weeks after the intervention, a transesophageal echocardiography or a computed tomography scan should be performed to discard the presence of thrombi in the device (that can appear in up to 2% to 4% of the cases) and significant peridevice leaks (> 5 mm).⁸

Q.: Are there any significant differences among the different devices available?

A.: The need for antithrombotic therapy post-LAAC shows that there is room for improvement because this procedure maintains the bleeding risk for a longer period of time, and it is still unclear what the optimal protocol should be. The PROTECT AF and the PREVAIL clinical trials kept patients on warfarin and acetylsalicylic acid for 45 days followed by a 6-month course of dual antiplatelet therapy and then acetylsalicylic acid for life.

The guidelines published by the ESC⁶ recommend acetylsalicylic acid permanently, clopidogrel between 1 and 6 months after the procedure and, for the Watchman device, in cases of low-risk of bleeding, a 45-day course of OA after implantation.

The consensus document published by the EHRA⁸ includes general recommendations that are very similar to those from the guidelines published by the ESC.⁶ It also claims that in patients with very high-risk of bleeding the use of single antiplatelet therapy could be an option (acetylsalicylic acid or clopidogrel) for short periods of time. However, this should always be an informed decision and the patient should think about it thoroughly.

Q.: Please tell us about any relevant ongoing clinical trials. In your professional opinion, what type of study should be conducted?

A.: The main ongoing trials are the ASAP-TOO that is assessing the LAAC in 888 patients with AF considered ineligible for OA; the OPTION trial, that is studying 1600 patients with AF to see if the LAAC with the Watchman FLX device is a reasonable option to OA (including DAOAs) after pulmonary vein ablation; and the CATALYST and CHAMPION-AF clinical trials, that will be conducting a long-term comparison between the Amulet (Abbott Vascular, United States) and the Watchman FLX device with DAOAs in patients with an indication for anticoagulant therapy due to AF.

Future clinical trials should prioritize the study of new devices comparing them to DAOAs since they are currently the therapy of choice to prevent strokes in patients with AF, especially those with relative or absolute contraindications to anticoagulation therapy. The use of these devices in patients with ischemic stroke despite the proper anticoagulation therapy should be analyzed too by associating the LAAC with an DAOA and then comparing it to an isolated DAOA. Finally, it is essential to clarify antithrombotic therapy after implantation in order to minimize it, above all, in patients with high risk of bleeding, while still keeping its efficacy.

FUNDING

No funding was received for this work.

CONFLICTS OF INTEREST

None.

REFERENCES

1. Holmes DR, Reddy VY, Turi ZG, et al. PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet*. 2009;374: 534-542.
2. Holmes DR Jr, Kar S, Price MJ, et al. Prospective randomized evaluation of the WATCHMAN Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. *J Am Coll Cardiol*. 2014;64:1-12.
3. Reddy VY, Doshi SK, Kar S, et al.; PREVAIL and PROTECT AF Investigators. 5-Year Outcomes After Left Atrial Appendage Closure. From the PREVAIL and PROTECT AF Trials. *J Am Coll Cardiol*. 2017;70:2964-2975.
4. Osmancik P, Herman D, Neuzil P, et al. Left atrial appendage closure versus direct oral anticoagulants in high-risk patients with atrial fibrillation. *J Am Coll Cardiol*. 2020;75:3122-3135.
5. Freeman JV, Varosy P, Price MJ, et al. The NCDR Left Atrial Appendage Occlusion Registry. *J Am Coll Cardiol*. 2020;75:1503-1518.
6. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2020;42:373-498.
7. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Circulation*. 2019;140:e125-e151.
8. Glikson M, Wolff R, Hindricks G, et al. ESC Scientific Document Group, EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion – an update. *Europace*. 2020;22:184.



Debate: Percutaneous left atrial appendage closure. The interventional cardiology perspective

A debate: Cierre percutáneo de la orejuela izquierda. Perspectiva desde el intervencionismo

Tomás Benito-González*

Servicio de Cardiología, Complejo Asistencial Universitario de León, León, Spain



SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000199>

QUESTION: Briefly, what is the evidence behind the percutaneous left atrial appendage closure (LAAC) regarding oral anticoagulation (OA)? Is there any evidence on direct-acting oral anticoagulants (DAOAs)?

ANSWER: The LAAC has been compared to OA regarding the prevention of thromboembolic events in patients with nonvalvular atrial fibrillation (NVAF) in 3 randomized clinical trials: the PROTECT AF, the PREVAIL, and the PRAGUE-17. The first 2 ones randomized 1114 patients with NVAF and CHADS₂ ≥ 1 on a 2:1 ratio to receive the Watchman device (Boston Scientific, United States) or warfarin. In an intention-to-treat meta-analysis of aggregate individual data from the 2 studies with 5-year follow-ups no differences were seen between both strategies in the primary composite endpoint of stroke, systemic embolism, and cardiovascular or unexplained death (hazard ratio [HR], 0.82; 95% confidence interval [95%CI], 0.58-1.17; *P* = .27).¹ In the secondary endpoint analysis a higher—though not statistically significant—rate of ischemic stroke or systemic embolism was reported in the device group (HR, 1.71; 95%CI, 0.94-3.11; *P* = .08). On the contrary, the LAAC was associated with a lower rate of hemorrhagic (HR, 0.20; 95%CI, 0.07-0.56; *P* = .002) or incapacitating stroke (HR, 0.45; 95%CI, 0.21-0.94; *P* = .034), major hemorrhage unrelated to the procedure (HR = 0.48; 95%CI 0.32-0.71; *P* < 0.001), cardiovascular or unexplained death (HR, 0.59; 95%CI, 0.37-0.94; *P* = .027), and all-cause mortality (HR, 0.73; 95%CI, 0.54-0.98; *P* = .035).

The results of the PRAGUE17 clinical trial have been recently published. This study randomized 402 patients on a 1:1 ratio with NVAF and an indication for OA to LAAC with the Amplatzer Amulet (Abbott Vascular, United States) (61.3%) or the Watchman device (38.7%) or to a DAOA, mainly apixaban (95.5%).² This trial only included patients considered of high risk with some of the following criteria: history of bleeding that required intervention or hospitalization, past medical history of embolism despite treatment with OA or CHA₂DS₂-VASc scores ≥ 3 with HAS-BLED ≥ 2. During the mean follow-up of 20.8 months ± 10.8 months no differences

were seen in the composite primary endpoint (stroke, transient ischemic attack, systemic embolism, cardiovascular death, major or clinically relevant bleeding or procedural or device-related complications) reaching criteria of non-inferiority (HR, 0.84; 95%CI, 0.53-1.31; *P* = .44; *P* for non-inferiority = .004). No differences between both groups were seen either in any of the events included in the composite primary endpoint separately.

Currently, there are 4 ongoing different randomized clinical trials that will be assessing the benefits of the LAAC with the Watchman FLX device (CHAMPION-AF [NCT04394546]), the Amplatzer Amulet device (CATALYST [NCT04226547]) or with either one of the 2 (OCCLUSION-AF [NCT03642509], CLOSURE-AF [NCT03463317]) vs DAOA therapy in patients with NVAF.

Q.: Which are the current indications for the LAAC? Should the clinical guidelines most recently published be changed somehow?

A.: The European guidelines on the management of AF published in 2020 suggest that the LAAC could be considered in patients with NVAF and a contraindication to OA (IIb level of recommendation, C level of evidence).³ Regarding this indication, I think a few considerations should be made. In the first place, the evidence available on the LAAC is limited basically because of the non-inferiority design of the clinical trials available with a limited number of patients. Also, due to the great heterogeneity of the antithrombotic therapy indicated post-LAAC, that could be conditioning the applicability of the results obtained. Secondly, the guidelines were written before the results of the PRAGUE-17 trial came out, that are consistent with the efficacy and safety profile of the procedure, also vs DAOAs (although in a limited 2-year follow-up) that is currently the treatment of choice to prevent thromboembolic events in patients with AF with, at least, moderate risk. Thirdly, since it is a «prophylactic» therapy, procedural success should be high, and the rate of related complications should be low. In this sense, in the largest registry published to this date of over 38000 patients, the rate of procedural success was 98.3% and the rate of

* **Corresponding author:** Servicio de Cardiología, Complejo Asistencial Universitario de León, Altos de Nava s/n, 24017 León, Spain.
E-mail address: tomasbenito@outlook.com (T. Benito-González).

Online: 24-02-2021.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

major complications, 2.16%.⁴ Finally, the lack of compliance to medical therapy and under or overdosing are common problems in our routine clinical practice, which have a significant impact on the efficacy of OA and are probably not reported in the randomized clinical trials as well.

Q.: Which is the common practice at your center?

A.: The patient's profile eligible for this procedure is that of an elderly patient with an indication for OA due to NVAF with a previous episode of intracranial or gastrointestinal bleeding. Other less common cases are patients with chronic anemia or high bleeding risk with an indication for OA or dual or triple antithrombotic therapy. Finally, more and more patients with stroke despite being on OA are being reported. We perform a transesophageal echocardiogram (TEE) prior to the procedure in all the cases. We often perform implantation with mild sedation and TEE guidance with microprobe. Antithrombotic therapy upon discharge is based on every particular patient and followed-up at the specific structural heart disease consultation within the first year including TEE sometime within the first 3 months after hospital discharge.

Q.: How valuable are imaging modalities in the selection of patients and procedural guidance?

A.: The preprocedural study of left atrial appendage aims at determining the anatomical feasibility for implantation purposes, providing the right dimensions for a proper sizing of the device, and excluding the existence of thrombi. To this end, a 3D imaging modality should be used, usually a TEE or a computed tomography scan. The selection of one or the other will depend on its accessibility, experience of every center, and certain characteristics of the patient like the presence of kidney disease. Regarding the computed tomography scan, a 2-stage acquisition protocol with sensitivity and specificity rates close to 100% for the detection of thrombi should be conducted.

In most cases, the LAAC is performed with TEE guidance. However, this imaging modality has complications: on the one hand, the prolonged use of the probe can cause non-negligible oropharyngeal lesions. On the other hand, general anesthesia is required in many patients with the corresponding complications and increased procedural duration and costs. In this sense, as we have been gaining experience on device implantation, new options have come up to minimize these limitations like the TEE microprobe and the intracardiac echocardiography. The microprobe provides slightly lower quality of image compared to conventional TEE but is better tolerated by the patient and requires no general anesthesia. The drawback is that no 3D images can be acquired, which means that a previous study capable of providing 3D images is necessary. Regarding intracardiac echocardiography, the latest machines available provide better quality of images, some even the possibility of 3D reconstructions (still not on the market). They do not require the presence of an imaging specialist at the cath lab or use of a transesophageal probe either. On the other hand, both the cost of the device and its disposable nature reduce its utility in the routine clinical practice. Several ongoing prospective registries will be shedding light on the safety, feasibility, and possible technical advantages.

Q.: Are there any significant differences among the different devices available?

A.: Despite the technical advances made in the procedure, there are still pending challenges or, at least, room for improvement: *a)* great anatomical variability in the left shape, orientation, and size of left atrial appendage; *b)* risk of perforation with pericardial effusion; *c)* device embolization; *d)* persistent residual leak after implantation; and *e)* rate of device related thrombosis. For all these reasons, there

are many devices to perform LAAC available today or in the pipeline that try to improve some of these aspects. Generally speaking, 2 important types of design can be distinguished here: tamponade-like devices like the Watchman, and anchor-disc shaped devices like the Amplatzer Amulet. In principle, the latter can be more versatile in complex anatomies while the first one has a growing body of evidence. Regarding procedural results, the observational data obtained do not suggest differences in the implantation success rate or in the rate of serious complications, device thrombosis or significant residual leak reported between the 2 most widely used devices to this date. However, the results from comparative studies AMULET IDE [NCT02879448] and SWISS-APERO [NCT03399851]⁵ will bring us more data on this regard.

There are many other devices available with scarce evidence and limited used, but with technical advances and very promising designs: extreme sizes, antithrombotic expanded polytetrafluoroethylene covering, self-adaptable configuration to the left atrial appendage ostium, small anchor with large disc configuration, highly flexible or articulated devices... Given the great anatomical variability of the left atrial appendage, maybe some devices will be complementary in the future. Therefore, if the volume of cases allows it, it can make sense to use more than just 1 type of device in every patient, the one more suitable to his anatomy.

Q.: Please tell us about any relevant ongoing clinical trials. In your professional opinion, what type of study should be conducted?

A.: There is no doubt that the most significant randomized clinical trials that are being conducted today are those comparing the LAAC to DAOAs. These trials will eventually determine the actual benefit of this procedure. Another very important aspect to elucidate is the optimal antithrombotic therapy to prevent device thrombosis. In this sense, the following randomized clinical trials should be highlighted: *a)* the SAFE-LAAC trial [NCT03445949] will assess the 6-month efficacy profile of dual antiplatelet therapy vs a 1-month course of dual antiplatelet therapy plus 5 months of single antiplatelet therapy; *b)* the ANDES trial [NCT03568890] will analyze the DAOA strategy vs an 8-week course of dual antiplatelet therapy; *c)* the FADE-DRT trial [NCT04502017] will be comparing the efficacy profile of 3 strategies consisting of a 6-week course of OA followed by a 6-month course of dual antiplatelet therapy, half-dose DAOA plus genotype-guided dual targeted therapy (acetylsalicylic acid + clopidogrel or half-dose DAOA depending on clopidogrel resistance or not); and *d)* the ASPIRIN-LAAO trial [NCT03821883] that will be analyzing the benefit of keeping single antiplatelet therapy starting 6 months after the procedure.

Another particularly interesting randomized clinical trial is the OPTION [NCT03795298] that will be randomizing 1600 patients treated with ablation due to AF to receive the Watchman FLX device or OA. Finally, from a theoretical point of view, evidence is still scarce in some potentially LAAC-eligible patients as it is in patients with recurring thromboembolic events despite OA or with NVAF and chronic kidney disease on dialysis. Both groups are characterized by a very high thrombotic risk. There is lack of consensus regarding the most adequate antithrombotic strategy that is empirically administered in most of the cases. Also, patients on dialysis have a high hemorrhagic risk and, unlike the general population, OA does not seem to benefit them. Some observational studies suggest that the LAAC can be safe and effective in these subgroups of patients. However, to this date, no randomized clinical trial has studied this therapy compared to others.

FUNDING

The author received no financial support for this work.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Reddy VY, Doshi SK, Kar S, et al. 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. *J Am Coll Cardiol.* 2017;70:2964-2975.
2. Osmancik P, Herman D, Neuzil P, et al. Left Atrial Appendage Closure Versus Direct Oral Anticoagulants in High-Risk Patients With Atrial Fibrillation. *J Am Coll Cardiol.* 2020;75:3122-3135.
3. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2020:ehaa612.
4. Freeman JV, Varosy P, Price MJ, et al. The NCDR Left Atrial Appendage Occlusion Registry. *J Am Coll Cardiol.* 2020;75:1503-1518.
5. Basu Ray I, Khanra D, Shah S, et al. Meta-Analysis Comparing Watchman™ and Amplatzer Devices for Stroke Prevention in Atrial Fibrillation. *Front Cardiovasc Med.* 2020;7:89.

Utility of balloon-assisted tracking in radial arterial Access

Utilidad del avance asistido con balón en el acceso arterial radial

Pau Federico Zaragoza,* Francisco Pomar Domingo, Teresa Castelló Víguer, Luis Martínez Ortiz de Urbina, and Enrique Peris Domingo

Servicio de Cardiología, Hospital Universitario La Ribera, Alzira, Valencia, Spain

To the Editor,

Currently, transradial approach is the most widely used access route both in coronary angiographies and percutaneous coronary interventions.¹ However, it is not rare to find anatomical difficulties like severe spasm, small-caliber vessel, loops or tortuosities that cannot be overcome with the usual techniques and lead to access route changes eventually.² In these situations, the advance of the catheter can dissect or perforate the artery and cause hematomas or even compartmental syndrome, although this entity is rare.³

As the main cause of resistance when advancing the catheter, Patel et al.⁴ identified the so-called razor effect exerted by the catheter distal border on the vessel wall (figure 1A), a mechanism that has been confirmed in optical coherence tomography studies.⁵ These same authors described the balloon-assisted tracking (BAT) technique⁴ that consists of inflating an angioplasty balloon that partially protrudes across the catheter distal border to keep its coaxial position with the artery avoiding the razor effect and providing better maneuverability (figure 1B). Therefore, the anatomical difficulty is crossed using a 0.014 in soft tip angioplasty guidewire. Afterwards, a 1.5 mm to 2.0 mm semicompliant balloon is inflated between 6 and 8 atm at the tip of the catheter and advanced en bloc beyond the anatomical problem (figure 2). Once the difficulty has been overcome with the catheter, both the balloon and the guidewire are retrieved to continue the procedure with the usual technique. All of it should be performed under strict fluoroscopic follow-up.

During the period from January 2019 through January 2020 we used this technique in 28 patients (2.3% of all transradial approaches attempted). In all of them, after the correct canalization of the artery, it was impossible to advance the catheter. Table 1 shows the patients' clinical characteristics, and reasons why the BAT technique was used. On 2 occasions it was used in the primary percutaneous coronary intervention setting. Informed consent was obtained from patients by telephone for the dissemination of the data included in the study.

To proceed with the BAT technique, 2 mm × 12 mm semicompliant balloons were used in 6-Fr catheters and 1.5 mm × 12 mm semicompliant balloons in 5-Fr catheters.

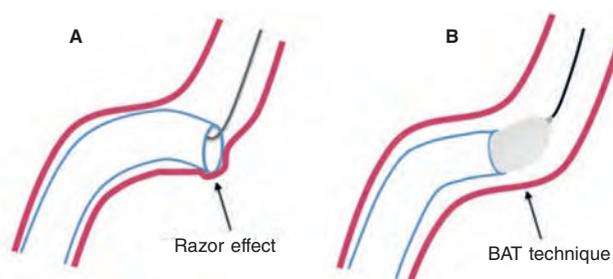


Figure 1. A: Razor effect of the catheter distal border over the vessel wall. **B:** correction of the razor effect with an angioplasty balloon inflated at the tip of the catheter. BAT, balloon-assisted tracking.

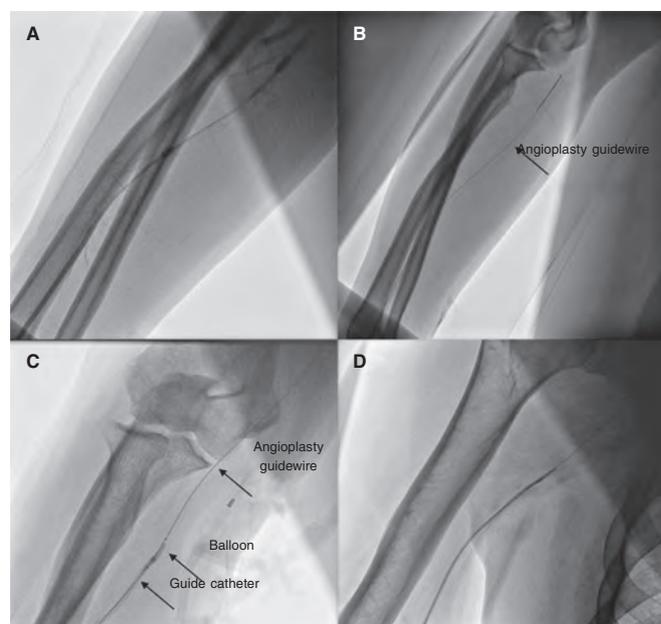


Figure 2. A: diffuse severe spasm of radial artery. **B:** advance of the angioplasty guidewire. **C:** catheter with balloon inflated in the distal border. **D:** crossing of the anatomical difficult.

* Corresponding author: Servicio Cardiología, Hospital Universitario La Ribera, Ctra. Corbera km 1, 46600 Alzira, Valencia, Spain. E-mail address: pau@comv.es [P. Federico Zaragoza].



Table 1. Clinical profile and reasons to proceed with balloon-assisted tracking (BAT) technique

Demographic characteristics	N = 28
Age (years)	67 ± 14 [36-91]
Women	15 (54)
Arterial hypertension	16 (57)
Smoking	10 (36)
Diabetes mellitus	8 (29)
Dyslipidemia	7 (25)
Peripheral arteriopathy	13 (46)
Access using the right radial artery	15 (54)
Acute coronary syndrome	22 (79)
Percutaneous coronary intervention	18 (64)
<i>Difficult moment during radial access</i>	
Advance of 0.035 in guidewire	1 (4)
Advance of 5-Fr diagnostic catheter	10 (36)
Exchange of 5-Fr diagnostic catheter for 6-Fr therapeutic catheter	17 (61)
<i>Indication for using the BAT technique</i>	
Unsolved severe spasm	
Small caliber	7 (25)
Severe radial or brachial tortuosity	3 (11)
Radial loop	3 (11)
Subclavian loop	1 (4)

Data are expressed as no. (%), mean ± standard deviation or median [interquartile range].

The success of the technique, defined as the overcome of the anatomical difficulty to be able to perform the procedure without having to change the access route, was achieved in 93% of the cases. In only 2 patients it was necessary to change the access route: one case of a heavily calcified small-caliber radial artery that made it impossible to advance the 0.014 in guidewire (indispensable step to use the BAT technique) and another case of a subclavian loop plus severe aortic elongation that could not be overcome with the BAT technique. None of the patients had vascular complications associated with the technique.

Therefore, we agree with other authors that the BAT is an easy-to-use technique that can improve the rates of success of radial access.⁶ Although in our group of patients there were only 2 cases of primary percutaneous coronary intervention, this scenario is especially sensitive to the need for access route change where the BAT technique also proved efficient.⁷ It is essential that in cases of minimal resistance while advancing the catheter an angiography should be performed to assess the anatomical difficulty and, once the problem has been defined, the BAT should be used early on to reduce the rate of complications.

FUNDING

None.

AUTHORS' CONTRIBUTIONS

All authors have contributed substantially to the idea, design and data acquisition of the study.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Cid Álvarez AB, Rodríguez Leor O, Moreno R, Pérez de Prado A. Spanish Cardiac Catheterization and Coronary Intervention Registry. 28th Official Report of the Spanish Society of Cardiology Working Group on Cardiac Catheterization and Interventional Cardiology (1990-2018). *Rev Esp Cardiol.* 2019;72:1043-1053.
2. Azzalini L, Khan R, Al-Hawwas M, et al. Effect of radial-to-femoral access crossover on adverse outcomes in primary percutaneous coronary intervention. *Am J Cardiol.* 2014;114:1165-1173.
3. Goirigolzarri Artaza J, Casado Álvarez R, Benítez Peyrat J, León Aliz E, Goicolea J, García Touchard A. Síndrome compartimental agudo de la mano tras un cateterismo transradial. *Rev Esp Cardiol.* 2017;70:672-673.
4. Patel T, Shah S, Pancholy S, Rao S, Bertrand OF, Kwan T. Balloon-assisted tracking: a must-know technique to overcome difficult anatomy during transradial approach. *Catheter Cardiovasc Interv.* 2014;83:211-220.
5. Merella P, Lorenzoni G, Casu G. Inside the "Razor Effect": Lessons From Optical Coherence Tomography-What Does Angiography Hide? *JACC Cardiovasc Interv.* 2019;12:409-410.
6. Wojciuk J, Beijk MA, Goode G, et al. Balloon-assisted tracking technique as 'a way forward' for transradial intervention. *Coron Artery Dis.* 2019;30:440-447.
7. Obaid D, Hailan A, Chase A, et al. Balloon-Assisted Tracking Use Reduces Radial Artery Access Failure in an Experienced Radial Center and is Feasible During Primary PCI for STEMI. *J Invasive Cardiol.* 2017;29:219-224.

<https://doi.org/10.24875/RECICE.M20000150>

Prognostic impact of zero coronary calcium score in stable patients



Significado pronóstico de la puntuación de calcio coronario nula en pacientes estables

Víctor Manuel Becerra-Muñoz,^{a,b,*} Mercedes Millán-Gómez,^{a,b} Germán Berteli-García,^{a,b} José Algarra-García,^c Nieves Alegre-Bayo,^c and Manuel Jiménez-Navarro^{a,b}

^a Unidad de Gestión Clínica del Corazón, Hospital Universitario Virgen de la Victoria, Instituto de Investigación Biomédica de Málaga (IBIMA), Universidad de Málaga, Málaga, Spain

^b Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain

^c Unidad de Radiodiagnóstico, Hospital Universitario Virgen de la Victoria, Universidad de Málaga, Málaga, Spain

To the Editor,

Coronary computed tomography angiography (CCTA) is one of the main imaging modalities used to discard coronary artery disease in patients with stable symptoms; thanks to its excellent negative predictive value, it can characterize atheromatous plaques and the degree of stenosis they cause.¹ In some imaging facilities, the CCTA is used after measuring the coronary calcium score often through the Agatston score that does not require initially the injection of contrast. Studies suggest that patients with stable symptoms and lack of coronary calcium (CCS = 0 or Agatston = 0) don't usually have significant coronary stenoses but a have better prognosis. This is indicative that a CCTA with the corresponding injection of contrast would not provide relevant information in most of the cases.²⁻⁴ Therefore, our objectives were to describe the prevalence and characteristic of patients with CCS = 0; also, to assess the findings obtained in the subsequent contrast study and invasive coronary angiography if any; finally, we studied the events occurring at the long-term follow-up in this group of patients.

Therefore, we conducted an observational cohort study that included all procedures (CCS and subsequent CCTA) performed in a tertiary center between 2008 and 2016. The authors declare that they acted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients. All patients were referred with chest pain and a past medical history of ischemic heart disease. The Philips CT Brilliance 64-multislice detector computed tomography scanner and Heartbeat-CS software (Philips Medical Systems, United States) were used. The CCS was assessed using the Agatston score. Stenoses that were > 70% quantitatively were considered significant coronary lesions.

Five hundred and forty studies were conducted of which 268 showed Agatston scores = 0 (49.4%) (figure 1). Patients were mostly women (62.7% vs 50.4%), younger (55.1 years vs 64.9 years), and with a lower prevalence of cardiovascular risk factors (table 1). No differences were seen in the intraprocedural characteristics.

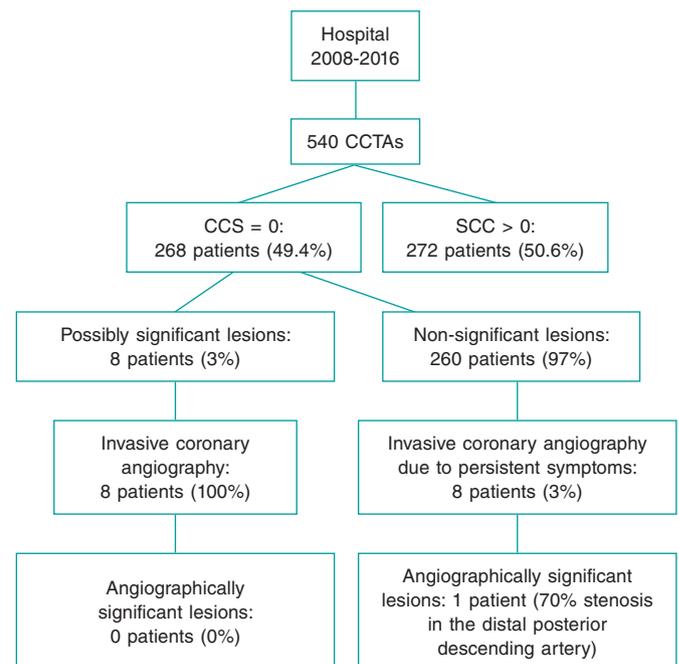


Figure 1. Flowchart of patients included in the study. CCTA, coronary computed tomography angiography; CCS: coronary calcium score.

Among the patients with zero CCS, only 8 patients showed images suggestive of significant lesions (3%) on the subsequent study with contrast (CCTA). Afterwards, the invasive coronary angiography performed in these cases confirmed the lack of significant lesions in all of the patients. Another 8 patients without significant lesions on the CCTA underwent an invasive coronary angiography because of their persistent symptoms, yet only 1 patient had significant stenosis: a male patient with a coronary anomaly consisting of a left anterior descending coronary artery originated at the right coronary artery with a 70% stenosis in the distal posterior

* Corresponding author: Unidad de Gestión Clínica del Corazón, Hospital Clínico Universitario Virgen de la Victoria, Campus de Teatinos s/n, 29010 Málaga, Spain. E-mail address: vmbecerram@gmail.com (V.M. Becerra-Muñoz).

Online: 21-09-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Table 1. Clinical, intraprocedural, and follow-up characteristics

	Total (N = 540)	Agatston = 0 (N = 268)	Agatston > 0 (N = 272)	P
Clinical characteristics				
Women	305 (56.5)	168 (62.7)	137 (50.4)	.004
Age (years)	59.98 ± 11.16	55.07 ± 11.28	64.86 ± 8.67	< .001
Arterial hypertension	248 (46.1)	90 (33.7)	158 (58.3)	< .001
Type 2 diabetes mellitus	91 (16.9)	25 (9.3)	66 (24.3)	< .001
Dyslipidemia	143 (26.5)	60 (22.4)	83 (30.5)	.032
Smoking	78 (14.4)	41 (15.3)	37 (13.6)	.136
Previous treatment				
Hypolipemiant drugs	85 (15.8)	31 (11.7)	54 (19.9)	.009
Antihypertensive drugs	114 (21.1)	42 (15.7)	72 (26.5)	.002
Antiplatelet therapy	124 (23)	54 (20.1)	70 (25.7)	.123
Analytical values				
Creatinine (mg/dL)	0.87 ± 0.3	0.83 ± 0.31	0.9 ± 0.29	.009
Glycemia (mg/dL)	104.49 ± 33.76	98.01 ± 31.57	110.36 ± 34.81	< .001
Total cholesterol levels (mg/dL)	197.44 ± 44.24	202.41 ± 39.48	192.93 ± 47.95	.020
LDL-C (mg/dL)	118.16 ± 37.26	122.69 ± 32.61	114.27 ± 40.72	.014
HDL-C (mg/dL)	51.64 ± 14.7	53.14 ± 14.06	50.32 ± 15.11	.039
Triglycerides (mg/dL)	146.08 ± 80.57	142.03 ± 84.91	148.73 ± 75.79	.373
Intraprocedural characteristics				
Step and shoot	419 (77.6)	213 (79.5)	206 (75.7)	.297
Atrial fibrillation	9 (1.7)	3 (1.1)	6 (2.2)	.324
Heart rate (bpm)	60.59 ± 8.39	60.79 ± 7.97	60.49 ± 8.77	.689
Systolic arterial pressure (mmHg)	126.52 ± 19.41	124.63 ± 18.88	128.49 ± 19.86	.051
Diastolic arterial pressure (mmHg)	68.86 ± 11.73	69.38 ± 1.5	68.39 ± 12.04	.410
Allergic reaction	5 (0.9)	3 (1.1)	2 (0.7)	.644
Clinical follow-up				
N (%)	510 (94.7)	252 (94.03)	258 (94.9)	
Follow-up period (months)	34.79 ± 24.39	32.72 ± 25.08	36.72 ± 23.52	.062
Mortality				
Cardiovascular causes	0 (0)	0 (0)	0 (0)	NS
Non-cardiac causes	1 (0.2)	1 (0.4)	0 (0)	NS
Cardiovascular events				
Acute myocardial infarction	2 (0.4)	0 (0)	2 (0.8)	.161
Heart failure	2 (0.4)	0 (0)	2 (0.8)	.161
Ischemic stroke	7 (1.4)	3 (1.2)	4 (1.6)	.914
Total	11 (2.2)	3 (1.2)	8 (3.1)	.138

bpm, beats per minute; HDL-C, high-density lipoprotein bound cholesterol; LDL-C, low-density lipoprotein bound cholesterol; NS, non-significant. Data are expressed as no. (%) or mean ± standard deviation.

interventricular branch that could not be revascularized. At the median 35-month follow-up [12 months to 56 months], no significant differences were seen regarding the events occurred between patients with CCS = 0 and those with CCS \geq 1.

Therefore, patients with CCS = 0, almost half of those referred, had no significant lesions on the CCTA or the invasive coronary angiography. This is consistent with former studies like the one conducted by Hulten et al.,² that reported a prevalence of potentially obstructive lesions of 1.5% in patients with CCS = 0 or Mittal et al.'s study,³ where 52.2% of the 2730 patients studied had zero CCS and significant lesions were only seen on the CCTA and the subsequent invasive coronary angiography in 4 (0.3%). Regarding prognosis, this study also showed a higher survival rate in the group with zero CCS (99% vs 94.5%).³

Similarly, the CONFIRM study confirmed an event-free survival rate of 99% within the first 2 years.⁴ Such a good survival rate was confirmed in our study, although without statistically significant differences regarding patients with calcium. This was probably due to the lower number of patients and the low percentage of events of both groups, maybe due to the inclusion of patients at lower risk.

The direct implication of these findings is that patients with zero CCS > may not have to undergo CCTA with the corresponding cost and time savings while avoiding venous puncture, the injection of iodinated contrast, the administration of bradycardia inducing drugs, and the use of more ionizing radiation. However, the main limitation for this is the possibility that the cause for the symptoms is a ruptured plaque where the presence of calcium is not indispensable.⁵ However, cumulative experience on this regard confirms that its finding in stable patients with low pre-test probabilities is highly unlikely.

Therefore, in our own opinion, the techniques should be adapted to the characteristics of each particular study patient. On the one hand, in patients at higher risk, the CCTA could be suggested right from the start given the currently relatively low doses of radiation; on the other hand, in low-risk patients (low pre-test probabilities with stable symptoms) a CCS with an Agatston score = 0 may spare the CCTA, thus reducing radiation and avoiding the injection of contrast.

FUNDING

There was no funding for this research project.

AUTHORS' CONTRIBUTIONS

V. M. Becerra-Muñoz, data collection, statistical analysis and manuscript drafting;;M. Millán-Gómez and G. Berteli-García, data collection and manuscript drafting; J. Algarra-García and N. Alegre-Bayo, reading of computerized tomography studies and revision of the final draft; M. Jiménez-Navarro, data collection, reading of computerized tomography studies and revision of the final draft.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest with respect to this study.

REFERENCES

1. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease. *Eur Heart J.* 2013;34:2949-3003.
2. Hulten E, Bittencourt MS, Ghoshhajra B, et al. Incremental prognostic value of coronary artery calcium score versus CT angiography among symptomatic patients without known coronary artery disease. *Atherosclerosis.* 2014;233:190-195.
3. Mittal TK, Pottle A, Nicol E, et al. Prevalence of obstructive coronary artery disease and prognosis in patients with stable symptoms and a zero-coronary calcium score. *EHJ Cardiovasc Imaging.* 2017;18:922-929.
4. Villines T, Hulten E, Shaw L, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM registry. *J Am Coll Cardiol.* 2011;58:2533-2540.
5. Gottlieb I, Miller J, Arbab-Zadeh A, et al. The absence of coronary calcification does not exclude obstructive coronary artery disease or the need for revascularization in patients referred for conventional coronary angiography. *J Am Coll Cardiol.* 2010;55:627-634.

<https://doi.org/10.24875/RECICE.M20000152>

Thrombus aspiration in the left atrial appendage: an option or a walk on the tightrope?



Tromboaspiración en orejuela izquierda: ¿opción o paseo en la cuerda floja?

Rafael J. Ruiz-Salmerón,* Sergio Rodríguez de Leiras, Rafael García de la Borbolla, César Carrascosa-Rosillo, Manuel Vizcaíno-Arellano, and Carlos Robles-Pérez

Servicio Endovascular, Hospital Virgen Macarena, Seville, Spain

To the Editor,

The presence of a thrombus in the left atrial appendage is a formal contraindication for its percutaneous closure and poses a serious dilemma during the therapeutic management of the patient. The option of intensifying anticoagulation to achieve the dissolution of the thrombus whether through better monitoring of the international normalized ratio (INR) parameters or through the introduction of direct anticoagulants is not often possible in most patients eligible for the percutaneous closure of the left atrial appendage. Therefore, the possibility of closing the left atrial appendage in certain cases of thrombosis (mural thrombus away from the landing zone) by using a modified technique to deploy the Amplatzer Amulet device (Abbott, United States) has been described.¹

In a non-closure setting, a percutaneous method for thrombus aspiration in the left atrial appendage with a large caliber device (22-Fr) and extracorporeal circulation has been reported.²

This is the case of an 86-year-old male patient (former smoker) with hypertension and non-valvular atrial fibrillation for which he was being anticoagulated with vitamin K antagonists. The previous month, the patient had suffered a cardioembolic ischemic stroke despite anticoagulation. During that admission, the cerebral magnetic resonance performed showed cerebral amyloid angiopathy with evidence of multiple microhemorrhages and superficial siderosis. Anticoagulation was withdrawn and the patient remained on acetylsalicylic acid only. During the current admission, the patient presented with serious heart failure. In this patient with persistent stroke,³ without anticoagulation, and a high ischemic and hemorrhagic risk (CHA₂DS₂-VASc and HAS-BLED values of 5 and 4, respectively), doctors suggested the percutaneous closure of the left atrial appendage. The patient was informed about the characteristics and purposes of the procedure, and his informed consent was obtained for both the procedure and the processing of his data for scientific purposes.

Due to the patient's frailty, the procedure was fluoroscopy guided only. The value of the image fusion technique has been suggested as coadjuvant to transesophageal ultrasound to guide the procedure.⁴ Our group, that has no intracardiac ultrasound machines available, has gained experience closing the left atrial appendage

with fluoroscopy guidance only using the image fusion technique (i-Pilot, Siemens, Germany).

Rotational angiography revealed a left atrial appendage with wind-sock morphology and a larger diameter in the landing zone of 31 mm. However, it was surprising to see the presence of a mobile filling defect at the left atrial appendage main lobe of circular appearance and an approximate diameter of 1 cm (figure 1 and video 1 of the supplementary data).

It was decided to continue the procedure with an Amplatzer Amulet device. Exchange was conducted with a 14-Fr 45° Amplatzer TorqVue delivery sheath (Abbott, United States) with a 4.8-mm internal lumen by bringing its tip towards the left atrial appendage ostium as seen using the image fusion technique. A mandatory step to avoid gas embolization in a low-pressure cavity like the left atrial appendage is to place the sheath proximal border below cardiac level, thus generating a negative pressure gradient that facilitates the outflow of blood. After a mild hemorrhagic retrograde flow, it stopped. On suspected sheath occlusion due to thrombus, a 50 mL Luer-Lock syringe was connected. Aspiration was performed with extraction of very organized thrombotic material of spherical appearance like the one seen during the angiography (figure 2).

With the guidance provided by the image fusion technique an no additional angiography, the 34 mm Amplatzer Amulet device was deployed in the first attempt with good results (video 2 of the supplementary data).

The patient did not have any complications during the procedure, and he was discharged on single antiplatelet therapy with acetylsalicylic acid. At the 1-year follow-up, no new events have been reported.

In conclusion, this was the first case ever reported by the medical literature of a successful thrombus aspiration of thrombotic material in the left atrial appendage during its percutaneous closure. The maneuver was successful thanks to 3 factors: the characteristics of the thrombus (organized and mobile); the negative pressure through a catheter of large internal lumen initially exerted by the pressure gradient and then by the aspiration with the syringe; and finally, the value of the image fusion technique to guide the procedure

* Corresponding author: Servicio Endovascular, Hospital Virgen Macarena, Dr. Fedriani 3, 41009 Seville, Spain. E-mail address: rjruizsalmeron@yahoo.es (R.J. Ruiz-Salmerón).

Online: 21-09-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

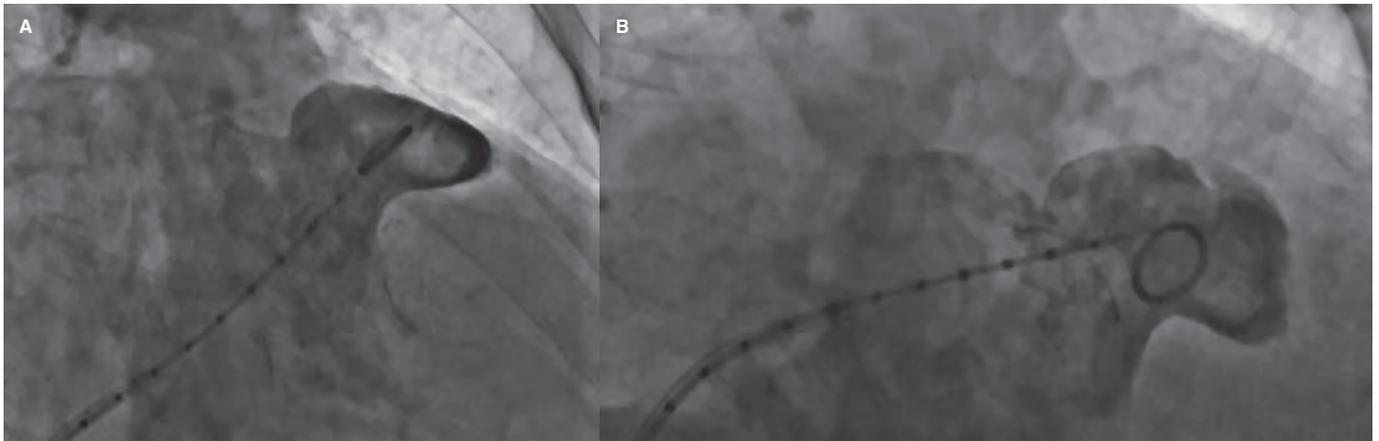


Figure 1. Angiographic image in the oblique anterior right cranial (A) and caudal (B) projections. A round radiolucent image immediately distal to the pigtail catheter of approximately 10 mm in diameter can be seen.

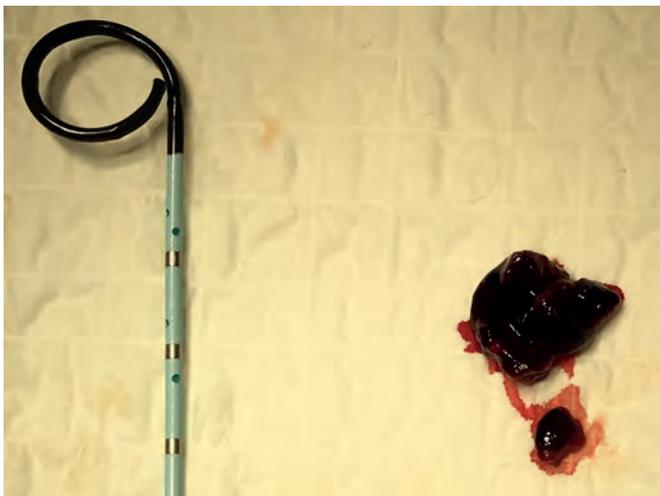


Figure 2. Organized thrombus originated at the left atrial appendage after its aspiration through a 34-Fr sheath.

without any additional angiographies. However, the success achieved with this particular case should not be mixed up with its recommendation: the lack of control over the thrombus behavior makes the use of cerebral embolic protection measures essential during the closure of the left atrial appendage.

FUNDING

No funding related to this work.

AUTHORS' CONTRIBUTION

R.J. Ruiz-Salmerón: author of the manuscript; S. Rodríguez de Leiras, R. García de la Borbolla, C. Carrascosa-Rosillo, M. Vizcaíno-Arellano, and Carlos Robles-Pérez: critical review.

CONFLICTS OF INTEREST

R.J. Ruiz-Salmerón is proctor for Abbott for left atrial appendage closure with Amulet.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000152>.

REFERENCES

1. Bordignon S, Bologna F, Chen S, et al. Percutaneous left atrial appendage closure in the presence of thrombus: A feasibility report. *J Cardiovasc Electrophysiol.* 2019;30:2858-2863.
2. So CY, Wang DD, Kang G, Villablanca PA, Frisoli T, O'Neill WW. Vacuuming the LAA: Left Atrial Appendage Thrombectomy Using AngioVac to Facilitate Percutaneous Mitral Balloon Valvuloplasty. *Structural Heart.* 2020; 4:243-244.
3. Cruz-González I, González-Ferreiro R, Freixa X, et al. Cierre de la orejuela izquierda por ictus pese a la anticoagulación oral (ictus resistente): resultados del registro Amplatzer Cardiac Plug. *Rev Esp Cardiol.* 2020;73:28-34.
4. Cruz-González I, Trejo-Velasco B, González-Ferreiro R. Utilidad del dynamic road-mapping en el cierre de la orejuela izquierda. *Rev Esp Cardiol.* 2020;73:255.

<https://doi.org/10.24875/RECICE.M20000185>

COVID-19 and spontaneous coronary artery dissection: causality?



La COVID-19 y la disección coronaria espontánea: ¿causalidad?

Álvaro Aparisi,^{a,*} Cristina Ybarra-Falcón,^a Pablo Elpidio García-Granja,^{a,b} Aitor Uribarri,^{a,b} Hipólito Gutiérrez,^{a,b} and Ignacio J. Amat-Santos^{a,b}

^a Departamento de Cardiología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

^b Centro de Investigación en Red de Enfermedades Cardiovasculares (CIBERCV), Spain

To the Editor,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the coronavirus disease 2019 (COVID-19) and is responsible for the current global outbreak. Although COVID-19 causes viral pneumonia mainly, alarms have gone off about its potential to damage the cardiovascular system with myocardial injury as a risk factor for mortality. Several are the potential causes of COVID-19 related myocardial injury including type I and type II myocardial infarction.¹

This is the case report of an apparent spontaneous coronary artery dissection (SCAD) in a patient with COVID-19 (informed consent obtained) followed by a systematic review of the medical literature available.

This is the case of a 40-year-old male without any known past medical history or cardiovascular risk factors who was admitted to our tertiary hospital with fever and cough. The patient tested positive in the reverse transcriptase-polymerase chain reaction test for SARS-CoV-2 infection, and the chest x-ray performed showed bilateral opacities (figure 1A). The patient was admitted to the intensive care unit due to a rapidly deteriorating clinical course within the first 72 hours despite initial supportive therapy that

required early intubation. The laboratory work showed severe lymphopenia ($0.5 \times 10^3/L$), troponin-T levels of 42 ng/dL, D-dimer levels $> 10\,000$ ng/mL, CRP levels > 300 mg/dL, and ferritin levels > 3000 ng/mL. Although corticosteroids and remdesivir were administered, the patient's hemodynamic status deteriorated with signs of acute respiratory distress syndrome and cardiogenic shock (CS). Concomitant inotropic and vasopressor support was initiated, and a transthoracic echocardiography performed revealed the presence of severe biventricular dysfunction with intraventricular thrombus without segmental wall motion abnormalities. After heart team discussion, a veno-arteriovenous extracorporeal membrane oxygenation (VAV-ECMO) was implanted. Within the first week after VAV-ECMO implantation a new electrocardiogram performed showed diffuse T-wave inversion in precordial leads (figure 1B). The patient's successful progression allowed the withdrawal of VAV-ECMO, adrenergic drugs, and mechanical ventilation.

Two months after the index event a cardiac magnetic resonance imaging performed discarded any signs of inflammation or fibrosis, a left ventricular ejection fraction of 35%, and resolution of the intraventricular thrombus. The endomyocardial biopsy performed tested negative for myocarditis (figure 1C). The coronary angiography performed (figure 1D,E; video 1 of the supplementary data) to discard concomitant coronary artery disease showed an isolated

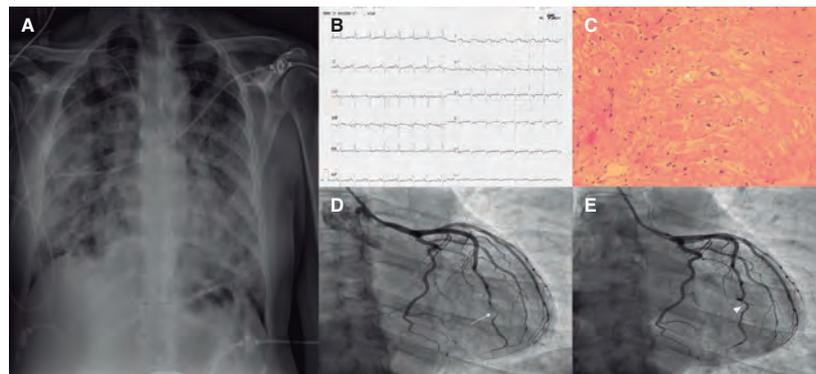


Figure 1. **A:** chest x-ray showing bilateral patchy infiltrates. **B:** electrocardiogram with diffuse T-wave inversion. **C:** endomyocardial biopsy without leukocyte infiltrate suggestive of myocarditis. Some freezing artifacts can be seen (asterisk). **D:** coronary angiogram, the arrow indicates the presence of significant stenosis of the distal portion of the LAD, which is compatible with a type II SCAD. **E:** follow-up with invasive coronary imaging showing the SCAD complete resolution (arrowhead).

* Corresponding author: Instituto de Ciencias del Corazón (ICICOR), Hospital Clínico Universitario de Valladolid, Ramón y Cajal 3, 47005 Valladolid, Spain. E-mail address: alvaro_aparisi@hotmail.com (Á. Aparisi Sanz).

Online: 21-12-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Table 1. Systematic review of the medical literature on spontaneous coronary artery dissections in patients with COVID-19

Authors	Journal/year	Age/sex	LVEF at admission	Previous predisposing factors*	Symptoms/signs at admission	COVID-19 severity	In-hospital treatment	Coronary angiogram	Management of SCAD
Courand P-Y et al. ³	<i>JACC Cardiovasc Interv</i> 2020	55/male	Preserved	Peripheral artery disease	Fever, dyspnea, and cough	Mild	Unreported	Mid-RCA dissection (confirmed on the OCT)	Conservative Aspirin, statins, and beta-blockers
Gasso LF et al. ⁴	<i>Eur Heart J</i> 2020	39/male	50% to 55%	None	Fever, dyspnea, cough, chest pain, and myalgia	Severe	Hydroxychloroquine, azitromycin, lopinavir/ritonavir, tocilizumab	Multivessel dissection (no intracoronary imaging)	Conservative Dual antiplatelet therapy
Kumar K et al. ⁵	<i>Catheter Cardio Int</i> 2020	48/female	45% to 55%	Migraine Dyslipidemia	Chest pain	Mild	Unreported	Mid-to-distal LAD dissection (confirmed on the computed tomography scan)	Conservative Dual antiplatelet therapy LifeVest, beta-blockers, and amiodarone after sustained PVT
Reported patient	2020	40/male	Severe (< 30%)	None	Fever, and dyspnea	Severe (mixed shock)	Hydroxychloroquine, azitromycin, lopinavir/ritonavir, corticosteroids, remdesivir, inotropic and vasopressor agents, VAV-ECMO	Distal LAD dissection (no intracoronary imaging)	Conservative Aspirin, and guideline-directed medical therapy for HF The follow-up CA confirmed the complete resolution

CA, coronary angiogram; COVID-19, coronavirus disease 2019; HF, heart failure; LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction; OCT: optical computed tomography; PVT, polymorphic ventricular tachycardia; RCA, right coronary artery.

* Prior to admission.

lesion of the distal segment in a tortuous left anterior descending coronary artery (LAD) that was compatible with a type II SCAD. Intravascular images were discarded after risk-benefit analysis, and conservative management was adopted. The patient was discharged and after an uneventful 3-month follow-up a control coronary angiography confirmed the complete resolution of the case.

Myocardial injury is a common finding in patients with COVID-19 and is associated with adverse events.¹ Previous coronavirus and influenza viral infections may trigger or aggravate a wide range of major cardiovascular events though the mechanisms responsible are yet to be elucidated. SCAD is an underreported coronary event with an estimated prevalence around 4%. There are several possible triggers, but emotional and physical stressors are the ones most commonly reported.

A case of bilateral carotid artery dissection in a patient with SARS-CoV-2 infection has been reported before. Single case-control cohort studies have reported on a potential association between upper respiratory tract infections and carotid dissection;² however, no conclusive study has been able to confirm whether infections are a predisposing condition for SCAD. Interestingly, 3 cases of SCAD and SARS-CoV-2 infection have been reported in the medical literature³⁻⁵ with different clinical course and disease severity (table 1). The potential mechanisms responsible for SCAD in patients with COVID-19 are still poorly understood, but they are probably not associated with a single factor as causality is a highly complex process.

SCAD has been associated with autoimmune and inflammatory diseases, which may be the result of eosinophilic infiltration with lytic enzyme secretion.⁶ The key of COVID-19 is an intense inflammatory burden and endothelial dysfunction.¹ However, SCAD may

be due to other contributing factors typically seen in critically ill patients. For instance, an overactive sympathetic system can cause intimal dissection. Also, SCAD could be the result of high-dose corticosteroid therapy, broadly used in COVID-19, due to the spontaneous rupture of a weakened arterial wall.⁶ Finally, a direct SARS-CoV-2 related endothelial damage cannot be discarded either.

Although SCAD is more common in females, 3 out of 4 cases reported are males, which could be explained by the higher incidence of COVID-19 reported in males. Chest pain is the most common symptom of SCAD and is present in 2 of the cases reported; however, the case reported by Courand PY et al. and our own case did not show specific symptoms of acute coronary syndrome.³ Whether SCAD is the cause of CS and severe ventricular dysfunction, in our case, is still under discussion. A previous unknown cardiomyopathy or transient ventricular dysfunction are possible causes since the SCAD was found in a distal small portion of the LAD. In any case, regardless of the severity of COVID-19, conservative management is a safe strategy. Morbidity is high as Kumar K et al. reported polymorphic ventricular tachycardia,⁵ and our patient presented with CS. We chose single antiplatelet therapy with aspirin, and guideline-directed medical therapy for heart failure like Courand PY et al. did,³ but different from the other 2 cases reported that chose dual antiplatelet therapy.^{4,5} It may raise concerns whether anticoagulation is a safe strategy as COVID-19 is associated with prothrombotic state.

In conclusion, SCAD is a potential cause of type II myocardial infarction in patients with COVID-19, but more studies are needed to establish causality. Infection-related SCAD may occur at any time during index events and could be difficult to diagnose. Conservative management seems like a safe strategy, although CS and ventricular arrhythmias can occur.

FUNDING

None.

AUTHORS' CONTRIBUTION

Á. Aparisi, C. Ybarra-Falcón, P.E. García-Granja, drafting the article or revising it critically for important intellectual content. All authors contributed substantially to the conception and design, and interpretation of data, and to the final approval of the version to be published.

CONFLICTS OF INTEREST

Nothing to declare.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000185>.

REFERENCES

1. Sandoval Y, Januzzi JL, Jaffe AS. Cardiac Troponin for the Diagnosis and Risk-Stratification of Myocardial Injury in COVID-19: JACC Review Topic of the Week. *J Am Coll Cardiol.* 2020;76:1244-1258.
2. Morassi M, Bigni B, Cobelli M, Giudice L, Bnà C, Vogrig A. Bilateral carotid artery dissection in a SARS-CoV-2 infected patient: causality or coincidence? *J Neurol.* 2020. <http://dx.doi.org/10.1007/s00415-020-09984-0>.
3. Courand P-Y, Harbaoui B, Bonnet M, Lantelme P. Spontaneous Coronary Artery Dissection in a Patient with COVID-19. *Jacc Cardiovasc Interventions.* 2020;13:e107-e108.
4. Gasso LF, Melon NMM, Cebada FS, Solis J, Tejada JG. Multivessel spontaneous coronary artery dissection presenting in a patient with severe acute SARS-CoV-2 respiratory infection. *Eur Heart J.* 2020;41:3100-3101.
5. Kumar K, Vogt JC, Divanji PH, Cigarroa JE. Spontaneous coronary artery dissection of the left anterior descending artery in a patient with COVID-19 infection. *Catheter Cardio Inte.* 2021;87:E249-E252.
6. Krittanawong C, Kumar A, Johnson KW, et al. Conditions and Factors Associated with Spontaneous Coronary Artery Dissection (From a National Population-Based Cohort Study). *Am J Cardiol.* 2018;123:249-253.



Shock after immediate TAVI implantation. Do we know what we are dealing with?

Shock tras implante inmediato de TAVI. ¿Sabemos a qué nos enfrentamos?

M. Isabel Barrionuevo Sánchez,^{a,*} Juan G. Córdoba Soriano,^b Arsenio Gallardo López,^b Juan C. García López,^b Miguel J. Corbí Pascual,^b and Jesús Jiménez Mazuecos^b

^a Servicio de Cardiología, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

^b Servicio de Cardiología, Hospital Universitario de Albacete, Albacete, Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000160>

<https://doi.org/10.24875/RECICE.M20000161>

CASE PRESENTATION

Eighty-four-year-old woman with hypertension, dyslipidemia, a past medical history of bronchial asthma, stroke in the left middle cerebral artery territory without negative side effects, and moderate chronic kidney disease (glomerular filtration rate, 42 mL/min/1.73 m² according to the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] equation). Also, the patient has a past medical history of non-ST-segment elevation acute myocardial infarction with revascularization of the left circumflex artery proximal segment with a conventional stent back in 2006 without an impaired ventricular function. The patient also showed moderate aortic stenosis for which she was regularly monitored by her cardiologist with a rate of progression of valvular heart disease in ranges of severity (peak gradient, 110 mmHg; mean gradient, 74 mmHg; continuity equation valve area, 0.75 cm² and indexed, 0.45 cm²/m²) with preserved ventricular function (left ventricular ejection fraction of 67% measured using Simpson's method). The echocardiography (figure 1) revealed the presence of left ventricular hypertrophy (a 19 mm interventricular septum and a 13 mm posterior wall) and a reduced ventricular cavity (a 38 mm end-diastolic diameter).

The patient remained asymptomatic with New York Heart Association functional class III, which is why the case was brought to the heart team. Given the high surgical risk involved (logistic EuroSCORE, 26.2%, Surgeon Thoracic Score, 7.3%) it was decided to proceed with transcatheter aortic valve implantation (TAVI). The study was completed with a coronary angiography (patent stent without de novo lesions), a transesophageal echocardiography, and a computed tomography scan that confirmed the presence of a suitable caliber to use the iliofemoral access and a borderline distance between the aortic annulus and the left main coronary artery of 10 mm with a suitable diameter of both the valvular sinuses and the aortic annulus (22.1 mm). The patient gave her verbal consent for the dissemination of the clinical case for teaching and scientific purposes.

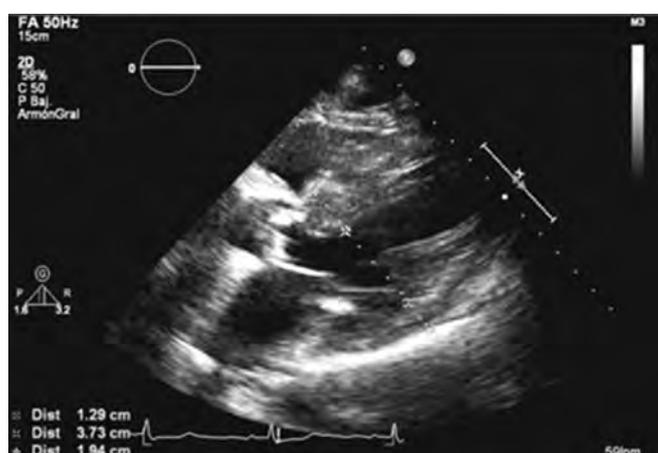


Figure 1. Parasternal long-axis view. Hypertrophy of septal predominance with small ventricular cavity. Severe aortic calcification.

* **Corresponding author:** Servicio de Cardiología, Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat, Barcelona, Spain. E-mail address: bsanchezmarisa@gmail.com (M.I. Barrionuevo Sánchez).

Online: 27-10-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

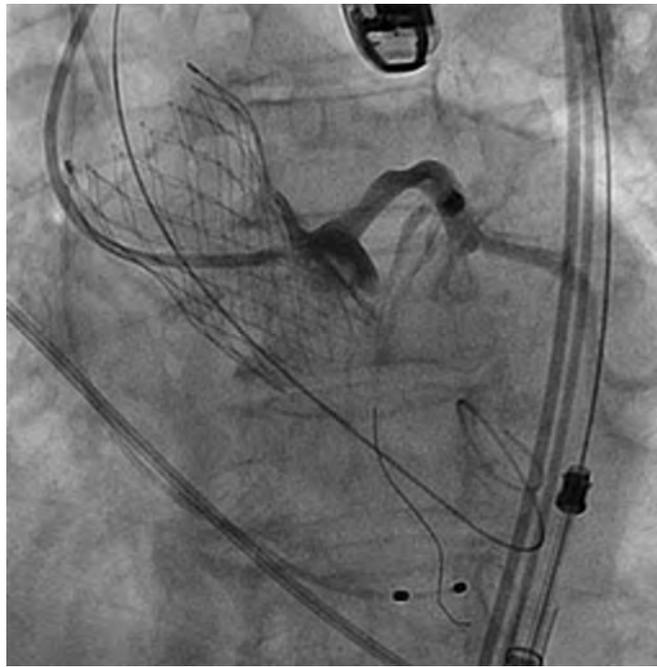


Figure 2. Screening of complications: diagnostic angiography on left coronary artery.



Figure 3. Screening of complications: transesophageal echocardiography on the transgastral view.

Since the patient was eligible for this procedure, a 26 mm CoreValve Evolut self-expanding aortic valve (Medtronic; Minneapolis, MN, United States) was implanted via transfemoral access after valvuloplasty with a 17 mm balloon. Femoral pre-closure as performed using a Prostar XL 10 device (Abbott Vascular; Reedwood City, CA, United States). Given the left main coronary artery maximum height and the possibility of a coronary occlusion, the heart team decided to use an angioplasty guidewire allocated in the left anterior descending coronary artery through a 3.5-Fr EBU XB guiding catheter (Medtronic, United States) for protection purposes. The procedure was uneventful and without immediate complications with proper penetration of the borders and a trivial degree of aortic regurgitation as seen on the transesophageal echocardiography.

After implantation and while at the cath lab, the patient showed early and sudden arterial hypotension (60/40 mmHg). Competence was confirmed between the rhythm paced by a temporary pacemaker and sinus rhythm without atrioventricular conduction disorders or apparent signs of acute ischemia. Taking into consideration the borderline distance to the left main coronary artery, the injection occurred through the guiding catheter inserted (figure 2). Similarly, the angiography performed discarded any vascular access complications.

The rapid echocardiographic evaluation performed discarded pericardial effusion (figure 3) and confirmed the integrity of the mitral valvular apparatus and lack of compromised aortic annulus without aortic dissection or rupture; the good positioning and proper functioning of the valve were confirmed without significant aortic regurgitation (figure 4) and no changes with respect to the immediate study following the implant.

Ventricular function proved to be hyperdynamic with flow acceleration (videos 1 and 2 of the supplementary data).



Figure 4. Screening of complications: transesophageal echocardiography, short-axis view.

FUNDING

No funding.

AUTHORS' CONTRIBUTION

All authors prepared and revised the article.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000159>.

<https://doi.org/10.24875/RECICE.M20000160>

Shock after immediate TAVI implantation. Do we know what we are dealing with? How would I approach it?



Shock tras implante inmediato de TAVI. ¿Sabemos a qué nos enfrentamos? ¿Cómo lo haría?

Mariano Larman*

Sección de Hemodinámica, Policlínica Gipuzkoa, San Sebastián, Guipúzcoa, Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000159>

<https://doi.org/10.24875/RECICE.M20000161>

* **Corresponding author:** Sección de Hemodinámica, Policlínica Gipuzkoa, Paseo de Miramón 174, 20009 San Sebastián, Guipúzcoa, Spain.

E-mail address: mariano.larman@gmail.com (M. Larman).

Online: 27-10-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

HOW WOULD I APPROACH IT?

This is a case of transcatheter aortic valve implantation (TAVI) (26 mm CoreValve Evolut). During the implant, the patient developed severe hypotension while at the cath lab. Both the angiography and the echocardiography performed discarded the common causes of hypotension after TAVI:

- Tamponade (the most common one, due to the pacemaker). There is no pericardial effusion.
- Aortic rupture: it is caused during the valvuloplasty before and after the dilatations with self-expanding valves. There is no pericardial effusion or suggestive images on the echocardiography.
- Coronary occlusion: it is discarded by injecting the left main coronary artery (LMCA). When the LMCA needs to be protected, the best thing to do is to leave a stent all the way into the left anterior descending coronary artery that should be long enough to provide coverage from before the LMCA bifurcation until above the leaflets of the implanted valve.
- Vascular complications with hemorrhage. They can be discarded on an angiography.
- Severe aortic regurgitation due to paravalvular leak or leaflet dysfunction of the transcatheter aortic valve. In this case only non-significant aortic regurgitation is seen.
- Other less common causes of hypotension such as mitral regurgitation due to chordal or papillary muscle ruptures and acute thrombosis of the valve can be discarded on the echocardiography.

Once the most common causes have been discarded, a rare complication called suicide left ventricle (SLV) remains.

Patients with aortic stenosis (AS) develop an adaptation of the LV to pressure overload that induces hypertrophy and impaired diastolic relaxation. Within the first few hours following surgical aortic valve replacement, changes in the dynamics of the LV can occur that can trigger the appearance of dynamic intraventricular gradients in up to 15% of the patients.¹ For this reason, at times, aortic valvular replacement and septal myectomy are performed.

The appearance of dynamic intraventricular gradients is associated with small LVs, asymmetric hypertrophy, high ejection fractions, and high valvular gradients.¹ This case has a gradient of 110 mmHg, left ventricular hypertrophy (a 19 mm septum and a 13 mm posterior wall), and a reduced ventricular cavity (a 38 mm end-diastolic diameter). We should remember that up to 10% of all aortic stenoses are accompanied by asymmetric septal hypertrophy.

Also, some patients with AS may have underlying hypertrophic cardiomyopathy. That is why we should think of this entity in the presence of a fast gradient that does not match the natural progression of a calcified AS (reduced aortic valve area > 0.12 cm² to 0.19 cm² per year).

Patients with AS related hypertrophic cardiomyopathy have worse in-hospital results (regarding mortality, cardiogenic shock, and kidney disease) after TAVI.

The echocardiography reveals the presence of severe left ventricular hypertrophy with ventricular collapse and end-systolic left ventricular outflow tract obstruction (LVOTO). Also, it shows a mosaic pattern that affects the entire LVOT compatible with pathological flow acceleration. No systolic anterior motion (SAM) of the mitral valve was reported.

If the suspected cardiogenic shock is due to a dynamic intraventricular gradient, the following measures should be implemented:

- Serotherapy to keep left ventricular filling pressures higher than normal.
- Withdraw positive inotropic drugs and use medication to increase postload (phenylephrine in infusion to maintain systemic vascular resistances).
- Monitor heart rate with cardioselective beta-blockers without vasodilator effect (metoprolol).
- Consider the use of disopyramide that has proven effective to reduce the dynamic gradient.
- In case of atrioventricular block or sinus bradycardia, implant a dual chamber pacemaker to keep atrioventricular synchrony and recover the contribution of the atrial systole to ventricular filling. This is especially important in the presence of mid-ventricular obliteration with flow acceleration in the LVOT.²
- In patients with SAM, if cardiogenic shock persists with the use of the optimal medical treatment, we would still have more therapeutic options available: alcohol septal ablation, lower implantation of TAVI into the LVOT, emergency surgical myectomy, and implantation of MitraClip.
- Alcohol septal ablation. Using a guidewire in the left anterior descending coronary artery, the injection of alcohol in the septal branches would be pretty fast. The final outcome of septal ablation won't be seen for another 6 months after the procedure. However, promising results have been reported in the emergency management of LVOTO after the transcatheter implantation of mitral valves,³ and also in a few cases of obstruction after TAVI. If the ablation of a septal branch does not do any good, another branch may be ablated with alcohol (especially in cases with very diffuse septal hypertrophy). Cases of ablation after TAVI have been reported at the follow-up as being asymptomatic. In patients showing LVOT dynamic obstructions and requiring TAVI, performing alcohol septal ablation between 3 and 6 months after the implantation is advised.

- New deeper TAVI to reduce the LVOTO. Very few cases have been published, all with CoreValve, in an attempt to avoid SAM (reported after TAVI and transcatheter implantation of mitral valves). A case of CoreValve collapse due to dynamic obstruction treated with a new CoreValve implanted a little deeper has been reported.
- MitraClip to treat SAM (reported in some of the cases published). This is difficult to perform in an emergency procedure.
- Emergency surgical myectomy: given the patient's age and past medical history, it does not seem indicated.

Although rare, dynamic obstructions following TAVI can be a complication not easy to solve. The cases with echocardiographic criteria of suspicion should be prevented by implementing the following measures:¹

- Proper hydration prior to the implant. Avoid diuretics.
- Use rigid guidewires with not very small curves and place them in the middle of the ventricle.
- Cardioselective IV beta-blockers without vasodilator effects (metoprolol) and keep a low heart rate.
- Avoid positive inotropic drugs.
- Pacing should be performed with a pacemaker in the right cavities and pacing with the guidewire in the LV should be avoided. Atrioventricular sequential pacing should be ready for use.

In the case presented here, if shock persists with the use of the optimal medical treatment and atrioventricular sequential pacing even in the absence of systolic anterior motion (SAM) of the mitral valve, the septal ablation of 1 or several septal branches should be taken into consideration.

FUNDING

No funding was received for this work.

CONFLICTS OF INTEREST

M. Larman is proctor for Edwards Lifesciences and Boston Scientific.

REFERENCES

1. Lopez Ayerbe J, Ewangelista Masid A, Armada Romero E, et al. Predictive factors of abnormal dynamic interventricular gradient after valve replacement in severe aortic stenosis. *Rev Esp Cardiol.* 2002;55:127-134.
2. Ibrahim H, Barker CM, Reardon MJ, et al. Suicide Left Ventricle Due to Conduction Disturbance Following Transcatheter Aortic Valve Replacement and Reversal With Restoration of Sinus Rhythm: Is There Life After Death? *J Invasive Cardiol.* 2015;27:E107-109.
3. Guerrero M, Wang DD, Himbert D, et al. Short term results of alcohol septal ablation as a bail-out strategy to treat severe left ventricular outflow tract obstruction after transcatheter mitral valve replacement in patients with severe mitral annular calcification. *Catheter Cardiovasc Interv.* 2017;90:1220-1226.

<https://doi.org/10.24875/RECICE.M20000161>

Shock after immediate TAVI implantation. Do we know what we are dealing with? Case resolution



Shock tras implante inmediato de TAVI. ¿Sabemos a qué nos enfrentamos? Resolución

M. Isabel Barrionuevo Sánchez,^{a,*} Juan G. Córdoba Soriano,^b Arsenio Gallardo López,^b
Juan C. García López,^b Miguel J. Corbí Pascual,^b and Jesús Jiménez Mazuecos^b

^a Servicio de Cardiología, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

^b Servicio de Cardiología, Hospital Universitario de Albacete, Albacete, Spain

SEE RELATED CONTENT:

<https://doi.org/10.24875/RECICE.M20000159>

<https://doi.org/10.24875/RECICE.M20000160>

* **Corresponding author:** Servicio de Cardiología, Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907, L'Hospitalet de Llobregat, Barcelona, Spain.
E-mail address: bsanchezmarisa@gmail.com (M.I. Barrionuevo Sánchez).

Online: 27-10-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

CASE RESOLUTION

Immediate shock after transcatheter aortic valve implantation (TAVI) is a rare complication that requires quick diagnosis and treatment.

The causes are alterations of the area adjacent to the implant (aortic regurgitation, aortic annulus complications or ischemia due to occlusion or coronary artery embolism), complications distant from the implant area (perforations associated with the pacemaker or the support guidewire in the left ventricle or mitral apparatus alterations) or vascular complications (in the femoroiliac access or the aorta). All of these complications were discarded in our female patient.

The videos of the case presentation suggested a suspected rare cause for the shock: suicide left ventricle consisting of ventricular collapse that triggers dynamic obstruction (video 1 of the supplementary data). The intraventricular gradient (figure 1) can generate anterior systolic movement of the mitral valve and severe mitral regurgitation (figure 2). A catheter was advanced to the apex that confirmed the severe intraventricular dynamic gradient (figure 3).

Targeted therapy with fluid therapy was used to optimize preload followed by IV esmolol, and phenylephrine. Also, the rhythm itself was optimized in order to keep atrioventricular synchrony and extend the diastolic filling period. This made the gradient go away (figure 4) and improved the patient's hemodynamic situation.

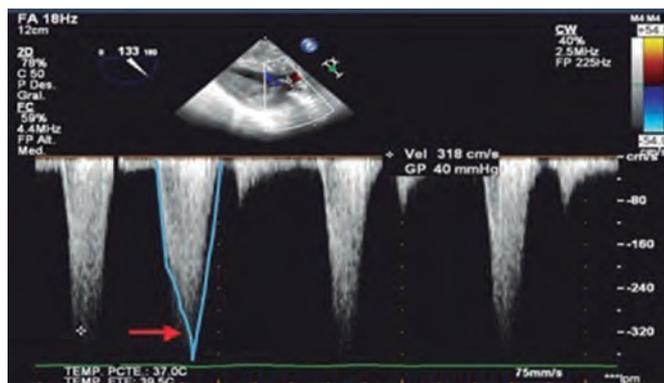


Figure 1. Intraventricular dynamic gradient with late peak (arrow).

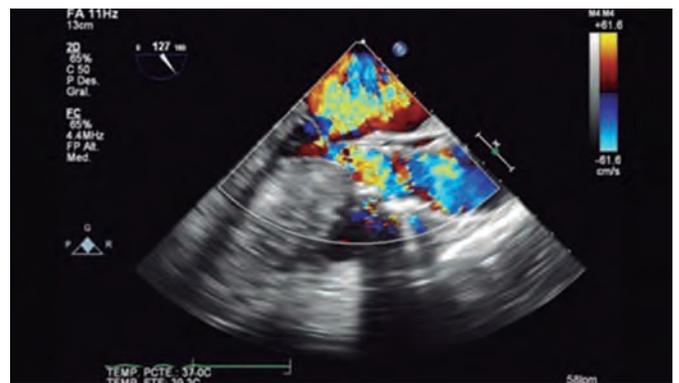


Figure 2. Flow acceleration due to dynamic obstruction, anterior systolic movement of the mitral valve, and severe mitral regurgitation.



Figure 3. Registry of aortic and left ventricular pressures immediately after TAVI: intraventricular dynamic gradient with late peak (arrows). No withdrawal, multimodal diagnosis.



Figure 4. Registry of aortic and left ventricular pressures after treatment; gradient resolution.

Progression was good and sustained in time. The control echocardiography performed at the hospital discharge showed a minimum dynamic gradient without anterior systolic movement of the mitral valve treated with atenolol (25 mg/day).

The chronic increase of ventricular postload due to aortic stenosis can trigger myocardial hypertrophy and intraventricular gradient that are masked by a fixed valvular obstruction.¹ However, after implanting the valve it triggers a series of hemodynamic changes that can unmask this gradient² and eventually lead to hemodynamic collapse.^{1,3}

The importance of the case is that in the presence of sudden hypotension, vasopressor drugs are often used. However, they can deteriorate both the intraventricular gradient and hypotension by increasing inotropism; that is why it is essential to be aware of this condition and use beta-blockers.¹

There are echocardiographic data available on the baseline study to predict the higher risk of developing suicide left ventricle:^{1,3} small end-diastolic diameter, hyperdynamic left ventricular ejection fraction, asymmetric hypertrophy (septal predominance) and very high valvular gradients. We should mention that, once the acute phase is over, ventricular hypertrophy decreases within the first month, and in 94% of the patients, the dynamic gradient is solved at the 3-month follow-up.¹

FUNDING

No funding.

AUTHORS' CONTRIBUTION

All authors prepared and revised the article.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000161>.

REFERENCES

1. Suh WM, Witzke CF, Palacios IF. Suicide left ventricle following transcatheter aortic valve implantation. *Catheter Cardiovasc Interv.* 2010;76:616-620.
2. Alfonso F, Domínguez L, Rivero F, et al. Severe intraventricular dynamic gradient following transcatheter aortic valve implantation: Suicide ventricle? *EuroIntervention.* 2015;11:e1.
3. Gerckens U, Pizzulli L, Raisakis K. Alcohol septal ablation as a bail-out procedure for suicide left ventricle after transcatheter aortic valve implantation. *J Invasive Cardiol.* 2013;25:E114-E117.

TAVI and compromised left main coronary artery. IVUS-guided “ping-pong” resolution



TAVI y tronco común comprometido. Resolución ping-pong guiada con IVUS

Iván J. Núñez-Gil,* Rafael Vera, Pilar Jiménez-Quevedo, Luis Nombela-Franco, and Antonio Fernández-Ortiz

Departamento de Cardiología Intervencionista, Hospital Clínico San Carlos, Universidad Complutense de Madrid, Madrid, Spain

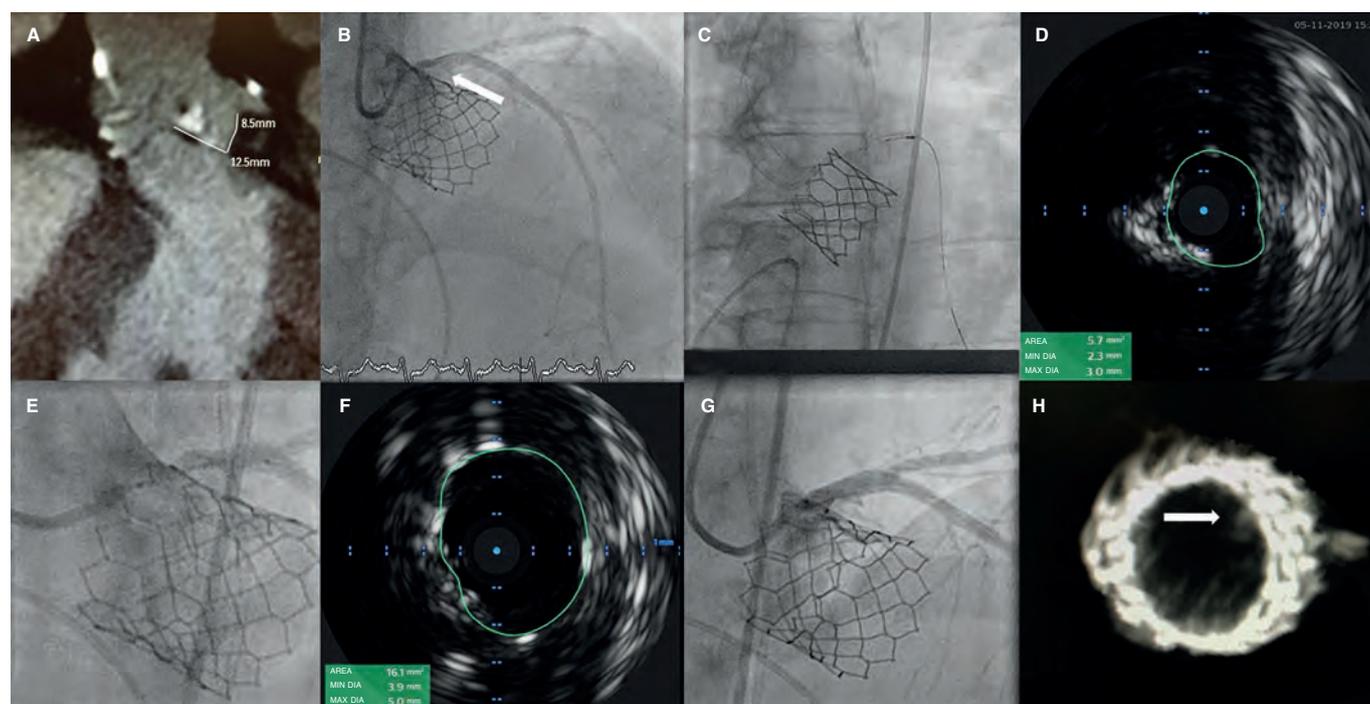


Figure 1.

A 76-year-old male was admitted to undergo a transfemoral aortic valve implantation. Left main coronary artery (LMCA) was low (8.5 mm) with a long (12.5 mm) and thick left leaflet in the aortic valve (figure 1A), and small aortic sinuses, therefore the LMCA was protected with a guidewire. After implanting an Edwards-S3 valve (N29; -1cc) and despite patent LMCA with normal coronary flow the coronary angiography still showed inconclusive images (arrow, figure 1B and video 1 of the supplementary data).

Intravascular ultrasound (IVUS) was performed, but the transducer could not be crossed easily because the guidewire was jailed. Using the therapeutic introducer, we were able to engage the LMCA through the prosthesis open cells (figures 1C,D and videos 2,3 of the supplementary data). The IVUS confirmed the presence of ostial LMCA compromise (area: 5.7 mm²) by the native leaflet. Stent implantation (4 x 12 mm with 5 x 10 mm proximal optimization) was decided with a slight stent-protrusion inside the valve (figure 1E and video 4 of the supplementary data). The IVUS and the angiography confirmed the good results (figure 1F,G and video 5 of the supplementary data) and the patient was discharged 3 days later. Informed consent was obtained from the patient for the publication of his case.

* Corresponding author: Departamento de Cardiología Intervencionista, Hospital Clínico San Carlos, Prof. Martín Lagos s/n, 28040 Madrid, Spain. E-mail address: ibnsky@yahoo.es (I.J. Núñez-Gil).

Received 18 January 2020. Accepted 24 March 2020. Online: 05-05-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

Currently, coronary artery compromise is a growing concern. To prevent it consider careful sizing, a proper ring-sinuses-leaflet length in relation to the coronary ostia, wire protection or even using the snorkel/chimney technique. Still, late occlusions have been reported. Our patient illustrates the value of IVUS to decide how to treat these compromised ostia possibly avoiding this late complication. On the other hand, compared to the snorkel technique the "ping-pong" technique allows a safe stenting inside the stent of the prosthesis (arrow, [figure 1H](#)), causes less distortion to its structure, and facilitates access to the coronaries in the future.

FUNDING

None.

AUTHORS' CONTRIBUTION

I.J. Núñez-Gil: conceptualization, case operator, preparation of the manuscript, and image processing. R. Vera: case operator, revision of the manuscript, and processing of computed tomography. P. Jiménez-Quevedo and L. Nombela-Franco: critical review of the manuscript. A. Fernández-Ortiz: case operator and critical review of the manuscript.

CONFLICTS OF INTEREST

None.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000120>.

Complicating a very late stent thrombosis

Complicando una trombosis muy tardía de stent

Pablo Salinas,* Pedro Martínez-Losas, Hernán Mejía-Rentería, Luis Nombela-Franco, Iván J. Núñez-Gil, and Antonio Fernández-Ortiz

Servicio de Cardiología, Hospital Clínico San Carlos e Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain



A 61-year-old male with a drug-eluting stent (DES) implanted 5 years ago (no further information) was admitted with anterior myocardial infarction. The emergent coronary angiography performed revealed the presence of very late stent thrombosis (VLST) (figure 1A, stent in green arrows, [video 1 of the supplementary data](#)). A Sion wire (Asahi Intecc) was easily advanced, but thromboaspiration catheter failed to cross. A 2.5 mm compliant balloon that crossed easily was used to restore the flow (figure 1B, [video 2 of the supplementary data](#)). Intravascular ultrasound (IVUS) revealed the presence of proximal stent deformation (partial crush) (figure 2A, red arrows indicating crushed struts); and significant undersizing or underexpansion (average stent diameter of 2.75 mm, green arrows and 4.5 mm reference diameter, blue line, [figure 2B](#)). Stent enhancement confirmed the IVUS findings. Given the deformation of the stent and the mismatch between the stent and the vessel size, we dilated with a 4 mm non-compliant balloon (20 atm) and implanted a new 4 mm x 28 mm DES with excellent final results ([figure 3, video 3 of the supplementary data](#)). Presence of possible distal myocardial bridging.



Figure 1.

* Corresponding author: Servicio de Cardiología, Hospital Clínico San Carlos, Prof. Martín Lagos s/n, 28040 Madrid, Spain.
E-mail address: salinas.pablo@gmail.com (P. Salinas).

Received 20 March 2020. Accepted 22 April 2020. Online: 06-09-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

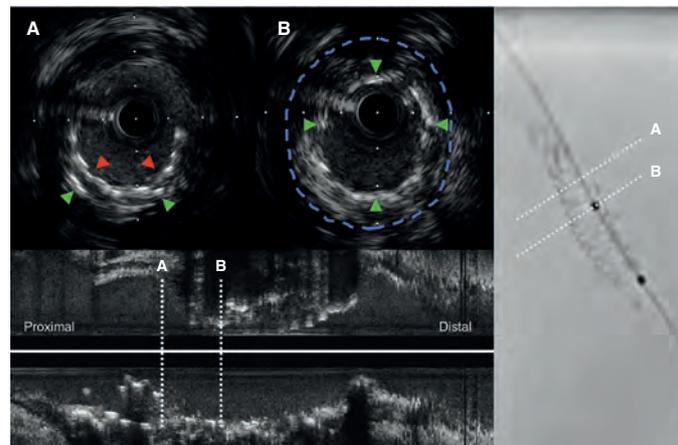


Figure 2.

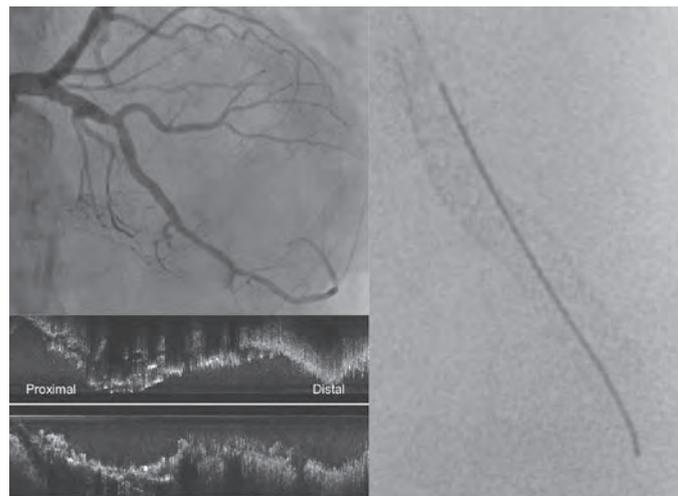


Figure 3.

Although the optical coherence tomography is the gold standard for late stent failure imaging, in selected cases, IVUS may be better for stent thrombosis. IVUS is not affected by thrombus and has higher penetration, which is critical to assess the true diameter of the vessel. In this case, the curve and malapposition facilitated an unnoticed peculiar wire crossing that facilitated the distortion of the stent. The IVUS provided essential information to assess the mechanical factors associated with VLST and successfully guide such a complex intervention. Crossing with a bent wire tip or imaging after crossing could have prevented the complication. Written informed consent was obtained from the patient for the procedure and the assignment of anonymous images for scientific dissemination.

FUNDING

No funding was received for this work.

AUTHORS' CONTRIBUTION

P. Salinas, and P. Martínez-Losas conceived and made the draft of the article. H. Mejía-Rentería, L. Nombela-Franco, and I.J. Núñez-Gil obtained, edited and made the graphic composition with the figures. A. Fernández-Ortiz conducted the critical review of the manuscript. All authors reviewed and approved the final version of the article.

CONFLICTS OF INTEREST

None.

SUPPLEMENTARY DATA



Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.24875/RECICE.M20000129>.



Percutaneous closure of coronary fistulae using different devices

Cierre percutáneo de fístulas coronarias con distintos dispositivos

Luis Fernández González,* Roberto Blanco Mata, Koldobika García San Román, Juan Carlos Astorga Burgo, Aída Acin Labarta, and Josune Arriola Meabe

Unidad de Cardiología Intervencionista, Hospital Universitario de Cruces, Baracaldo, Vizcaya, Spain

Two-month baby recently treated with closure of perimembranous interventricular communication with congestive clinical signs in the postoperative period and echocardiographic suspicion of possible right coronary artery-to-right ventricle fistula confirmed on the cardiac computed tomography and catheterization with nonselective coronary angiography. Parents' informed consent was obtained for the dissemination of the case. A large coronary fistula—eligible for percutaneous closure—can be seen exiting the right coronary artery marginal branch and entering the right ventricular cavity with great dilatation of the right coronary artery proximal segment (figure 1). A 4-Fr carrier catheter is inserted into the right coronary artery and a guidewire is advanced towards the right ventricle. Assisted by an angioplasty balloon, the carrier catheter is then advanced towards the fistula proximal zone where eventually a 4 × 6 Amplatzer Vascular Plug (AVP4) device (Abbott, United States) is delivered resulting in the total occlusion of the defect with no interference with the distal right coronary artery (figure 2).

Seventy-year-old male patient with an incidental finding on the transthoracic and transesophageal echocardiography of a large mass in the right atrium with abundant vascular component. Patient' informed consent was obtained for the dissemination of the case. The cardiac CT performed confirmed the finding of an arteriovenous malformation. The coronary angiography performed shows afference from the

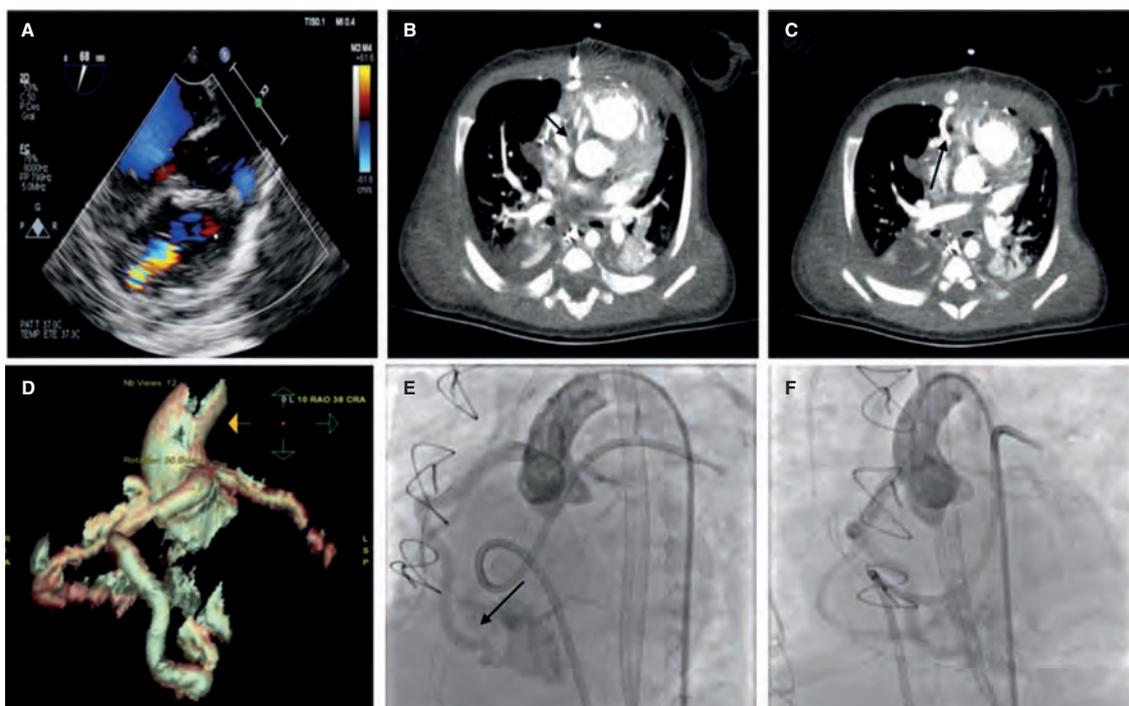


Figure 1.

* Corresponding author: Unidad de Cardiología Intervencionista, Plaza Cruces s/n, 48903 Baracaldo, Vizcaya, Spain.
E-mail address: luisfg82@hotmail.com (L. Fernández González).

Received 23 April 2020. Accepted 17 June 2020. Online: 21-09-2020.

2604-7322 / © 2020 Sociedad Española de Cardiología. Published by Permanyer Publications. This is an open access journal under the CC BY-NC-ND 4.0 license.

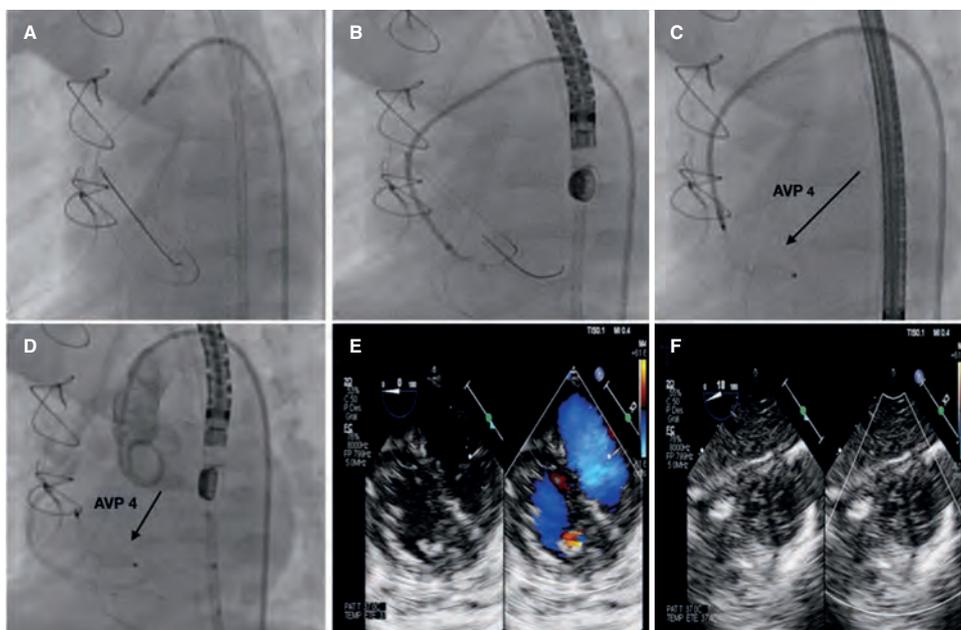


Figure 2.

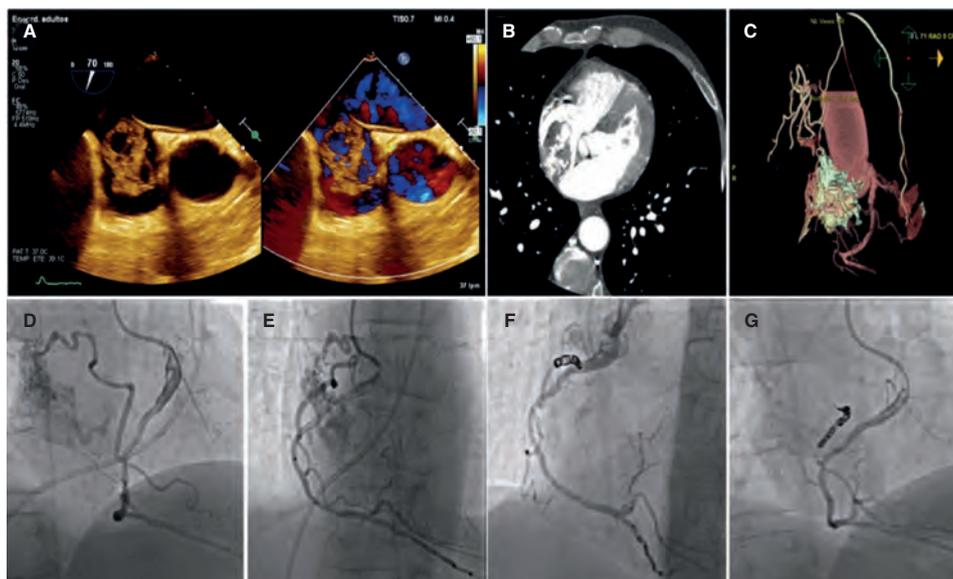


Figure 3.

mid-right coronary artery towards the atrial mass and percutaneous closure is decided. The closure is performed by advancing a micro-catheter towards the afferent branch mid-section and protecting the mid-right coronary artery through the inflation of the angioplasty balloon. Ten Hilal Coils (Cook Medical, United States) are delivered with good results and complete closure of the defect (figure 3).

FUNDING

No funding to declare.

AUTHORS' CONTRIBUTION

All authors have contributed to the elaboration, drafting and revision of the manuscript.

CONFLICTS OF INTEREST

None declared.