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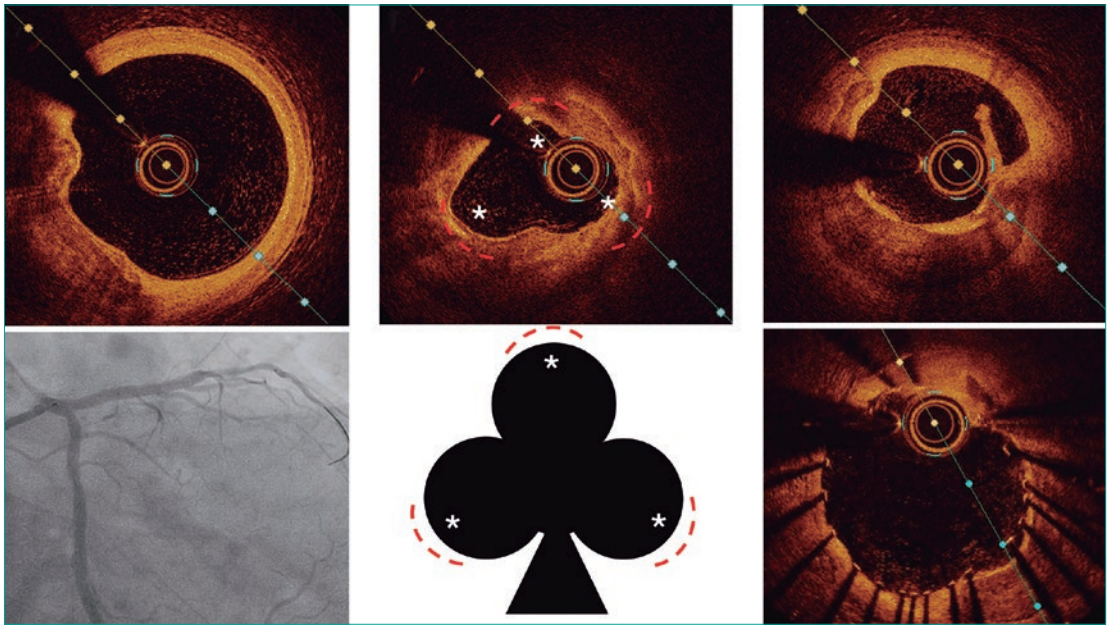

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Editorial

Expanding the role of drug-coated balloons in native large coronary artery disease

Balones farmacoactivos: a la conquista de la enfermedad coronaria de vaso grande

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We have witnessed a remarkable evolution in the field of percutaneous coronary intervention (PCI) over the past half a century, transitioning from the first cases of balloon angioplasty to bare metal stents and, most notably, to the widespread use of drug-eluting stents (DES). The advent of DES substantially reduced restenosis rates by providing a mechanical scaffold combined with sustained release of an antiproliferative drug, eg, taxanes and then rapamycin derivatives. Considering their permanent and static nature, such metallic implants are not without limitations, including the potential for delayed healing, chronic inflammation, inhibition of positive vessel remodeling, and the need for prolonged antithrombotic therapy.[1,2] Following this, the concept of bioresorbable vascular scaffolds emerged, promising a temporary scaffold that would "leave nothing behind". Nonetheless, their initial promise was hampered by late scaffold thrombosis and a high rate of target lesion failure.[3] At the same time, drug-coated balloons (DCB) emerged as a "metal-free" alternative delivering an antiproliferative drug to the vessel wall without leaving a permanent implant, thus preserving vessel anatomy, function, and allowing for adaptive remodeling. Currently, DCB are established in percutaneous coronary intervention (PCI) for in-stent restenosis (ISR) and, subsequently, for small-vessel native disease. Their role in larger native coronary arteries, however, remains debated, given the limited evidence from small randomized controlled trials (RCTs) with relatively short follow-up.[4]

In this context, in a recent paper published in *REC: Interventional Cardiology*, Sorolla Romero et al. report a timely and rigorous meta-analysis of RCT comparing DCB with DES in patients with native large coronary artery disease (PROSPERO CRD42024602012).[5] A total of 2961 patients (n = 1476 for DCB and n = 1485 for DES) from 7 RCT published from 2016 through 2024 were included, and, compared with DES, DCB were associated with a similar risk of the primary endpoint of target lesion revascularization, and all-cause and cardiovascular mortality, myocardial infarction, and major adverse cardiovascular events, but a > 2-fold risk of target vessel revascularization. For angiographic outcomes, although DCB caused less late lumen loss, they were associated with a smaller minimal lumen diameter at follow-up. In light of these results, we hereby hope to provide current and future perspectives on the role of DCB for treatment of native large coronary artery disease.

LESION CHARACTERISTICS

The type of lesions included in the analyzed RCT is a key determinant of the external validity of the study findings, and we outline key considerations below.

- Across the 7 RCT, patients with high clinical and anatomical complexity were consistently excluded (table 1).[6-12] Notably, patients with extensive coronary artery disease (eg, long or multiple lesions, 3-vessel disease, or those requiring multiple devices), severe calcification, left main involvement, or chronic total occlusions were not evaluated. Additional characteristics that appeared among exclusion criteria, and could instead arguably represent favorable scenarios for DCB angioplasty, are requirement for hemodialysis, bifurcations lesions requiring treatment of both branches, and severe coronary artery tortuosity. This selective enrollment underscores the contrast with recent observational studies of DCB use in native large coronary artery disease, which have examined more complex scenarios in which DES may be less effective, technically challenging to deliver, or best avoided to limit long stent segments or multiple overlapping implants (figure 1).[13-15]

- The degree of inter-study variability is also of note, particularly given the disproportionate contribution of individual RCT. As appropriately highlighted by the authors, REC-CAGE-FREE I[7] alone accounts for approximately 75% of the total patient population, and leave-one-out analyses yield different results. Moreover, enrollment periods span 8 years (2014–2022), introducing potential variability in procedural techniques, device technology, and adjunctive pharmacotherapy. The observed prediction intervals and measures of heterogeneity further support this consideration.

- We acknowledge the clinical variability in defining "large" coronary artery disease. This meta-analysis applied a ≥ 2.5 mm-cutoff to define large vessels, which is at the lower end of what many would consider large. In several of the included studies, patients were eligible for enrollment regardless of treated vessel diameter, with some RCT allowing lesions within reference vessel diameters as small as 2.0 mm (table 1).

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Table 1. Clinical, angiographic and procedural characteristics excluding patients from each study included in the meta-analysis

Characteristics	Nishiyama et al.[6] (CCS) N = 60	REC-CAGEFREE I[7] (45%, CCS; 55%, ACS) N = 2271	Yu et al.[8] (11%, CCS; 89%, ACS) N = 170	REVELATION[9] (STEMI) N = 120	Wang et al.[10] (STEMI) N = 184	Gobić et al.[11] (STEMI) N = 75	Hao et al.[12] (STEMI) N = 80
Age, years					> 70		> 80
Hemodialysis	X						
Previous MI					X		
Previous PCI/CABG						Within 6 months	Within 6 months
Vessel size, mm			< 2.25 or > 4.0		< 2.0 or > 4.0		< 2.5 or > 4.0
Lesion length, mm	≥ 25		> 30				
No. of DES or DCB/total DES or DCB length, mm		≥ 3/> 60					
Extensive CAD		≥ 3 lesions/vessels				X	
Severe calcification or atherectomy	X	X		X			X
Left main coronary artery	X	X					
CTO	X	X					
Bifurcation requiring treatment in both branches		X					
Grafts		X					
Severe coronary artery tortuosity						X	

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCS, chronic coronary syndrome; CTO, chronic total coronary occlusion; DCB, drug-coated balloon; DES, drug-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

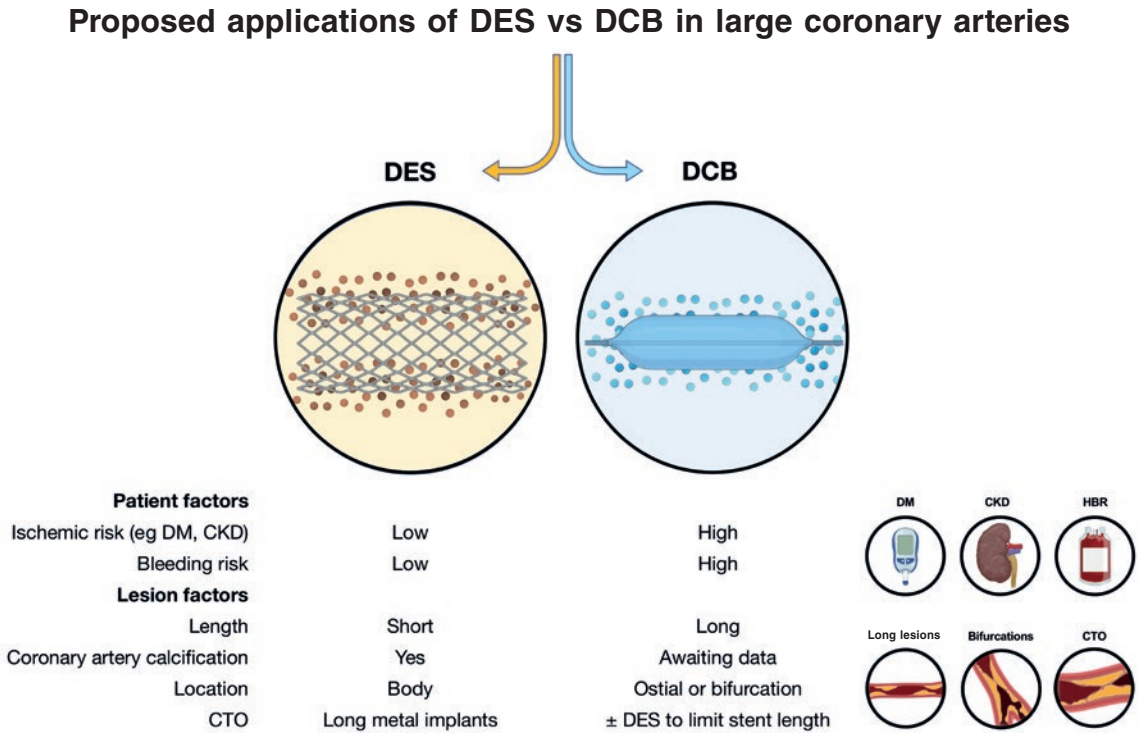

Figure 1. Patient and lesion factors to be taken into consideration when evaluating native large coronary artery disease for percutaneous coronary intervention. Presence of any one of the factors highlighted beneath DCB should lead the operator to contemplate an approach to limit the number of permanent coronary artery implants. ACS, acute coronary syndrome; CKD, chronic kidney disease; CTO, chronic total coronary occlusion; DCB, drug-coated balloon; DES, drug-eluting stent; DM, diabetes mellitus; HBR, high bleeding risk.

Subgroup analyses within individual studies provide more specific insights into patients treated with larger devices. Given the significant interaction *P* value in the vessel size subgroup analysis of the largest included RCT,[7] it is reasonable to question whether the overall results would have been superimposable had the analysis been limited to larger vessels. These observations should be interpreted in the context of the earlier discussion on the type of lesions included. Finally, this aspect may have sex-specific relevance: although women generally have smaller coronary vessels, a vessel of a given diameter may be more proximal and supply a larger myocardial territory in women than in men, potentially amplifying its clinical significance.[16]

LESION PREPARATION

Lesion preparation is a point of significant heterogeneity among the RCT included in the meta-analysis. For example, the REVELATION trial,[9] conducted on patients with ST-segment elevation myocardial infarction, permitted proceeding with DCB angioplasty with a 50% residual percent diameter stenosis after predilation, and thrombectomy if visible thrombus was present, which contrasts with the more commonly embraced ≤ 30% threshold.[5] Further complicating the procedural comparison is the timing of patient randomization, as 2 studies randomized patients before assessing the outcome of lesion preparation.[10,11] Moreover, the specific methods of lesion preparation varied, with 1 study supporting the use of semicompliant balloon angioplasty before DCB inflation.[12] The success of DCB angioplasty depends on a dedicated procedural strategy that hinges on meticulous lesion preparation and careful postoperative assessment, a nuance often lost when comparing outcomes across various methodologies.[15,17,18]

DCB CHARACTERISTICS

The field is characterized by a diversity of DCB platforms, antiproliferative agents and coatings. While the included RCT largely focus on paclitaxel-coated balloons, a growing body of evidence highlights differences in vascular response, downstream effects, and pharmacokinetics across different DCB, indicating that the choice of drug and coating technology could arguably influence clinical outcomes. Sirolimus-coated balloons have recently shown promising results in various clinical settings. Moving forward, future efforts should continue to differentiate between different technologies, as their clinical performance may not be uniform.[19,20] Of note, the balloon coating and mechanism of drug release are also key aspects that should be taken into consideration. The DCB technologies assessed in this meta-analysis all used paclitaxel coating but different in platform; only 3 trials evaluated the same device (DCB; SeQuent Please, B. Braun, Germany) whereas the remaining studies used distinct systems, including an ultrasound-controlled paclitaxel delivery platform.[10] Finally, inflation time is important for drug delievery and this was not uniform in the studies included in the meta-analysis, with recommended DCB inflation times as low as 30 seconds.[6] Recommendations among studies currently enrolling (MAGICAL SV [NCT06271590] and Prevail Global [NCT06535854]) are also slightly different, and whether this might have clinical implications is still to be elucidated.

ANGIOGRAPHIC AND CLINICAL OUTCOMES

DES implantation typically provides a larger acute gain in lumen diameter than balloon angioplasty, a concept highlighted also within the REVELATION trial,[9] where the residual percent diameter stenosis to define a successful procedure was different after DCB angioplasty (< 30%) and DES implantation (< 20%). While the meta-analysis reports the endpoint late lumen loss, we recognize that this metric may not fully capture the relative efficacy of these 2 technologies. The use of endpoints, such as net lumen gain, providing a more comprehensive and meaningful comparison between these 2 fundamentally different strategies by focusing on the overall therapeutic effect on the vessel lumen, rather than just the restenotic response following the intervention, should be implemented in upcoming studies. In addition, we acknowledge the limitation in comparing the incidence rate of composite endpoints such as major adverse cardiovascular events when these include different single components across the studies. Finally, we highlight the importance for future studies to concentrate on the reporting of any target vessel thrombosis, a key safety endpoint which remained underreported in the meta-analysis. Still, a significant concern in clinical practice and a key factor impacting the wider implementation of a DCB-based strategy (COPERNICAN [NCT06353594]).

CONCLUSIONS

The meta-analysis by Sorolla Romero et al. provides a timely summary of the current evidence on the use of DCB in large native coronary arteries, and its findings provide hypothesis-generating evidence that challenges the long-standing paradigm of DES as the default choice for any lesion. This work underscores that the evolution of PCI is ongoing and invites reconsideration of therapeutic algorithms toward a more personalized approach, in which the choice between DCB and DES is guided by patient- and lesion-specific factors (figure 1). Moving forward, the focus must shift towards refining patient selection, optimizing procedural techniques, and conducting further RCT with long-term follow-up to clarify the role of DCB in this new therapeutic paradigm.

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CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Colombo A, Leone PP. Redefining the way to perform percutaneous coronary intervention: a view in search of evidence. *Eur Heart J*. 2023; 44:4321-4323.
2. Colombo A, Leone PP, Ploumen EH, von Birgelen C. Drug-coated balloons as a first choice for patients with de novo lesions: pros and cons. *EuroIntervention*. 2024;20:e120-e122.
3. Regazzoli D, Latib A, Ezhumalai B, et al. Long-term follow-up of BVS from a prospective multicenter registry: Impact of a dedicated implantation technique on clinical outcomes. *Int J Cardiol*. 2018;270:113-117.
4. Camaj A, Leone PP, Colombo A, et al. Drug-Coated Balloons for the Treatment of Coronary Artery Disease: A Review. *JAMA Cardiol*. 2025; 10:189-198.
5. Sorolla Romero JA, Novelli L, LLau Garcia J, et al. Drug-coated balloons vs drug-eluting stents for the treatment of large native coronary artery disease. Meta-analysis of randomized controlled trials. *REC Interv Cardiol*. 2025. https://doi.org/10.24875/RECICE.M25000527.
6. Nishiyama N, Komatsu T, Kuroyanagi T, et al. Clinical value of drug-coated balloon angioplasty for de novo lesions in patients with coronary artery disease. *Int J Cardiol*. 2016;222:113-118.
7. Gao C, He X, Ouyang F, et al. Drug-coated balloon angioplasty with rescue stenting versus intended stenting for the treatment of patients with de novo coronary artery lesions (REC-CAGEFREE I): an open-label, randomised, non-inferiority trial. *Lancet*. 2024;404:1040-1050.

8. Yu X, Wang X, Ji F, et al. A Non-inferiority, Randomized Clinical Trial Comparing Paclitaxel-Coated Balloon Versus New-Generation Drug-Eluting Stents on Angiographic Outcomes for Coronary De Novo Lesions. *Cardiovasc Drugs Ther*. 2022;36:655-664.
9. Vos NS, Fagel ND, Amoroso G, et al. Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent in Acute Myocardial Infarction: The REVELATION Randomized Trial. *JACC Cardiovasc Interv*. 2019;12:1691-1699.
10. Wang Z, Yin Y, Li J, et al. New Ultrasound-Controlled Paclitaxel Releasing Balloon vs. Asymmetric Drug-Eluting Stent in Primary ST-Segment Elevation Myocardial Infarction-A Prospective Randomized Trial. *Circ J Off J Jpn Circ Soc*. 2022;86:642-650.
11. Gobić i D, Tomulić V, Lulić D, et al. Drug-Coated Balloon Versus Drug-Eluting Stent in Primary Percutaneous Coronary Intervention: A Feasibility Study. *Am J Med Sci*. 2017;354:553-560.
12. Hao X, Huang D, Wang Z, Zhang J, Liu H, Lu Y. Study on the safety and effectiveness of drug-coated balloons in patients with acute myocardial infarction. *J Cardiothorac Surg*. 2021;16:178.
13. Leone PP, Oliva A, Regazzoli D, et al. Immediate and follow-up outcomes of drug-coated balloon angioplasty in de novo long lesions on large coronary arteries. *EuroIntervention*. 2023;19:e923-e925.
14. Tartaglia F, Gitto M, Leone PP, et al. Validation of complex PCI criteria in drug-coated balloon angioplasty. *Clin Res Cardiol*. 2025;114:1059-1070.
15. Leone PP, Gitto M, Gao C, Sanz Sánchez J, Latib A, Colombo A. Rethinking coronary artery metal implants. *Prog Cardiovasc Dis*. 2025. https://doi.org/10.1016/j.pcad.2025.07.005.
16. Leone PP, Testa L, Greco A, et al. Two-Year Clinical Outcomes in Female and Male Patients After Sirolimus-Coated Balloon Angioplasty for Coronary Artery Disease. *Circ Cardiovasc Interv*. 2025;18:e014814.
17. Gitto M, Leone PP, Gioia F, et al. Coronary Artery Dissection in Drug-Coated Balloon Angioplasty: Incidence, Predictors, and Clinical Outcomes. *Am J Cardiol*. 2025;239:28-35.
18. Leone PP, Mangieri A, Regazzoli D, et al. Drug-Coated Balloon Angioplasty Guided by Postpercutaneous Coronary Intervention Pressure Gradient: The REDUCE-STENT Retrospective Registry. *JACC Cardiovasc Interv*. 2023;16:363-365.
19. Leone PP, Heang TM, Yan LC, et al. Two-year outcomes of sirolimus-coated balloon angiopla,sty for coronary artery disease: the EASTBOURNE Registry. *EuroIntervention*. 2024;20:e831-e833.
20. Leone PP, Calamita G, Gitto M, et al. Sirolimus- Versus Paclitaxel-Coated Balloons for Treatment of Coronary Artery Disease. *Am J Cardiol*. 2025;255:74-82.

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Editorial

The role of angiography-derived physiological assessment techniques in the post-FAVOR III Europe era?

Técnicas de evaluación fisiológica derivadas de la angiografía: ¿todavía tienen cabida después de la publicación del ensayo FAVOR III Europe?

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Currently, invasive coronary angiography is still the main technique to identify obstructive coronary artery disease. However, its diagnostic yield is limited by its inability to assess the functional relevance of intermediate stenoses.[1] The introduction of pressure guidewire-based physiological assessment was first enabled by the development of fractional flow reserve (FFR).[2] Within the following decade, a large body of evidence supported the benefit of FFR in revascularization decision-making, leading to its endorsement by clinical practice guidelines.[3-5] Still, a low penetrance of FFR was observed, due to scepticism in coronary physiology, the need for coronary instrumentation, adenosine infusion, and increased procedural time and costs.[6] These challenges led to the development of several non-hyperemic indices, avoiding the need for hyperemic agents, as well as angiography-derived physiological assessment techniques (ADPAT), which avoid both the use of adenosine and coronary guidewires. Over the past few years, several ADPAT modalities have emerged with the objective of estimating FFR by combining fluid dynamic equations, 3D models of the coronary tree and certain predefined boundary flow conditions.[7]

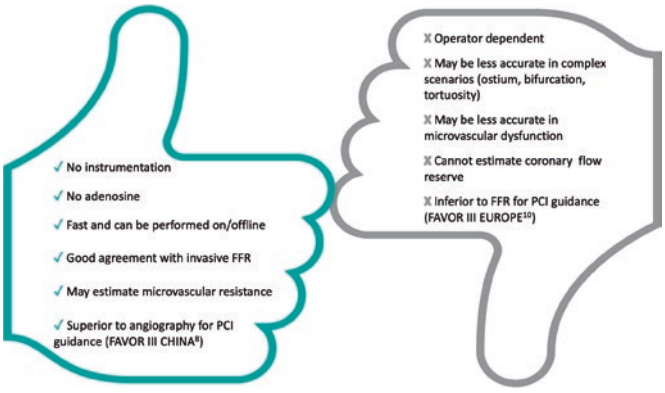

Figure 1. Advantages and disadvantages of ADPAT. ADPAT, angiography-derived physiological assessment techniques; FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

Most ADPAT have pivotal validation studies that compare them to FFR showing good diagnostic accuracy. Among these methods, quantitative flow ratio (QFR) has been evaluated in the largest number of studies and, importantly, the main clinical trials powered for cardiovascular events. In the randomized FAVOR III China trial, the QFR-guided revascularization of intermediate stenoses was superior to angiography-guided revascularization,[8] prompting a 1B recommendation for the use of QFR by the European clinical practice guidelines on the management of chronic coronary syndromes.[9] However, when QFR was compared with FFR for clinical events in the randomized FAVOR III Europe trial it not only failed to show non-inferiority, but also had a significantly worse rate of adverse events, with a hazard ratio of 1.67 for the composite primary endpoint and 1.84 for myocardial infarction (MI).[10] This has raised concerns about the reliability of QFR and its applicability as a substitute for FFR in the routine clinical practice. Figure 1 illustrates the known advantages and disadvantages of ADPAT.

In a recent article published in *REC: Interventional Cardiology*, Ruiz-Ruiz et al. provide a meta-analysis on the combined and individual accuracy of the most frequently used ADPAT software in the setting of functional interrogation of intermediate stenoses.[11] After applying eligibility criteria, a total of 27 papers were finally selected, including more than 4800 patients and more than 5400 vessel analysis. Although stable angina was the most prevalent indication, roughly a third of the patients exhibited acute coronary syndromes, mostly unstable angina. In more than half of the cases, the target vessel was the left anterior descending coronary artery. The ADPAT modalities included primarily QFR; 42.6% of vessels), angiography-derived FFR (15.5%), and vessel FFR (12.0%).

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The main results from the meta-analysis suggest a good diagnostic performance of the different ADPAT tools considered vs FFR. Overall sensitivity and positive predictive value were around 85%, whereas total specificity and negative predictive value exceeded 90%, highlighting a potential value of these techniques to identify functionally non-significant stenoses and defer revascularization. The area under the curve for predicting a significant FFR was remarkable (0.947). However, evidence quality on every ADPAT software was uneven and a large proportion of pivotal studies was included in the meta-analysis, precluding the results to properly represent a real-world patients' population. Furthermore, there were several exclusion criteria, such as > 10% prevalence of previous surgical revascularization, > 25% prevalence of atrial fibrillation, or > 30% of the patients exhibiting MI if time from the event to physiological evaluation was not specified, which means the studies included are highly selected and may not accurately reflect our routine clinical practice.

In any case, taken at face, these data of diagnostic accuracy for ADPAT seem encouraging. The pressure wire-based instantaneous wave-free ratio (iFR) demonstrated an area under the curve, as well as positive and negative predictive values very similar to those reported in this meta-analysis for ADPAT.[12] This would be indicative of a similar clinical value, which is why the negative results of the FAVOR III Europe trial came as such a shock. It is well established for FFR and iFR that much of the clinical benefit of physiology-based revascularisation derives from deferral of unneeded coronary interventions.[13] Similarly, the advantage of QFR over angiography in the FAVOR III China trial was associated with a lower number of lesions treated in the QFR arm.[8] However, data from the FAVOR III Europe trial questioned the ability of QFR to defer as many revascularizations as FFR. In this trial, median QFR values were lower than those of FFR, leading to more than 20% additional patients undergoing revascularization in the QFR group.[10] On the other hand, it could be that the inaccuracy goes both ways: a *post hoc* subanalysis of the trial revealed that QFR-based intervention deferral was associated with worse outcomes, especially in terms of unplanned revascularizations.[14] This suggests that excess events in the QFR arm of FAVOR III Europe trial might be attributed to both false positive and false negative measurements. For reproducibility, a pre-specified sub-study of the trial compared investigator-performed QFR measurements with repeated assessments by the core laboratory. Almost 30% disagreement was documented, including both significant and non-significant QFR values.[15] Of note, the study included a rigorous training and certification protocol for all the investigators involved in QFR assessment.

Clearly, the final word on these techniques has not yet been written. If we aim to predict and reduce the risk of adverse cardiovascular events, both microvascular dysfunction and plaque vulnerability are 2 factors that we should taken into consideration. The former, not only modifies the risk of cardiovascular events, but affects the accuracy of ADPAT measurements.[16] The latter is a major driver of adverse coronary events, may prompt percutaneous revascularization even in physiologically non-significant lesions,[17,18] and cannot be accurately estimated by any angiographic technique. In this regard, the use of intravascular imaging to assess both plaque vulnerability and physiological significance by means of dedicated algorithms seems promising.[19,20] Another important unsolved issue is the performance of physiology –of any kind– in clinical scenarios other than chronic coronary syndrome. Current clinical practice guidelines from the European Society of Cardiology do not support the use of FFR in ST-segment elevation MI due to conflicting evidence, and all other physiological indexes are lacking clinical trials in this setting. Of note, MI with and without ST-segment elevation accounts for more than half of revascularization procedures in most centers with a primary percutaneous coronary intervention program in our setting. The ongoing VULNERABLE trial[18] should shed light on this issue of whether physiology is sufficient to safely defer non-culprit lesions in ST-segment elevation MI, or rather a more proactive approach is needed to detect and treat vulnerable plaques. As we wait for the results of this and other trials, integrative efforts such as the meta-analysis conducted by Ruiz-Ruiz et al.[11] may contribute to expand knowledge and expertise on ADPAT.

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None declared.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Patel MR, Peterson ED, Dai D, et al. Low Diagnostic Yield of Elective Coronary Angiography. *N Engl J Med*. 2010;362:886–895.
2. Pijls NHJ, Van Gelder B, Van der Voort P, et al. Fractional Flow Reserve. *Circulation*. 1995;92:3183–3193.
3. Tonino PAL, De Bruyne B, Pijls NHJ, et al. Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention. *N Engl J Med*. 2009;360:213–224.
4. Toth G, Hamilos M, Pyxaras S, et al. Evolving concepts of angiogram: fractional flow reserve discordances in 4000 coronary stenoses. *Eur Heart J*. 2014;35:2831–2838.
5. De Bruyne B, Pijls NHJ, Kalesan B, et al. Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease. *N Engl J Med*. 2012;367:991–1001.
6. Demir OM, Schrieken C, Curio J, Rahman H. Behavioural determinants impacting the adoption rate of coronary physiology. *Int J Cardiol*. 2021;330:12–14.
7. Faria D, Hennessey B, Shabbir A, et al. Functional coronary angiography for the assessment of the epicardial vessels and the microcirculation. *EuroIntervention*. 2023;19:203–221.
8. Xu B, Tu S, Song L, et al. Angiographic quantitative flow ratio-guided coronary intervention (FAVOR III China): a multicentre, randomised, sham-controlled trial. *Lancet*. 2021;398:2149–2159.
9. Vrints C, Andreotti F, Koskinas KC, et al. 2024 ESC Guidelines for the management of chronic coronary syndromes. *Eur Heart J*. 2024;45:3415–3537.
10. Andersen BK, Sejr-Hansen M, Maillard L, et al. Quantitative flow ratio versus fractional flow reserve for coronary revascularisation guidance (FAVOR III Europe): a multicentre, randomised, non-inferiority trial. *Lancet*. 2024;404:1835–1846.
11. Ruiz-Ruiz J, Cortés-Villar C, Fernández-Cordón C, et al. Angiography-derived index versus fractional flow reserve for intermediate coronary lesions: a meta-analysis review. *REC Interv Cardiol*. 2025. https://doi.org/10.24875/RECICE.M25000523.
12. Sen S, Escaned J, Malik IS, et al. Development and Validation of a New Adenosine-Independent Index of Stenosis Severity From Coronary Wave–Intensity Analysis. *J Am Coll Cardiol*. 2012;59:1392–1402.
13. Escaned J, Ryan N, Mejía-Rentería H, et al. Safety of the Deferral of Coronary Revascularization on the Basis of Instantaneous Wave-Free Ratio and Fractional Flow Reserve Measurements in Stable Coronary Artery Disease and Acute Coronary Syndromes. *JACC Cardiovasc Interv*. 2018;11:1437–1449.
14. Andersen BK, Holm NR, Mogensen LJH, et al.; on behalf of the FAVOR III Europe Study Team. Coronary revascularisation deferral based on quantitative flow ratio or fractional flow reserve: a post hoc analysis of the FAVOR III Europe trial. *EuroIntervention*. 2025;21:e161–e170.
15. Kristensen SK, Holm MB, Maillard L, et al. Re-analysis and quality assessment of QFR in the FAVOR III Europe trial. The REPEAT-QFR study. In: EuroPCR 2025; 2025 May 20-23; Paris, France. Available at: https://www.

pcronline.com/Cases-resources-images/Resources/Course-videos-slides/2025/EuroPCR/How-coronary-physiology-may-help-in-guiding-treatment-of-NSTEMI. Accessed 9 Sep 2025.

16. Mejia-Renteria H, Lee JM, Choi K, et al. Coronary microcirculation assessment using functional angiography: Development of a wire-free method applicable to conventional coronary angiograms. *Catheter Cardiovasc Interv*. 2021;98:1027–1037.
17. Park S-J, Ahn J-M, Kang D-Y, et al. Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial. *Lancet*. 2024;403:1753–1765.
18. Gómez-Lara J, López-Palop R, Rúmiz E, et al. Treatment of functionally nonsignificant vulnerable plaques in multivessel STEMI: design of the VULNERABLE trial. *REC Interv Cardiol*. 2024. https://doi.org/10.24875/RECICE.M24000468.
19. Yu W, Tanigaki T, Ding D, Wu P, Du H, Ling L, Huang B, Li G, Yang W, Zhang S, et al. Accuracy of Intravascular Ultrasound-Based Fractional Flow Reserve in Identifying Hemodynamic Significance of Coronary Stenosis. *Circ Cardiovasc Interv*. 2021;14:e009840.
20. Jeremias A, Maehara A, Matsumura M, et al. Optical Coherence Tomography–Based Functional Stenosis Assessment: FUSION—A Prospective Multicenter Trial. *Circ Cardiovasc Interv*. 2024;17:e013702.

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Original article

Drug-coated balloons vs drug-eluting stents for the treatment of large native coronary artery disease. Meta-analysis of randomized controlled trials

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ABSTRACT

Introduction and objectives: To compare the effects of drug-coated balloon (DCB) vs drug-eluting stent (DES) in patients presenting with de novo large vessel coronary artery disease (CAD).
Methods: We conducted a systematic research of randomized controlled trials comparing DCB vs DES in patients with de novo large vessel CAD. Data were pooled by meta-analysis using a random-effects model. The prespecified primary endpoint was target lesion revascularization (TLR).
Results: A total of 7 trials enrolling 2961 patients were included. The use of DCB vs DES was associated with a similar risk of TLR (OR, 1.21; 95%CI, 0.44-3.30; I^2 = 48%), all-cause mortality (OR, 1.56; 95%CI, 0.94- 2.57; I^2 = 0%), cardiac death (OR, 1.65; 95%CI, 0.90-3.05; I^2=0%), myocardial infarction (OR, 0.97; 95%CI, 0.58-1.61; I^2 = 0%), major adverse cardiovascular adverse (OR, 1.19; 95%CI, 0.74-1.90; I^2 = 13.5%) and late lumen loss (standardized mean difference [SMD], −0.35; 95%CI, −0.74 to 0.04; I^2 = 81.4%). However, the DCB was associated with a higher risk of target vessel revascularization (OR, 2.47; 95%CI, 1.52-4.03; I^2 = 0%) and smaller minimal lumen diameter during late follow-up (SMD, −0.36; 95%CI, −0.56 to −0.15; I^2 = 34.5%). Nevertheless, prediction intervals included the value of no difference for both outcomes.
Conclusions: In patients with de novo large vessel CAD the use of DCB vs DES is associated with a similar risk of TLR. However, the DES achieves better late angiographic results.

Keywords: Drug-coated balloon. Drug-eluting stent. Coronary artery disease.

Balón farmacoactivo frente a *stent* farmacoactivo para el tratamiento de la enfermedad coronaria de vaso grande. Metanálisis de ensayos clínicos aleatorizados

RESUMEN

Introducción y objetivos: Comparar los efectos del balón farmacoactivo (BFA) frente al *stent* farmacoactivo (SFA) en pacientes con enfermedad arterial coronaria (EAC) de vaso grande *de novo*.
Métodos: Se realizó una búsqueda sistemática de ensayos clínicos aleatorizados comparando BFA frente a SFA en pacientes con EAC de vaso grande *de novo*. Los datos se agruparon mediante un metanálisis de efectos aleatorios. El objetivo primario fue la necesidad de revascularización de la lesión diana (RLD).

◊ Both authors contributed equally to this work.

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Resultados: Se incluyeron 7 ensayos con 2.961 pacientes. El uso de BFA, en comparación con SFA, se asoció con un riesgo similar de RLD (OR = 1,21; IC95%, 0,44-3,30; I^2 = 48%), muerte por todas las causas (OR = 1,56; IC95%, 0,94-2,57; I^2 = 0%), muerte de causa cardiovascular (OR = 1,65; IC95%, 0,90-3,05; I^2 = 0%), infarto de miocardio (OR = 0,97; IC95%, 0,58-1,61; I^2 = 0%), acontecimientos adversos cardiacos mayores (OR = 1,19; IC95%, 0,74-1,90; I^2 = 13,5%) y pérdida luminal tardía (DME = −0,35; IC95%, −0,74 a 0.04; I^2 = 81,4%). Sin embargo, el BFA se asoció a un mayor riesgo de revascularización del vaso diana (OR = 2,47; IC95%, 1,52-4,03; I^2 = 0%) y a un menor diámetro luminal mínimo en el seguimiento (DME: −0,36; IC95%, −0,56 a −0,15; I^2 = 34,5%), aunque los intervalos de predicción incluyeron el valor nulo para ambos resultados.
Conclusiones: En los pacientes con EAC de vaso grande *de novo,* el BFA comparado con el SFA se asoció a un riesgo similar de RLD, obteniendo el SFA mejores resultados angiográficos.

Palabras clave: Balón farmacoactivo. *Stent* farmacoactivo. Enfermedad arterial coronaria.

Abbreviations

CAD: coronary artery disease. **DCB:** drug-coated balloon. **DES:** drug-eluting stent. **MI:** myocardial infarction. **MLD:** minimum lumen diameter. **TLR:** target lesion revascularization.

INTRODUCTION

Drug-eluting stents (DES) remain the standard of treatment for patients undergoing percutaneous coronary intervention (PCI).[1,2] However, DES are associated with a gradually and permanent increased risk of adverse events, particularly due to late stent thrombosis and in-stent restenosis, with a 2% incidence rate per year with no plateau observed.[1] This risk is even higher when complex and long lesions are treated.[3] In recent years, drug-coated balloons (DCB) have emerged as a potential alternative treatment option to DES. Following adequate lesion preparation, unlike traditional stents, DCBs can release an antiproliferative drug into the vessel wall without leaving behind a permanent metal scaffold. Notably, permanent scaffolding can distort and constrain the coronary vessel, thus impairing vasomotion and adaptive remodelling, while also promoting chronic inflammation.[4] DCB-PCI is a well-established treatment for in-stent restenosis and small-vessel coronary artery disease (CAD).[5,6] However, its role in de novo large vessel CAD remains controversial. In a recent randomized clinical trial (RCT) with patients undergoing de novo CAD revascularization, a strategy of DCB-PCI did not achieve non-inferiority vs DES in terms of device-oriented composite endpoint driven by higher rates of target lesion revascularization (TLR).[7] Contrary to prior published research, our findings did not support similar clinical outcomes for DCB vs DES in patients with de novo large vessel CAD.[8,9] A recent meta-analysis of 15 studies compared DCB-PCI or hybrid angioplasty vs DES-PCI in patients with vessels > 2.75 mm in diameter showing no significant differences in the clinical endpoints of TLR, cardiac death, and MI.[10] However, 14 of the 15 included studies were non-RCT, and the recent previously reported RCT was not included. Nevertheless, individual non-inferiority studies often lack the statistical power needed to definitively compare these technologies, underscoring the need for a systematic appraisal of treatment effects and evidence quality. Therefore, we conducted a systematic review and meta-analysis of available RCT to provide a comprehensive and quantitative assessment of evidence on the efficacy of DCB vs the current-generation DES in de novo large vessel CAD in terms of adverse events at longest available follow-up.

METHODS

Search strategy and selection criteria

We conducted a meta-analysis of RCT according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 guidelines.[11] Two reviewers independently identified the relevant studies through an electronic search across the MEDLINE and Embase databases (from inception to October 2024). In addition, we employed backward snowballing (eg, reference review from identified articles and pertinent reviews). No language, publication date or publication status restrictions were imposed. This study is registered with PROSPERO and the search strategy is available in the supplementary data.

Study selection

Two reviewers independently assessed trial eligibility based on titles, abstracts, and full-text reports. Discrepancies in study selection were discussed and resolved with a third investigator. Eligible studies needed to meet the following pre-specified criteria: *a)* RCT comparing PCI with DCB and PCI with DES; *b)* study population including patients with de novo large vessel CAD (eg, defined as vessel diameter ≥ 2.5 mm);[12] *c)* availability of clinical outcome data (without restriction as to follow-up time). Exclusion criteria were *a)* lack of a randomized design; *b)* studies including patients undergoing treatment for in-stent restenosis; *c)* studies including patients with de novo small vessel CAD; *d)* lack of any clinical outcome data.

A reference vessel diameter ≥ 2.5 mm was established as the cut-off value to define large vessel based on a recent proposed standardized definition.[12]

Data extraction

Three investigators (J. Llau García, S. Huélamo Montoro and J. A. Sorolla Romero) independently assessed studies for possible inclusion, with the senior investigator (J. Sanz-Sánchez) resolving discrepancies. Non-relevant articles were excluded based on title and abstract. The same investigators independently extracted data on study design, measurements, patient characteristics, and outcomes using a standardized data-extraction form. Data extraction conflicts were discussed and resolved with the senior investigator.

Data on authors, year of publication, inclusion and exclusion criteria, sample size, patients' baseline patients, endpoint definitions, effect estimates, and follow-up time were collected.

Endpoints

The prespecified primary endpoint was TLR. Secondary clinical endpoints were all-cause mortality, cardiac death, myocardial infarction (MI), target vessel revascularization (TVR) and major adverse cardiovascular events (MACE). Secondary angiographic endpoints were minimum lumen diameter (MLD) and late lumen loss (LLL). Each endpoint was assessed according to the definitions reported in the original study protocols, as summarized in table 1 of the supplementary data. All the endpoints were assessed at the maximum follow-up available.

Risk of bias

The risk of bias in each study was assessed using the revised Cochrane risk of bias tool (RoB 2.0).[11] Three investigators (J. Llau García, S. Huélamo Montoro and J. A. Sorolla Romero) independently assessed 5 domains of bias in RCT: *a)* randomization process, *b)* deviations from intended interventions, *c)* missing outcome data, *d)* outcome measurement, and *e)* selection of reported results (table 2 of the supplementary data).

Statistical analysis

Odds ratios (OR) and 95% confidence intervals (95%CI) were calculated using the DerSimonian and Laird random-effects model, with the estimate of heterogeneity being obtained from the Mantel-Haenszel method. The presence of heterogeneity among studies was evaluated with the Cochran Q chi-square test, with $P \leq .10$ being considered of statistical significance, and using the I^2 test to evaluate inconsistency. A value of 0% indicates no observed heterogeneity, and values of ≤ 25%, ≤ 50%, > 50% indicate low, moderate, and high heterogeneity, respectively. Prediction intervals (95%) in addition to conventional 95%CI around ORs were calculated to assess residual uncertainty. Publication bias and the small study effect were assessed for all outcomes, using funnel plots. The presence of publication bias was investigated using Harbord and Egger tests and visual estimation with funnel plots. We performed a sensitivity analysis by removing one study at a time to confirm that the findings, when compared with DES, were not driven by any single study. To account for different lengths of follow-up across studies, another sensitivity analysis was performed using the Poisson regression model with random intervention effects to calculate inverse-variance weighted averages of study-specific log stratified incidence rate ratios (IRRs). Results were displayed as IRRs, which are exponential ratios of the regression model. Additionally, random-effect meta-regression analyses were performed to assess the impact of the following variables on treatment effect with respect to the primary endpoint: eg, percentage of patients with acute coronary syndrome (ACS), percentage of patients with diabetes mellitus, mean reference vessel diameter and follow-up duration. The statistical level of significance was 2-tailed $P < .05$. Stata version 18.0 (StataCorp LP, College Station, United States), was used for statistical analyses.

RESULTS

Search results

Figure 1 illustrates the PRISMA study search and selection process. A total of 7 RCT were identified and included in this analysis. The main features of included studies are shown in table 1.

All studies had a non-inferiority design. A clinical primary endpoint was selected in 1 study,[7] and an invasive functional endpoint was selected in another trial,[9] while angiographic primary endpoints were prespecified in the remaining studies.[8,13-16] The mean clinical and angiographic follow-up were 21.5 months and 8.9 months respectively. A total of 4 studies were conducted in the context of ACS[9,14-17] and 1 study in the context of chronic coronary syndrome (CCS).[13] Finally, 2 studies enrolled both ACS and CCS patients.[7,8] A total of 3 trials enrolled patients treated with second-generation DES (Firebird 2.0 [Microport, China], Xience Xpedition [Abbott Vascular, United States], Orsiro [Biotronik, Germany]),[7,9,13] and 2 studies enrolled patients treated with third-generation DES (Biomine [Meril Life Sciences, India], Cordimax [Rientech, China]).[14,15] One trial enrolled patients treated with second and third-generation DES (Xience Xpedition [Abbott Vascular, United States], Resolute Integrity, [Medtronic, United States], Firehawk, [MicroPort, China]).[8] All studies included patients who underwent paclitaxel-DCB-PCI ([Pantera Lux, Biotronik, Germany],[9,14] [SeQuent Please, B Braun, Germany],[7,8,13,15] [Bingo DCB, Yinyi Biotech,China]),[16] and none with sirolimus-DCB-PCI.

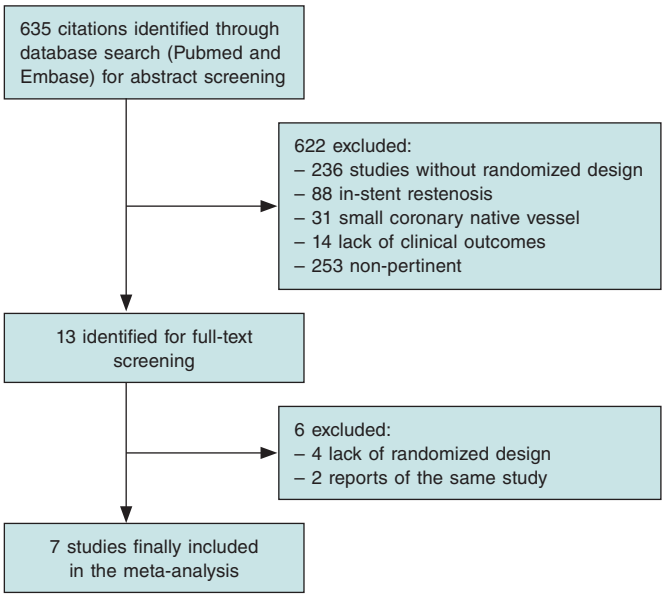

Figure 1. Flow diagram of the search for studies included in the meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement.

Baseline characteristics

A total of 2961 patients were included, 1476 of whom received DCB and 1485, DES for de novo large vessel CAD. The patients main baseline characteristics are shown in table 2.

Publication bias and asymmetry

Funnel-plot distributions of the pre-specified outcomes indicate absence of publication bias for all the outcomes (figures 1-8 of the supplementary data).

Risk of bias assessment

Table 2 of the supplementary data illustrates the results of the risk of bias assessment with the RoB 2.0 tool. One trial was considered at low overall risk of bias,[7] 5 raised some concerns[8,9,13,14,16] and 1 presented a high overall risk of bias.[15]

Table 1. Main features of included studies

Study	Year of publication	No. of patients		Type of Device	Reference vessel diameter (mean ± SD) (mm)	Multicenter	Clinical follow up (months)	Angiographic follow-up (months)
		DCB	DES					
REC-CAGEFREE I[7]	2024	1133	1139	Paclitaxel-DCB Sirolimus-DES	3.00 ± 0.55	YES	24	NO
Nishiyama et al.[13]	2016	30	30	Paclitaxel-DCB Everolimus-DES	2.80 ± 0.63	NO	8	8
Xue Yu et al.[8]	2022	85	85	Paclitaxel-DCB Everolimus-DES	2.89 ± 0.33	NO	12	9
REVELATION[9]	2019	60	60	Paclitaxel-DCB Sirolimus and everolimus DES	3.24 ± 0.50	NO	24	9
Gobic et al.[15]	2017	38	37	Paclitaxel-DCB Sirolimus-DES	> 2.50	NO	6	6
Hao et al.[16]	2021	38	42	Paclitaxel-DCB NA	> 2.50	NO	12	12
Wang et al.[14]	2022	92	92	Paclitaxel-DCB Sirolimus-DES	3.37 ± 0.52	NO	12	9

DCB, drug-coated balloon; DES, drug-eluting stent; NA, not available.

Table 2. Baseline clinical characteristics of included patients

Study	Age (years)	Male (%)	Diabetes (%)	Smoking (%)	Hypertension (%)	LVEF (%)	Clinical Presentation (CCS/ACS) (%)	Multivessel (%)	Complex lesion (%)
REC-CAGEFREE I[7]	62	69.3	27.3	45	60.1	60	44.9/55.3	4.8	0
Nishiyama et al.[13]	69	73.3	41.6	60	83.3	NA	0/100	NA	36
Xue Yu et al.[8]	63.3	69.3	24.1	54	63.9	> 40	11.1/88.9	84	44.1
REVELATION[9]	57	87	10	60	31	57.6	0/100	71.6	N/A
Gobic et al.[15]	57.4	87	10	49.5	33.4	50.2	0/100	NA	N/A
Hao et al.[16]	57.5	78.5	31.5	29.5	24	46	0/100	NA	N/A
Wang et al.[14]	49.5	93.5	81.6	81.5	71.8	NA	0/100	NA	N/A

ACS, acute coronary syndrome; CCS, chronic coronary syndrome; NA, not available.

Outcomes

Clinical outcomes

DCB use compared with DES was associated with a similar risk of TLR (OR, 1.21; 95%CI, 0.44-3.30; $I^2 = 48\%$), all-cause mortality (OR, 1.56; 95%CI, 0.94- 2.57; $I^2 = 0\%$), cardiac death (OR, 1.65; 95%CI, 0.90-3.05; $I^2 = 0\%$), MI (OR, 0.97; 95%CI, 0.58-1.61; $I^2 = 0\%$) and MACE (OR, 1.19; 95%CI, 0.74-1.90; $I^2 = 13.5\%$). However, DCB was associated with a higher risk of TVR (OR, 2.47; 95%CI, 1.52-4.03; $I^2 = 0\%$) (figure 2, figure 3 and figures 9-10 of the supplementary data).

Angiographic outcomes

Compared with DES, DCB use yielded significant smaller MLD (SMD, −0.36; 95%CI, −0.56 to −0.15; $I^2 = 34.5\%$) and similar risk of LLL (SMD, −0.35; 95%CI, −0.74 to 0.04; $I^2 = 81.4\%$) at follow-up (figure 4).

Prediction intervals were consistent with CI for all the outcomes except for TVR and MLD, which included the value of no difference.

Sensitivity analysis

A leave-one-out pooled analysis by iteratively removing one study at a time was performed for all endpoints. Treatment effects were consistent with the main analysis for TLR, all-cause mortality, cardiac death, MI and MLD. The risk of TVR was no longer significantly higher among patients undergoing DCB when removing the CAGEFREE I trial,[7] and the risk of LLL was significantly lower among patients undergoing DCB-PCI when removing the REVELATION trial.[9] However, an increased risk of MACE was observed among patients undergoing DCB-PCI when removing the study by Xue Yu et al.[18] (tables 3-10 of the supplementary data). A sensitivity analysis using estimated IRRs was performed to account for varying follow-up lengths, confirming that our main analysis findings remained unchanged (table 11 of the supplementary data).

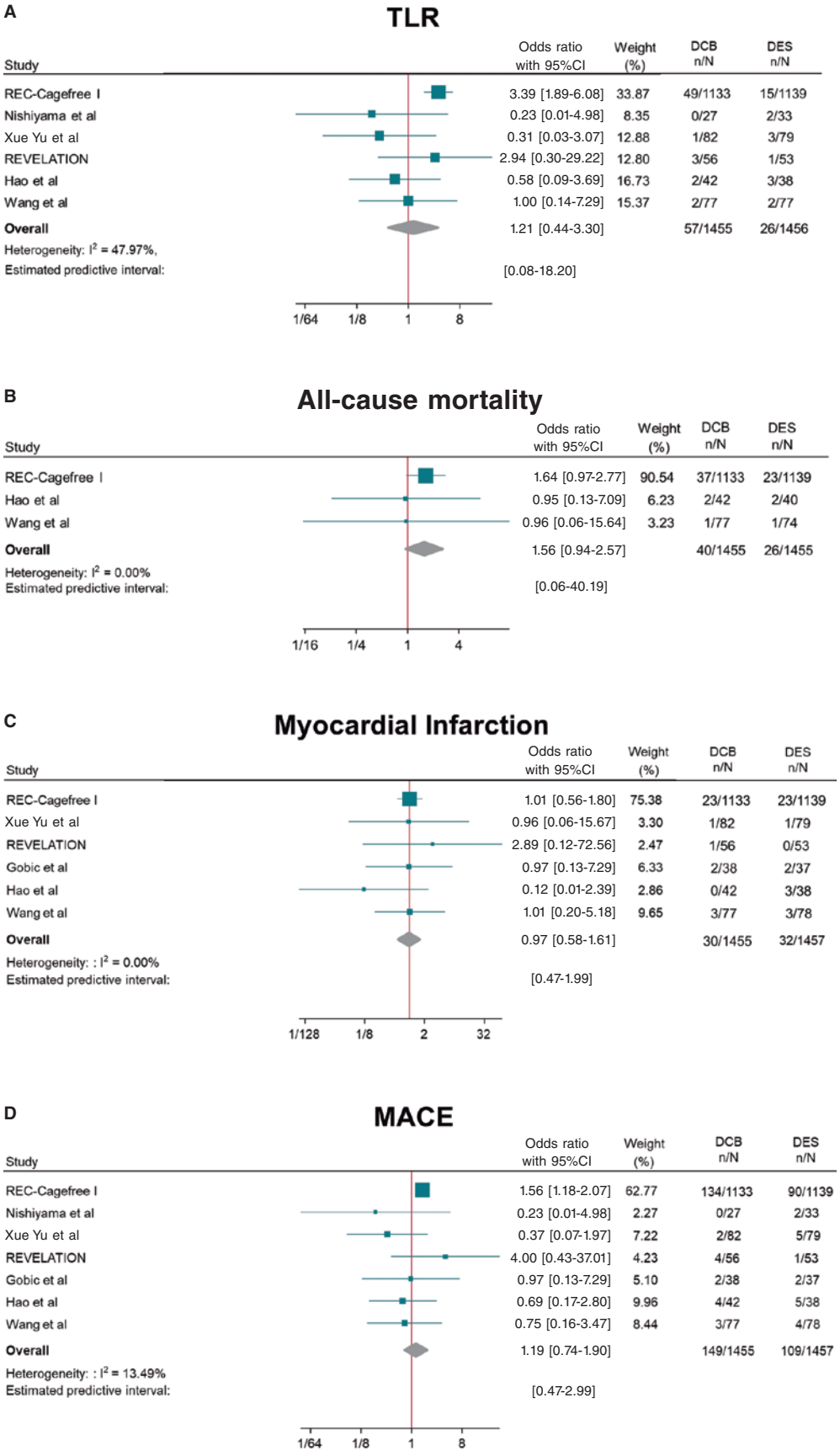

Figure 2. Forest plot reporting trial-specific and summary ORs with 95%CIs for the endpoint of A) target lesion revascularization; B) all-cause mortality; C) myocardial infarction; D) MACE. 95%CI, 95% confidence interval; DCB, drug-coated balloon; DES, drug-eluting stents; MACE, major adverse cardiovascular events; OR, odds ratio. References: REC-Cagefree I.,[7] Nishiyama et al.,[13] Xue Yu et al.,[8] REVELATION,[9] Hao et al.,[16] Wang et al.,[14] and Gobic et al.[15]

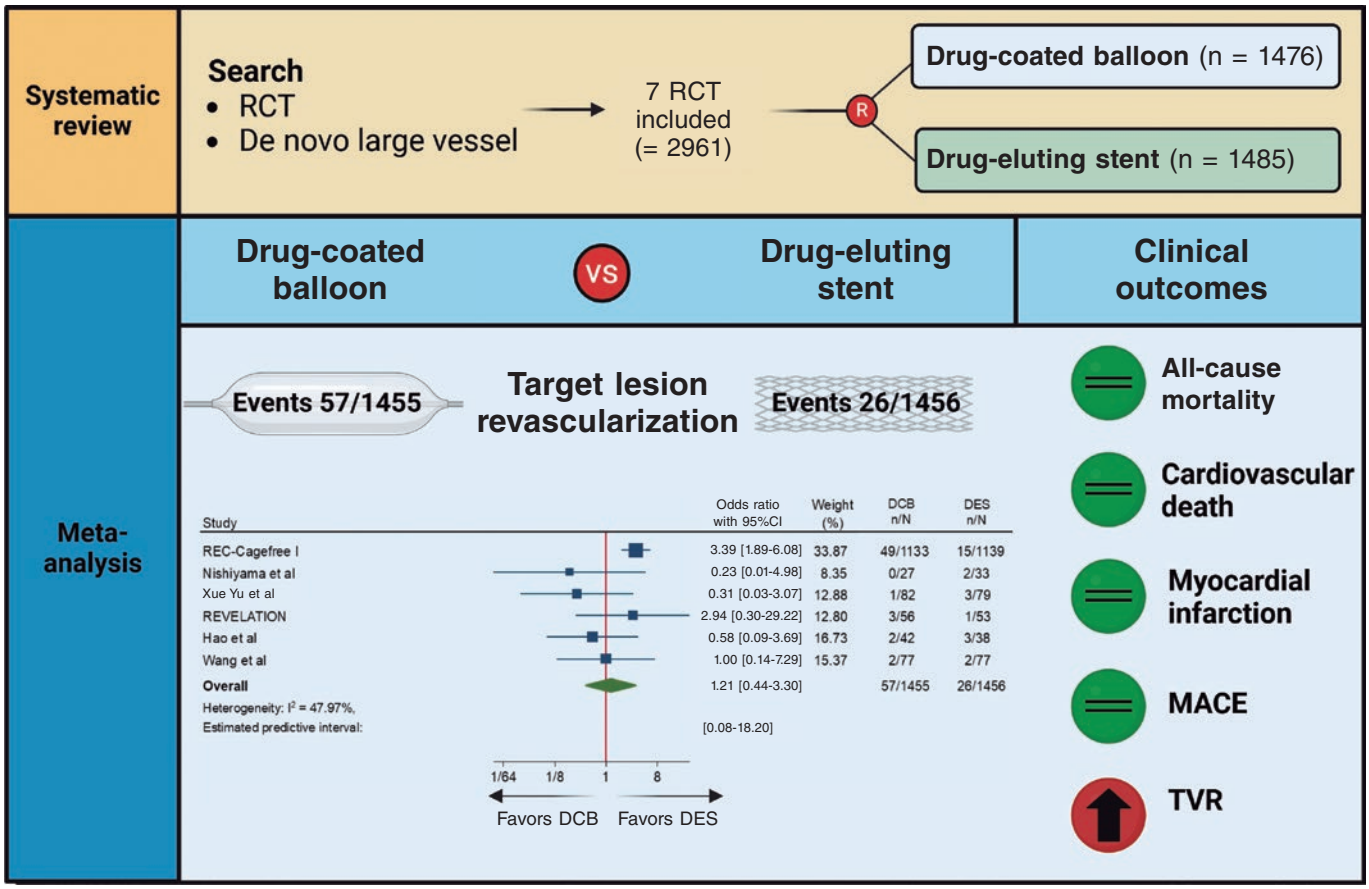

Figure 3. Central Illustration. DCB, drug-coated balloon; DES, drug-eluting stent; RCT, randomized clinical trial; TVR, target vessel revascularization. References: REC-Cagefree I.,[7] Nishiyama et al.,[13] Xue Yu et al.,[8] REVELATION,[9] Hao et al.,[16] and Wang et al.[14]

Random effect meta-regression analysis found no significant impact of the proportion of patients presenting with ACS (P = .882), diabetes mellitus (P = .641), mean reference vessel diameter (P = .985) and follow-up duration (P = .951) on treatment effect with respect to the primary endpoint.

DISCUSSION

This meta-analysis provides a comprehensive and updated quantitative analysis of available evidence on the comparison of DCB vs DES in de novo large vessel CAD, including data from 2961 patients enrolled in 7 RCT. The main findings of the study are:

a) The use of DCB was associated with a similar risk of clinical events vs DES except for TVR. However, data for this outcome was only available in 3 of the 7 included studies and the increased risk in patients undergoing DCB-PCI was not significant when the CAGEFREE I trial was removed. In addition, prediction intervals were not consistent with the CI. Therefore, the results of this outcome should be interpreted with caution.

b) The effect of DCB on the risk of TLR was not affected by the proportion of patients presenting with ACS or diabetes, as well as the mean reference vessel diameter or follow-up duration as assessed by meta-regression analysis.

c) DCB was associated with lower MLD at angiographic follow-up, but with similar LLL vs DES.

DES are the standard of treatment for patients undergoing PCI. However, complications such as stent thrombosis and in-stent restenosis still occur with rates estimated at 0.7-1% and 5-10% at the 10-year follow-up respectively.[19,20] Therefore, in recent years there has been a growing concern for developing strategies to reduce stent-related adverse events. In this context, DCBs have emerged as a potential treatment alternative based on a "leaving nothing behind" strategy. Nevertheless, data of patients presenting with de novo large CAD is scarce and conflicting. The CAGEFREE I is the only available clinically powered RCT that included 2272 patients undergoing de novo non-complex CAD revascularization across 40 centers in China. A strategy of DCB-PCI did not achieve non-inferiority vs DES in terms of device-oriented composite endpoint driven by higher rates of TLR in the DCB-PCI group (3.1% vs 1.2%, P = .002). On the other hand, in single-center RCT conducted by Nishiyama et al. with 60 patients with CCS undergoing elective PCI a trend toward lower rates of TLR in the DCB-PCI group (0% vs 6.1%, P = .193) was shown at the 8-mont follow-up.[13] Similarly, in a RCT including 170 patients undergoing PCI for de novo large CAD lower rates of TLR at the 12-month follow-up were found in patients undergoing DCB-PCI (1.6% vs 3.4%, P = .306).[14] In our analysis when pooling data from all available RCT, the risk of TLR was similar among patients undergoing DCB-PCI or DES-PCI. Notably, since this result was obtained with a moderate heterogeneity ($I^2 \approx 50\%$), it should be interpreted with caution regarding its general applicability. These findings remained unvaried at the leave-one-out analysis. In addition, prediction intervals were consistent with CI around ORs showing lack of residual uncertainty. Previous studies have shown that in-stent restenosis after DES is not a benign phenomenon, presenting as an ACS in

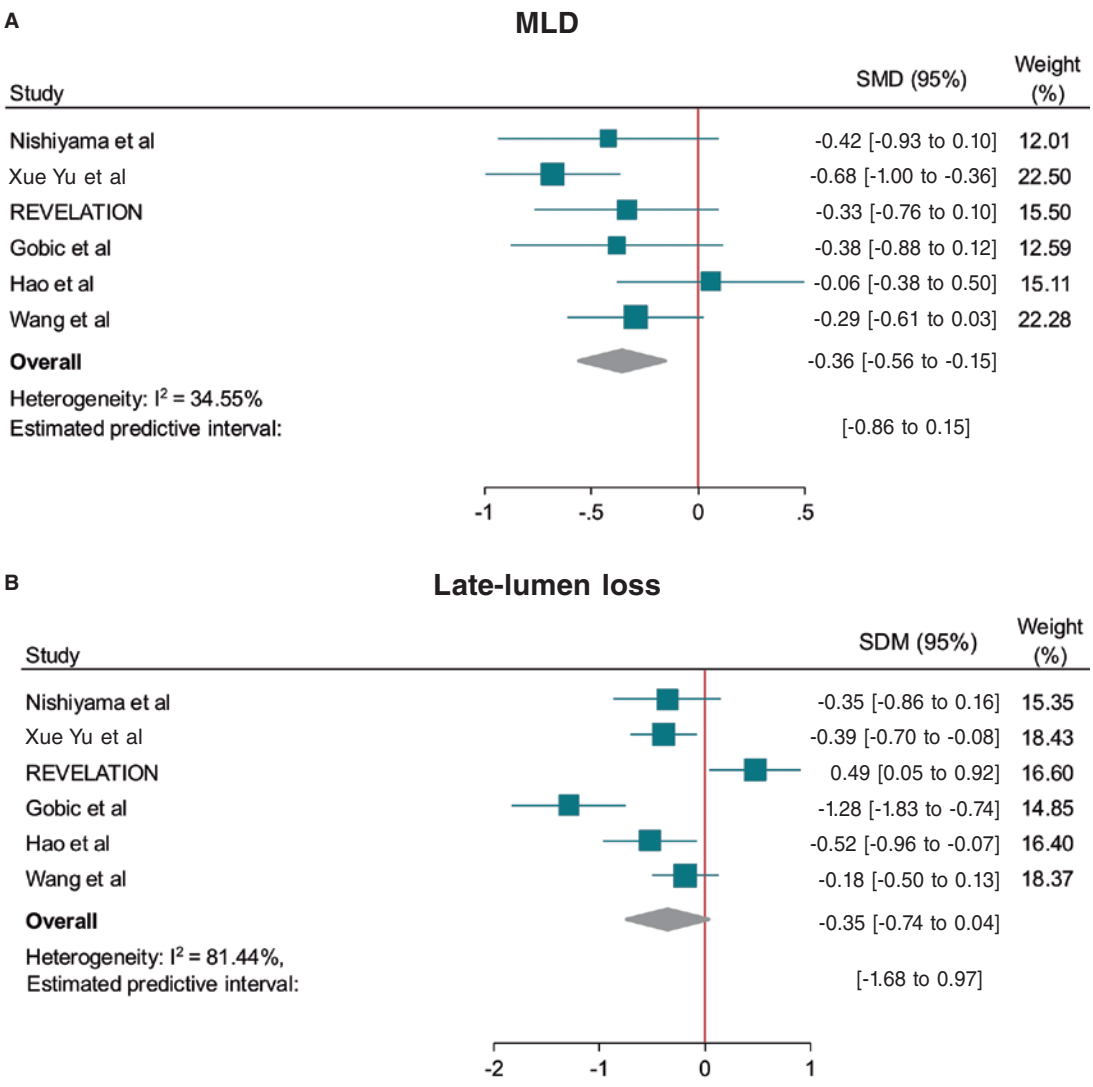

Figure 4. Forest plot reporting trial-specific and summary ORs with 95%CIs for the endpoint of **A**: minimum lumen diameter, and **B**: late-lumen loss. 95%CI, 95% confidence interval; DCB, drug-coated balloon; DES, drug-eluting stents; MACE, major adverse cardiovascular events; MLD, minimum lumen diameter; SMD, standardized mean difference; OR, odds ratio. References: Nishiyama et al.,[13] Xue Yu et al.,[8] REVELATION,[9] Gobic et al.,[15] Hao et al.,[16] and Wang et al.[14].

about 70% of the cases, with 5-10% of these resulting in MI.[21] We could speculate that the lack of permanent scaffold with DCB vs DES may predispose to a less aggressive pattern of restenosis and not increase the risk of thrombotic vessel closure beyond 3 months when vessel healing after DCB-PCI has occurred.[22]

Notably, 5 of the 7 studies included in this meta-analysis enrolled patients presenting with ACS. A total of 34% of the patients included in the CAGEFREE study presented with ACS, with 16% being STEMI cases.[7] Four other studies only included STEMI patients.[7,9,14-16] Although the performance of DCB in the STEMI scenario is unknown, its use in clinical practice is increasing.[23] Culprit lesion plaques in STEMI patients are usually soft and adequate plaque modification can be easily achieved through DCB-PCI (< 30% residual stenosis and low grade of dissection).[23] Moreover, the ruptured lipid rich plaque can potentially be an ideal reservoir for effective paclitaxel uptake.[24] On the other hand, DCBs carry specific risks for STEMI patients, such as acute recoil and culprit lesion closure, because they don't provide vessel scaffolding.

In our study, the proportion of patients presenting with ACS had no impact on treatment effects on the meta-regression analysis. Nevertheless, further RCT with adequate sample size are needed to obtain more solid evidence in this field. Of note, complex lesions (eg, severe calcification and bifurcations with planned two-stent technique) were excluded from the studies that included patients presenting with CCS.[7,8] Therefore, our findings might not be generalized to this population.

The better angiographic surrogate outcomes with DES-PCI vs DCB-PCI found in our meta-analysis after pooling data from 6 studies can be explained by the absence of a metal scaffold to expand the vessel lumen and the acute recoil following balloon angioplasty. This justifies the lower MLD achieved after DCB-PCI vs DES-PCI. While our analysis did not show significant differences regarding LLL during follow-up, the value of LLL was lower among patients undergoing DCB-PCI when excluding the REVELATION trial.[9,17] This study showed extremely low LLL in both DCB and DES groups vs other available evidence from RCT.[15,16] The presence of positive vessel remodeling with a late lumen enlargement after the use of DCB evaluated by intracoronary imaging modalities has been evidenced in multiple studies, and seems to be associated with small vessel disease, fibrous and layered plaques and a post-PCI medial dissection arc > 90°.[25,26,27] However, evidence of this

phenomenon in patients with large vessel CAD is less known.[22] It should, therefore, be noted that all studies in this meta-analysis used paclitaxel-DCB. While the evidence comparing sirolimus and paclitaxel-DCB is scarce, 2 recent RCT have shown better angiographic results with the lipophilic component. In the first one, with 121 patients with the novo small vessel CAD, sirolimus-DCB failed to achieve non-inferiority for net-lumen gain at 6 months.[28] In the second study, with 70 patients, the 2 devices showed similar results of LLL at 6 months, although patients treated with paclitaxel-DCB had more frequent late luminal enlargement.[29] Due to the small sample size and although there is not enough evidence to evaluate differences across clinical endpoints, we cannot assume that there is a class effect across all DCBs. There are larger ongoing RCT to evaluate the outcomes of sirolimus DCB vs DES in large vessels that will provide evidence in this field.[30,31]

Limitations

The results of our investigation should be interpreted in light of some limitations. First, this is a study-level meta-analysis providing average treatment effects. The lack of patient-level data from the included studies prevents us from assessing the impact of baseline clinical, angiographic and procedural characteristics on treatment effects. Second, minor differences in definition were present for some endpoints (eg, MACE), limiting the reliability of effect estimates. Third, one study which accounted for approximately 75% of all patients included did not included angiographic follow-up,[7] thus limiting the evaluation of DCB and DES on angiographic outcomes. Fourth, the clinical follow-up varied from 6 to 24 months. Ideally, outcomes such as TLR should be compared at uniform follow-up across studies (eg, at 1 year), which was not consistently possible in the current analysis. Nonetheless, these differences in follow-up duration were accounted with the IRRs, as detailed in the Methods section. However, longer follow-ups are needed to establish the safety and efficacy profile of DCB vs DES throughout time. Fifth, the definition of large vessel is inconsistent across trials, which might be a source of bias. Finally, the limited number of studies and patients, and the small event rate for some endpoints, such as all-cause mortality may reduce the power for detecting significant differences across groups.

CONCLUSIONS

This meta-analysis provides the most updated quantitative evidence on the use of DCB vs DES for the treatment of de novo large vessel CAD in both CCS and ACS. DCB-PCI is associated with similar TLR and LLL at mid-term follow-up representing an appealing treatment option for patients with large vessel CAD.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

Ethics approval was deemed unnecesary for this meta-analysis as all data were collected and synthesized from previous studies. Additionally, no informed consent was required as there were no patients involved in our work. The meta-analysis of RCT was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2009 guidelines. We confirm that sex/gender biases have been taken into consideration.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence has been used in the preparation of this article.

AUTHORS' CONTRIBUTIONS

J. Llau García, S. Huelamo Montoro and J.A. Sorolla Romero participated in literature research and study selection. J.A. Sorolla Romero, L. Novelli and J. Sanz Sánchez contributed to the conception, design, drafting and revision of the article. P. Rubio, J.L. Díez Gil, L. Martínez-Dolz, I.J. Amat Santos, B. Cortese, F. Alfonso, and H.M. Garcia-Garcia contributed to the critical revision of the intellectual content of the article.

CONFLICTS OF INTEREST

F. Alfonso is an associate editor of *REC: Interventional Cardiology;* the journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The authors declared no relevant relationships with the contents of this paper.

WHAT IS KNOWN ABOUT THE TOPIC?

- DCB are a well-established treatment for patients with small-vessel CAD.
- Available published evidence of patients with de novo large vessel CAD is scarce and shows conflicting results.

WHAT DOES THIS STUDY ADD?

- In this meta-analysis including data from 2961 patients enrolled in 7 RCT, DCB showed similar risk of clinical events at follow-up vs DES in the treatment of de novo large vessel CAD.
- The use of DCB might be considered as an alternative option to DES in patients undergoing PCI for non-complex de novo large vessel CAD.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000527.

REFERENCES

1. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J*. 2019;40:87-165.
2. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:e4-e17.
3. Kong MG, Han JK, Kang JH, et al. Clinical outcomes of long stenting in the drug-eluting stent era: patient-level pooled analysis from the GRAND-DES registry. *EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol*. 2021;16:1318-1325.
4. Kawai T, Watanabe T, Yamada T, et al. Coronary vasomotion after treatment with drug-coated balloons or drug-eluting stents: a prospective, open-label, single-centre randomised trial. *EuroIntervention*. 2022;18:e140-e148.

5. Jeger RV, Eccleshall S, Wan Ahmad WA, et al. Drug-Coated Balloons for Coronary Artery Disease: Third Report of the International DCB Consensus Group. *JACC Cardiovasc Interv*. 2020;13:1391-1402.
6. Sanz Sánchez J, Chiarito M, Cortese B, et al. Drug-Coated balloons vs drug-eluting stents for the treatment of small coronary artery disease: A meta-analysis of randomized trials. *Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv*. 2021;98:66-75.
7. Gao C, He X, Ouyang F, et al. Drug-coated balloon angioplasty with rescue stenting versus intended stenting for the treatment of patients with de novo coronary artery lesions (REC-CAGEFREE I): an open-label, randomised, non-inferiority trial. *Lancet Lond Engl*. 2024;404:1040-1050.
8. Yu X, Wang X, Ji F, et al. A Non-inferiority, Randomized Clinical Trial Comparing Paclitaxel-Coated Balloon Versus New-Generation Drug-Eluting Stents on Angiographic Outcomes for Coronary De Novo Lesions. *Cardiovasc Drugs Ther*. 2022;36:655-664.
9. Vos NS, Fagel ND, Amoroso G, et al. Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent in Acute Myocardial Infarction: The REVELATION Randomized Trial. *JACC Cardiovasc Interv*. 2019;12:1691-1699.
10. Gobbi C, Giangiacomi F, Merinopoulos I, et al. Drug coated balloon angioplasty for de novo coronary lesions in large vessels: a systematic review and meta-analysis. *Sci Rep*. 2025;15:4921.
11. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
12. Sanz-Sánchez J, Chiarito M, Gill GS, et al. Small Vessel Coronary Artery Disease: Rationale for Standardized Definition and Critical Appraisal of the Literature. *J Soc Cardiovasc Angiogr Interv*. 2022;1:100403.
13. Nishiyama N, Komatsu T, Kuroyanagi T, et al. Clinical value of drug-coated balloon angioplasty for de novo lesions in patients with coronary artery disease. *Int J Cardiol*. 2016;222:113-118.
14. Wang Z, Yin Y, Li J, et al. New Ultrasound-Controlled Paclitaxel Releasing Balloon vs. Asymmetric Drug-Eluting Stent in Primary ST-Segment Elevation Myocardial Infarction-A Prospective Randomized Trial. *Circ J Off J Jpn Circ Soc*. 2022;86:642-650.
15. Gobić D, Tomulić V, Lulić D, et al. Drug-Coated Balloon Versus Drug-Eluting Stent in Primary Percutaneous Coronary Intervention: A Feasibility Study. *Am J Med Sci*. 2017;354:553-560.
16. Hao X, Huang D, Wang Z, Zhang J, Liu H, Lu Y. Study on the safety and effectiveness of drug-coated balloons in patients with acute myocardial infarction. *J Cardiothorac Surg*. 2021;16:178.
17. Niehe SR, Vos NS, Van Der Schaaf RJ, et al. Two-Year Clinical Outcomes of the REVELATION Study: Sustained Safety and Feasibility of Paclitaxel-Coated Balloon Angioplasty Versus Drug-Eluting Stent in Acute Myocardial Infarction. *J Invasive Cardiol*. 2022;34:E39-E42.
18. Xue W, Ma J, Yu X, et al. Analysis of the incidence and influencing factors associated with binary restenosis of target lesions after drug-coated balloon angioplasty for patients with in-stent restenosis. *BMC Cardiovasc Disord*. 2022;22:493.
19. Coughlan JJ, Maeng M, Räber L, et al. Ten-year patterns of stent thrombosis after percutaneous coronary intervention with new- versus early-generation drug-eluting stents: insights from the DECADE cooperation. *Rev Esp Cardiol*. 2022;75:894-902.
20. Madhavan MV, Redfors B, Ali ZA, Prasad M, et al. Long-Term Outcomes After Revascularization for Stable Ischemic Heart Disease: An Individual Patient-Level Pooled Analysis of 19 Randomized Coronary Stent Trials. *Circ Cardiovasc Interv*. 2020;13:e008565.
21. Buchanan KD, Torguson R, Rogers T, et al. In-Stent Restenosis of Drug-Eluting Stents Compared With a Matched Group of Patients With De Novo Coronary Artery Stenosis. *Am J Cardiol*. 2018;121:1512-1518.
22. Antonio Sorolla Romero J, Calderón AT, Tschischke JPV, Luis Díez Gil J, Garcia-Garcia HM, Sánchez JS. Coronary plaque modification and impact on the microcirculation territory after drug-coated balloon angioplasty: the PLAMI study. *Rev Esp Cardiol. 2025;78:481-482*.
23. Merinopoulos I, Gunawardena T, Corballis N, et al. Assessment of Paclitaxel Drug-Coated Balloon Only Angioplasty in STEMI. *JACC Cardiovasc Interv*. 2023;16:771-779.
24. Maranhão RC, Tavares ER, Padoveze AF, Valduga CJ, Rodrigues DG, Pereira MD. Paclitaxel associated with cholesterol-rich nanoemulsions promotes atherosclerosis regression in the rabbit. *Atherosclerosis*. 2008;197:959-966.
25. Kleber FX, Schulz A, Waliszewski M, et al. Local paclitaxel induces late lumen enlargement in coronary arteries after balloon angioplasty. *Clin Res Cardiol Off J Ger Card Soc*. 2015;104:217-225.
26. Alfonso F, Rivero F. Late lumen enlargement after drug-coated balloon therapy: turning foes into friends. *EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol*. 2024;20:523-525.
27. Yamamoto T, Sawada T, Uzu K, Takaya T, Kawai H, Yasaka Y. Possible mechanism of late lumen enlargement after treatment for de novo coronary lesions with drug-coated balloon. *Int J Cardiol*. 2020;321:30-37.
28. Ninomiya K, Serruys PW, Colombo A, et al. A Prospective Randomized Trial Comparing Sirolimus-Coated Balloon With Paclitaxel-Coated Balloon in De Novo Small Vessels. *JACC Cardiovasc Interv*. 2023;16:2884-2896.
29. Ahmad WAW, Nuruddin AA, Abdul KMASK, et al. Treatment of Coronary De Novo Lesions by a Sirolimus- or Paclitaxel-Coated Balloon. *JACC Cardiovasc Interv*. 2022;15:770-779.
30. Spaulding C, Krackhardt F, Bogaerts K, et al. Comparing a strategy of sirolimus-eluting balloon treatment to drug-eluting stent implantation in de novo coronary lesions in all-comers: Design and rationale of the SELUTION DeNovo Trial. *Am Heart J*. 2023;258:77-84.
31. Greco A, Sciahbasi A, Abizaid A, et al. Sirolimus-coated balloon versus everolimus-eluting stent in de novo coronary artery disease: Rationale and design of the TRANSFORM II randomized clinical trial. *Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv*. 2022;100:544-552.

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Original article

Angiography-derived index versus fractional flow reserve for intermediate coronary lesions: a meta-analysis review

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ABSTRACT

Introduction and objectives: Assessment and treatment of intermediate coronary lesions, defined as those which represent 30%-90% of the vessel lumen, remains a clinical challenge. Physiological evaluation techniques, such as fractional flow reserve (FFR), non-adenosine-based methods, such as instantaneous wave-free ratio or resting full-cycle ratio, and angiography-derived physiological assessment techniques (ADPAT) have transformed the diagnostic landscape. This meta-analysis aimed to systematically review and compare the diagnostic performance of ADPAT and FFR evaluating intermediate coronary lesions.
Methods: We conducted a systematic review of comparative research on FFR and ADPAT from January through February 2024.
Results: A total of 27 studies were finally included in the meta-analysis for a total of 4818 patients and 5440 vessels. Overall, a strong correlation between the different ADPAT and FFR was observed (r = 0.83; 95%CI, 0.80-0.85), with a mean ADPAT value of 0.82; 95%CI, 0.81-0.83 and a mean FFR of 0.83; 95%CI, 0.82-0.85. The summary area under the curve for predicting significant FFR (≤ 0.80) was excellent at 0.947. The overall sensitivity rate was 85% (95%CI, 81-87) with a specificity rate of 93% (95%CI, 91-94). The positive predictive value was 86% (95%CI, 83-88) with a total negative predictive value of 92% (95%CI, 91-94).
Conclusions: ADPAT show good correlation and concordance with FFR for intermediate coronary lesion evaluation. However, due to unfavorable outcomes observed in the FAVOR III Europe trial[1] with quantitative flow ratio-guided revascularization, its clinical role should be reconsidered and potentially limited to scenarios where invasive assessment or adenosine use is not feasible. Further evaluation is warranted to confirm its diagnostic performance in broader clinical contexts.
Registered at PROSPERO: CRD420251042828.

Keywords: Clinical research. Fractional flow reserve. Angiographic/fluoroscopic. Meta-analysis.

Índice derivado de la angiografía frente a reserva fraccional de flujo en lesiones coronarias intermedias. Revisión de metanálisis

RESUMEN

Introducción y objetivos: La evaluación y el tratamiento de las lesiones coronarias intermedias, definidas como aquellas que comprometen entre el 30 y el 90% de la luz del vaso, continúan representando un desafío clínico. Las técnicas de evaluación fisiológica (como la reserva fraccional de flujo [RFF]), los métodos que no requieren adenosina (como el índice instantáneo libre de ondas o el índice de ciclo completo en reposo) y las técnicas de evaluación fisiológica derivadas de la angiografía (ADPAT) han transformado el panorama diagnóstico. Este metanálisis tuvo como objetivo revisar sistemáticamente y comparar el rendimiento diagnóstico de las ADPAT frente a la RFF en la evaluación de lesiones coronarias intermedias.
Métodos: Entre enero y febrero de 2024 se realizó una revisión sistemática de investigaciones comparativas entre RFF y ADPAT.
Resultados: Se incluyeron 27 estudios en el metanálisis, con un total de 4.818 pacientes y 5.440 vasos. En general, se observó una fuerte correlación entre las distintas ADPAT y la RFF (r = 0,83; IC95%, 0,80-0,85), con un valor medio de ADPAT de 0,82 (IC95%, 0,81-0,83) y un valor medio de FFR de 0,83 (IC95%, 0,82-0,85). El área bajo la curva resumen para predecir una RFF significativa (≤ 0,80) fue excelente, con un valor de 0,947. La sensibilidad global fue del 85% (IC95%, 81-87) y la especificidad fue del 93% (IC95%, 91-94). El valor predictivo positivo fue del 86% (IC95%, 83-88) y el valor predictivo negativo total fue del 92% (IC95%, 91-94).

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Conclusiones: Las ADPAT muestran una buena correlación y concordancia con la RFF en la evaluación de lesiones coronarias intermedias. Sin embargo, debido a los resultados desfavorables observados en el estudio FAVOR III Europe1 con la revascularización guiada por el índice cuantitativo de flujo, su papel clínico se debe reconsiderar y posiblemente limitar a escenarios en los que no sea factible realizar una evaluación invasiva ni utilizar adenosina. Se requiere una evaluación adicional para confirmar su rendimiento diagnóstico en contextos clínicos más amplios.
Registrado en PROSPERO: CRD420251042828.

Palabras clave: Investigación clínica. Reserva fraccional de flujo. Angiografía/fluoroscopia. Metanálisis.

Abbreviations

ADPAT: angiography-derived physiological assessment techniques. **AUC:** area under the curve. **FFR:** fractional flow reserve. **QFR:** quantitative flow ratio. **uFR:** Murray law-based quantitative flow reserve.

INTRODUCTION

Assessment and treatment of intermediate coronary lesions (those where percent diameter stenosis accounts for 30%-90% of the vessel lumen) remains a clinical challenge.[1] Over the past 10 years this field has undergone significant changes, primarily due to theoretical and technological advances in physiological evaluation techniques.[2,3]

Prior to the existence of these techniques, the assessment of intermediate lesions was based on the degree of relative narrowing of the vessel lumen vs healthy segments, being this reduction subjectively determined by the operator, without knowledge of its physiological repercussion.[2] The development of pressure guidewire methods, along with their validation and proven prognostic significance (particularly in the context of chronic coronary syndrome) from the late 1990s to the early 2000s,[4] has led to substantial progress in intermediate lesions evaluation, which has enabled a more accurate classification based on their clinical relevance.[5]

The initial method developed, and still considered the gold standard, is fractional flow reserve (FFR).[5] This technique estimates blood flow across a coronary lesion by measuring pressure differences.[6] To make this estimation between pressure and flow, maximal coronary vessel hyperemia, primarily achieved through adenosine infusion, is necessary.[6] FFR is defined as significant if flow difference across the lesion is > 20% (FFR ≤ 0.80).[6] Beyond merely identifying which lesions benefit from revascularization, FFR has shown improved survival vs revascularization based on relative narrowing assessment. Furthermore, it has allowed lesion exclusion where revascularization is deemed unnecessary, thus reducing stent implantation rates and any potential complications associated with both this procedure and antiplatelet therapy.[7]

Despite the clear benefits of using intracoronary physiology, the need for invasive pressure guidewires, IV adenosine (with its potential complications), the time required, and even the outright rejection by interventional cardiologist may have led to a lower than expected adoption.[8] These limitations triggered the appearance of non-adenosine-based methods, such as the instantaneous wave-free ratio (iFR) or resting full-cycle ratio.[9,10] These methods use a specific moment of the cardiac cycle (for example the iFR uses the diastolic wave-free period) where microvascular resistances are minimal, allowing correlation between pressures and flow without the use of adenosine.[11,12] However, despite eliminating this limitation, the use of pressure guidewires is still a barrier.[8]

Simultaneously with the development of these adenosine-free techniques, angiography-derived physiological assessment techniques (ADPAT) emerged, enabling the physiological evaluation of coronary lesions without the need for a guidewire or adenosine. These techniques, initially derived from those used in coronary lesion assessment in computational tomography,[13] are based on the computational evaluation of lesions through fluid dynamics in coronary angiography. Since then, multiple options have emerged including QFR, Murray law-based quantitative flow ratio (uFR), vessel fractional flow reserve (vFRR), fractional flow reserve derived from routine coronary angiography (FFRangio) and coronary angiography-derived fractional flow reserve (CaFFR). All of them have been validated and compared with the gold standard FFR in prospective direct comparative studies of diagnostic accuracy.[14-20]

The aim of this article was to provide a review of the different validation studies of ADPAT vs FFR and offer a meta-analysis on the accuracy of each option, both collectively and individually.

METHODS

Literature search strategy

We conducted a systematic review of comparative research on FFR and ADPAT from January through February 2024. The PubMed database was used to search for articles on concordance, agreement, and diagnostic accuracy. Multiple searches were conducted using the following algorithm: FFR/FFR permuted with each mainly commercialized tool (QFR, uFR, vFRR, FFRangio and CaFFR) while trying to avoid CT and articles developed mainly in acute coronary syndrome through the commands "NOT (CT) NOT ("acute coronary syndrome")". Date range was limited from January 2012 through December 2023. PRISMA statement guidelines were followed, and the review was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) with registration No. CRD420251042828.

Eligible criteria

A total of 4580 terms were identified through the entire search process. These terms and their combinations were carefully selected by 2 different operators to refine the search for articles comparing the main ADPAT from the main commercial vs FFR. Articles involving coronary computed tomography angiography and those where comparisons were mainly drawn within the context of acute coronary syndrome were also excluded by the operators. Based on these criteria, an initial pool of studies was established.

A total of 15 studies were subsequently excluded based on prespecified criteria, including those that specified the presence of patients

with concurrent or treated aortic stenosis, had more than 25% of patients diagnosed with atrial fibrillation, or involved angiography-derived physiological assessments for coronary lesions conducted within the first 29 days of acute myocardial infarction (either on the culprit lesion or non-culprit lesions).

In cases where the time elapsed from myocardial infarction to angiography-derived evaluation was nonspecific; articles were also excluded if more than 30% of patients had undergone coronary angiography due to acute myocardial infarction.

Furthermore, studies specifying the presence of 10% or more patients with prior surgical revascularization were excluded, as were those where the comparison between angiography-based physiological assessment methods and FFR was conducted on mammary artery grafts, radial artery grafts, or saphenous vein grafts.

After applying the selection criteria, a total of 29 articles were initially chosen for analysis. However, 2 articles (FAST [virtual FFR])[21] and Ai et al.[22] were subsequently excluded because they did not provide or calculate sensitivity and specificity data from their analyses. Consequently, the final analysis included 27 articles.

Two articles were divided and included as different items in the analysis as they showed 2 different analyzed cohorts on their studies: Smit et al.,[23] where QFR was compared with the FFR in 2 cohorts: 1 with diabetes mellitus and the other without the disease; Zuo et al.[24] divided patients in 2 cohorts based on whether the vessel was severely calcified or not. The uFR was compared with the FFR in each group. Each cohort was included in our analysis. Finally, the study by Emori et al.[25] "Diagnostic accuracy of quantitative flow ratio for assessing myocardial ischemia in prior myocardial infarction," presented 2 distinct cohorts based on the presence of prior myocardial infarction (≥ 30 days from coronary angiography). Although one cohort depicted an acute coronary syndrome scenario, it fulfilled our inclusion criteria, leading to the inclusion of both cohorts in the final analysis.

Statistical and methodologic analysis

The homogeneity across studies was contrasted using the QH statistic. Regarding the low sensitivity of this test, $P < .10$ values were considered significant. To overcome this limitation, the I2 statistic was estimated as well, which measures the proportion of the total variation of the studies, explained by the heterogeneity and its 95% confidence interval (95%CI). A random effects model was used for all cases using the pooled method of DerSimonian Laird. If heterogeneity was present, meta-regression analyses were conducted to explore the sources of heterogeneity (figure 1 of the supplementary data). The presence of publication bias was tested using the Deek funnelplot (figure 2 of the supplementary data).

From the reported values of sensitivity, specificity, negative predictive value, positive predictive value, accuracy, and the number of vessels assessed, all 2 × 2 tables for the 0.8 cutoff point of the tests were constructed. Subsequently, pooled estimates for sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were derived from these data.[26]

The confidence intervals of sensitivity and specificity were calculated using the F distribution method to compute the exact confidence limits for the binomial proportion (x/n). The summary receive operator curve (SROC) was also calculated from which we drew all the points of sensitivity and 1-specificity and adjusted the weighted regression curve using Moses' Model. Spearman correlation coefficient between sensitivity and specificity was used to assessed constant diagnostic odds ratio (positive likelihood ratio and negative likelihood ratio) employing a symmetric SROC.[27] The area under curve (AUC) was computed by numeric integration of the curve equation using the trapezoidal method. Additionally, we applied the bootstrap methods for estimated AUC of multiple SROC. We provided the resultant bootstrap *P* values and 95%CI of the AUC for pairwise comparisons of the different methods (table 1 of the supplementary data). Furthermore, we provided an influence diagnostic method based on the AUC by performing leave-one-study-out analyses (table 2 of the supplementary data). Pearson correlation coefficients were transformed into Fisher's z-values to calculate variance and we performed a meta-analysis and calculated the 95%CI (figure 3 of the supplementary data). Fagan's Nomogram (figure 4 of the supplementary data) was used to graphically estimate how the result from a diagnostic test altered the probability of a patient having a disease. We assessed applicability and risk of bias based on the modified version of the QUADAS-2 tool[28] (figure 5A,B of the supplementary data). All analyses were conducted using R Statistical Software (v4.2.0; R Core Team 2022) and performed using dmetatools R package (1.1.1; Noma H 2023), mada R package (0.5.11; Sousa-Pinto 2022) and TeachingDemos R package (2.13; Greg Snow 2024).

RESULTS

Finally, a total of 27 articles were suitable for inclusion, as illustrated in figure 1. From these articles, a total of 4818 patients and 5440 vessels were added to the analysis. The population characteristics and mean cardiovascular risk factors are detailed in table 1 highlighting the existence of 3189 (66.18%) patients with hypertension, 2438 (50.6%) with dyslipidemia, and 1263 (26.2%) with diabetes. Notably, most patients included in the study were men (68.86% of the sample).

Thirteen of the selected articles were prospective in design. The most extensively studied vessel was the left anterior descending coronary artery (2921; 53.69%), followed by the right coronary artery (1075; 19.61%) and the left circumflex artery (772; 14.2%). Additionally, 89 left main coronary arteries were analyzed, accounting for 1.6% of all vessels. Angiography was primarily performed for stable angina (2483; 51.53%). Of note, while 1475 (30.61%) angiographies were prompted by acute coronary syndrome, only 333 (6.9% of the total) were performed in the context of acute myocardial infarction with or without ST-segment elevation, and the remaining 1142 in the context of unstable angina. Indications for cardiac catheterization are shown in table 2. The left anterior descending coronary artery was the most frequently studied vessel, accounting for 2921 patients (53.7% of the total studies). Proportions for other vessels are available in table 3.

The QFR[15-17,23,25,29-34] (QAngio XA 3D QFR, Medis Medical Imaging System; The Netherlands) was the most widely used software with a total of 13 patient cohorts from 11 articles, comprising 1987 patients and 2315 vessels, which accounts for 41.2% and 42.6% of the total, respectively. The correlation between QFR and FFR was excellent, showing an r = 0.82 (95%CI, 0.77-0.877). The overall sensitivity rate of QFR was 84% (95%CI, 80-88) with a specificity rate of 90% (95%CI, 87-93). The positive predictive value was 81% (95%CI, 77-84) with a total negative predictive value of 92% (95%CI, 90-94). The AUC for this technique was 0.937.

The second most analyzed technique, with a total of 5 articles, was FFRangio[14,35-38] (Cathworks FFRangio, Israel), where this technology was employed in 696 patients and 841 vessels (14.4% and

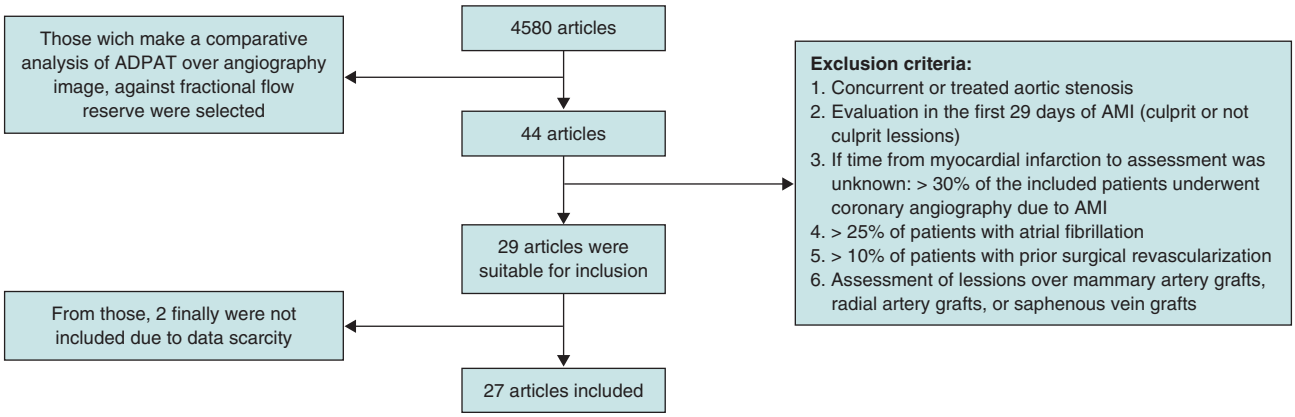

Figure 1. Selected articles flowchart and exclusion criteria. ADPAT, angiography-derived physiological assessment techniques; AMI, acute myocardial infarction.

Table 1. Patients' baseline characteristics

Patients' baseline characteristics (n = 4818)	
Characteristics (cohorts where this data is available)	**(± 95%CI) or %**
Mean age (26)	66.4 ± 1.3
Male (26)	3318 (68.9%)
Mean BMI (kg/m^2) (17)	26 ± 0.8
Hypertension (25)	3189 (66.2%)
Diabetes (25)	1263 (26.2%)
Dyslipidemia (21)	2438 (50.6%)
Mean LVEF (%) (10)	59.6 ± 3.3
Prior or current smoker (23)	1406 (29.2%)
Prior MI (20)	566 (11.7%)
Prior PCI (20)	1314 (27.3%)
Prior CABG (13)	47 (1%)

BMI, body mass index; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention. Data are expressed as mean value and standard deviation across the studies.

Table 2. Indications for cardiac catheterization

Indication for cardiac catheterization	(%)
Silent isquemia	323 (6.8)
Stable angina	2483 (51.5)
Acute coronary syndrome	1475 (30.6)
Unstable angina	1142 (23.7)
AMI	333 (6.9)
NSTEMI	204 (4.2)
STEMI	13 (0.3)
MI subtype not specified	116 (2.4)
Others	127 (2.6)

AMI, acute myocardial infarction; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

Table 3. Number of studies per vessel performed across the different studies

Vessel characteristics (n = 5440)	(%)
Left main coronary artery	89 (1.7)
Left anterior descending coronary artery	2921 (53.7)
Diagonal branch	52 (1)
Ramus intermedius	54 (1)
Left circumflex artery	772 (14.2)
Obtuse marginal branch	108 (2)
Right coronary artery	1075 (19.8)
Posterolateral branch	7 (0.1)
Interventricular branch	8 (0.15)

15.45% of the total, respectively). The overall sensitivity rate of FFRangio was 90% (95%CI, 83-94) with a specificity rate of 95% (95%CI, 91-97). The positive predictive value was 90% (95%CI, 85-93) with a total negative predictive value of 94% (95%CI, 91-96).

vFFR (Pie Medical Imaging, The Netherlands) on the other hand, had an excellent correlation with FFR across the 3 included studies,[20,39,40] contributing 647 patients and 663 vessels to the analysis (representing 13.42% of patients and 11.96% of vessels). The mean sensitivity and specificity rates were 82% (95%CI, 72-89) and 0.94% (95%CI, 89-97), respectively. The summary positive predictive value was 89% (95%CI, 82-93), and the summary negative predictive value, 91% (95%CI, 86-94).

Following its recent validation in 2022, the uFR (AngioPlus, Pulse Medical Imaging Technology, China) is supported by only 2 articles,[19,24] one of which includes 2 cohorts based on vessel calcification. The uFR had a sensitivity rate of 80% (95%CI, 69-87) and a specificity rate of 0.94 (95%CI, 89-97). The summary positive predictive value was 85% (95%CI, 79-90), and the summary negative predictive value, 91% (95%CI, 87-94).

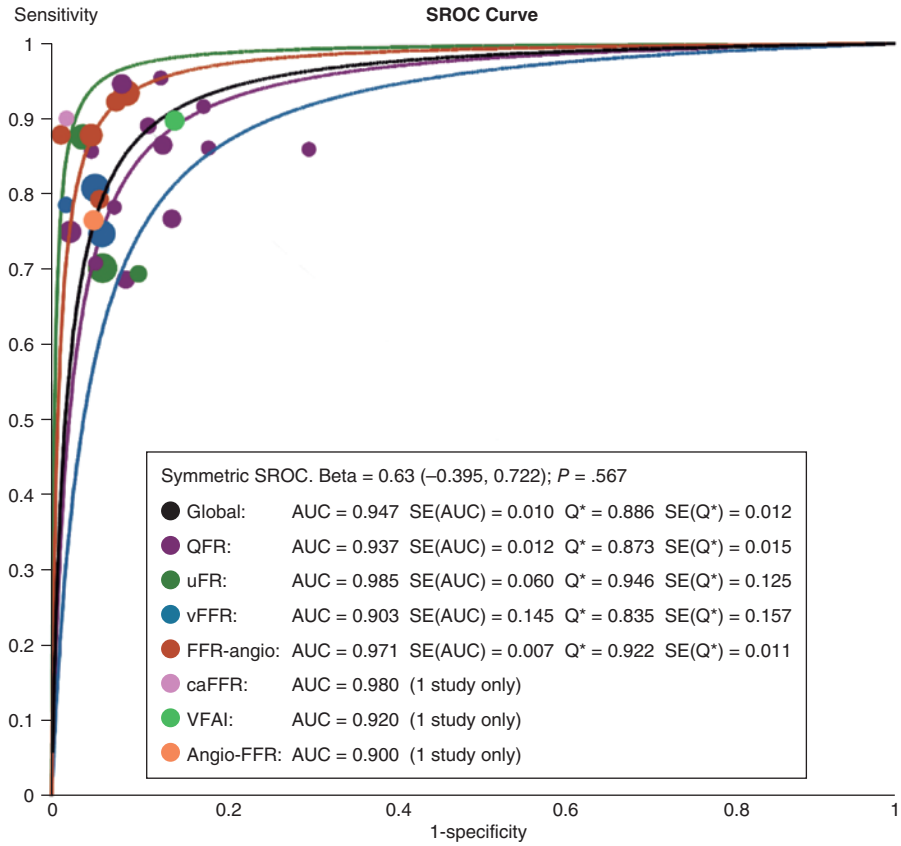

Figure 2. Summary receiver operating characteristic (SROC) curves and Q* index for subgroup analyses of software-derived coronary angiography-derived fractional flow reserve (caFFR); FFR, fractional flow reserve; QFR, quantitative flow ratio; uFR, Murray law-based quantitative flow reserve; VFAI, vessel fractional anatomy index; vFFR, vessel fractional flow reserve.

Only 1 article of CaFFR (Flashangio, Rainmed Ltd., China) was included.[18]

The analysis included 2 non-commercialized tools, VFAI[41] and AngioFFR,[42] which were not individually evaluated. Both were compared to FFR only once.

Overall, a strong correlation between the different ADPAT and FFR was observed (r = 0.83, 95%CI, 0.80-0.85), with a mean ADPAT value of 0.82 (95%CI, 0.81-0.83) (all the ADPAT set a value ≤ 0.80 for lesion significance) and a mean FFR of 0.83 (95%CI, 0.82-0.85).

The summary AUC for predicting significant FFR (≤ 0.80) was excellent at 0.947. The SROC for the different ADPAT is shown in figure 2.

The overall sensitivity rate was 85% (95%CI, 81-87) with a specificity rate of 93% (95%CI, 91-94). The positive predictive value was 86% (95%CI, 83-88) with a total negative predictive value of 92% (95%CI, 91-94). The main commercially available ADPAT values of sensibility, specificity, positive predictive value and negative predictive value are shown in figure 3 and figure 4.

DISCUSSION

Key findings

Our key findings were: *a)* ADPAT emerge as a reliable and practical method for assessing the physiological significance of intermediate coronary lesions, which is consistent with previous literature.[44-46] ADPAT consistently demonstrates agreement with the current gold standard (FFR) regarding mean values and lesion classification, without vasodilator medication or pressure guidance; *b)* By summarizing the diagnostic capabilities of each ADPAT from the included studies, we were able to perform the first direct comparison of various angiography-based methods for evaluating coronary lesions. We presented the main commercially available options and their respective diagnostic accuracies relative to FFR. Additionally, an overview of these techniques was provided; *c)* We also included innovative methods, such as uFR, based on Murray's Law, while offering a unique approach by using a single projection to estimate lesion significance, potentially overcoming a significant limitation of current techniques, which often require specific projections and a certain quality image.

The overall results confirmed that different ADPAT serve as an appropriate method for evaluating intermediate coronary lesions, as they demonstrated a strong correlation with FFR. This correlation extended to sensitivity, specificity, and predictive values as illustrated in figure 4. Notably, the studies exhibited homogeneity without significant discrepancies in their weighting within the analysis, as observed through the resampling techniques employed.

In comparative analysis, while ADPAT exhibit adequate sensitivity and positive predictive values regarding lesion significance, their specificity and negative predictive value exceed 90%. This high specificity allows ADPAT to more accurately identify physiologically non-significant lesions, thereby avoiding unnecessary revascularization.

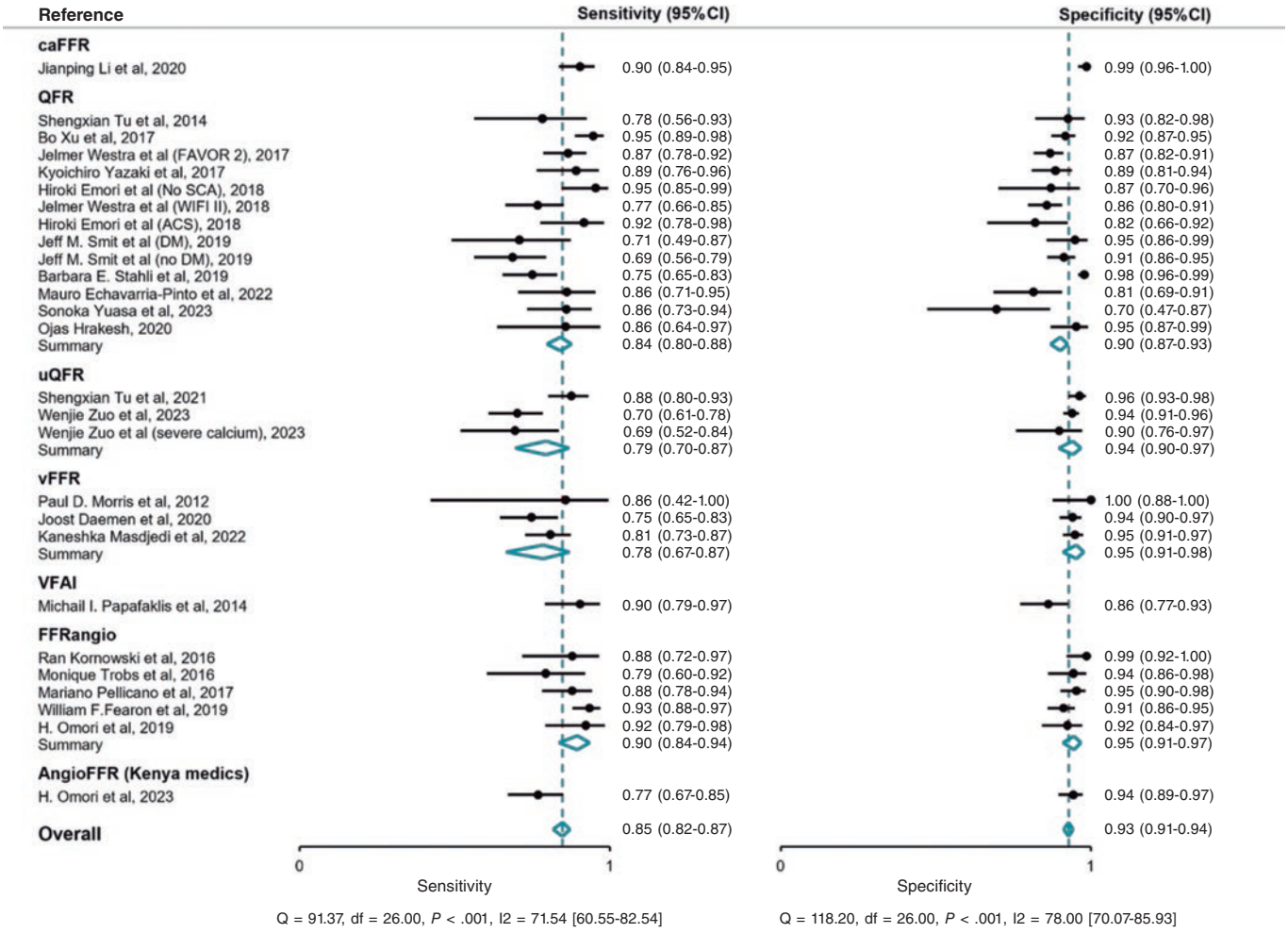

Figure 3. Forest plots and summary statistics for sensitivity and specificity estimates from a meta-analysis of FFR across different indices, using a random-effects model. 95%CI, 95% confidence interval; caFFR, coronary angiography–derived fractional flow reserve; FFR, fractional flow reserve; QFR, quantitative flow ratio; uFR, Murray law-based quantitative flow reserve; VFAI, vessel fractional anatomy index; vFFR, vessel fractional flow reserve. Xu et al.,[16] 2017; Fearon et al.,[36] 2019; Yuasa et al.,[33] 2023; Morris et al.,[39] 2013; Westra et al.,[29] 2018; Echavarría-Pinto et al.,[31] 2022; Stähli et al.,[34] 2019; Omori et al.,[35] 2019; Westra et al.,[17] 2018; Li et al.,[18] 2020; Pellicano et al.,[14] 2017; Emori et al.,[25] 2018; Tu et al.,[15] 2014; Zuo et al.,[24] 2024; Tu et al.,[19] 2021; Omori et al.,[42] 2023; Hrakesh et al.,[32] 2020; Kornowski et al.,[37] 2016; Masdjedi et al.,[20] 2022; Tröbs et al.,[38] 2016; Yazaki et al.,[30] 2017; Smit et al.[23] 2019; Daemen et al.,[43] 2022; and Papafaklis et al.,[41] 2014.

From a technical standpoint, it was notable that these results were primarily obtained from assessments of the left anterior descending coronary artery (53.6%), with only 1 dedicated study on the left main coronary artery. Despite this, left main coronary arteries contributed a significant proportion (1.66%) to the overall analysis, showcasing proficient classification of significant lesions (AUC = 0.82) and indicating the feasibility of applying tools in this context.

QFR was the most frequently included tool in the analysis, representing 13 out of 27 cohorts. Despite multiple validations vs the FFR in diverse contexts, most studies align closely, demonstrating a correlation between QFR and FFR.

Comparing results across different tools, minimal differences were observed, with FFRangio and CaFFR showing slightly superior overall results vs other methods. However, it's important to note that the results of the CaFFR are based solely on validation articles, and when considering only validation studies, results among tools are very similar.

Although QFR is frequently studied, its results might require more robust validation because there are limited articles on FFRangio, especially on chronic coronary syndrome in patient groups like those with left main disease or diabetes.

While ADPAT have been validated vs the FFR in various clinical scenarios, such as severe aortic stenosis, atrial fibrillation, or non-culprit coronary lesions in acute coronary syndrome, the inclusion of these scenarios in our analysis could potentially bias the results due to variations in study characteristics and the unique features of each disease affecting lesion assessment.

The limitation of this study stems from including a large proportion of pivotal studies for each analyzed tool, which were not performed under real-world clinical conditions. Consequently, the applicability of their results may be restricted, as demonstrated by a recent study from independent laboratories comparing the 5 main non-hyperemic indices with FFR under real-life conditions.[47]

Although the study demonstrated a good correlation between the indices and FFR, the levels of diagnostic accuracy reported in the pivotal studies were not achieved.

In this regard, QFR has been recently evaluated vs the FFR in the FAVOR III Europe trial,[1] which included 2000 patients who were

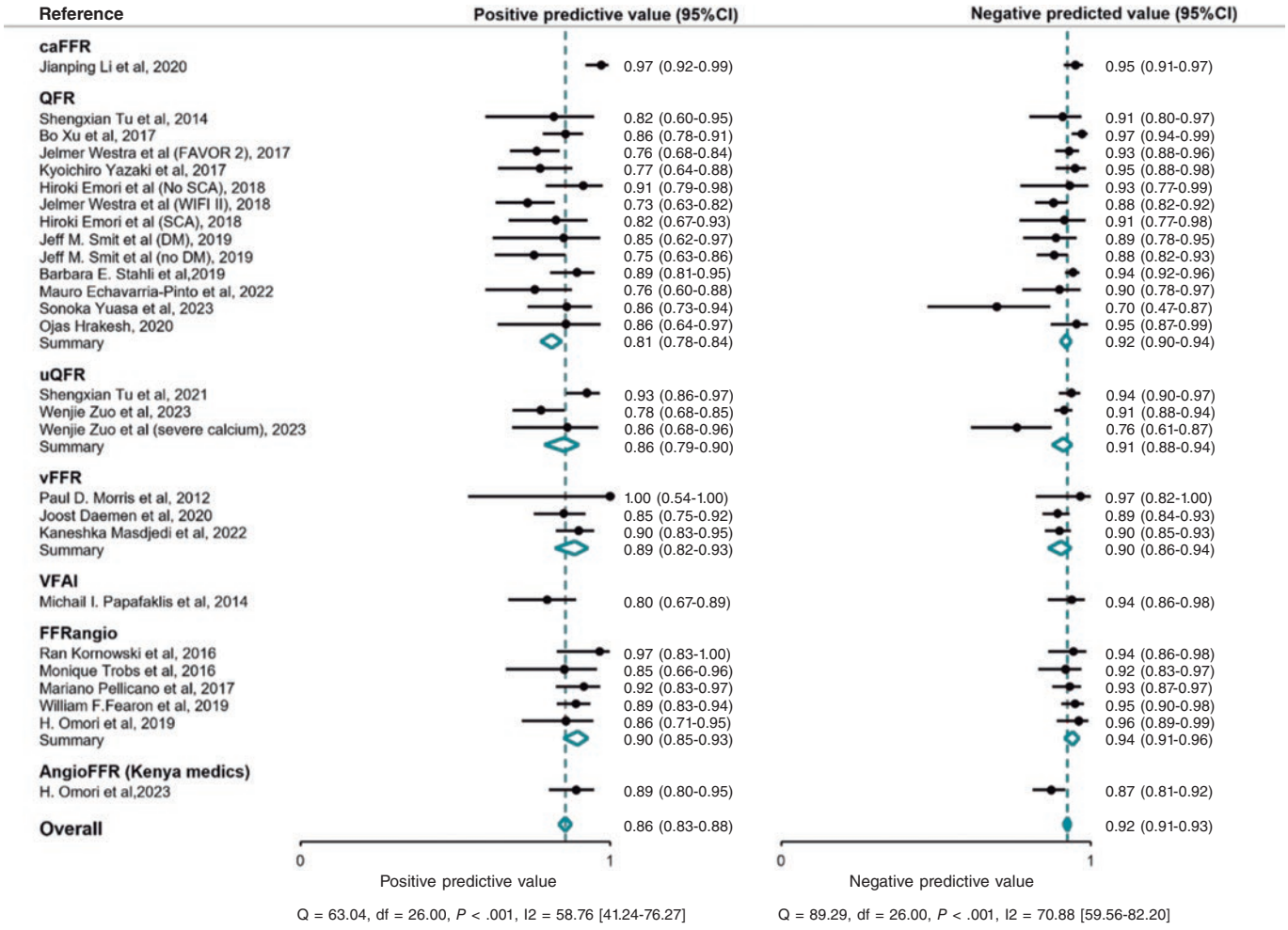

Figure 4. Forest plots and summary statistics for positive predictive value (PPV) and negative predictive value (NPV) estimates from a meta-analysis of FFR across different indices, using a random-effects model. 95%CI, 95% confidence interval; caFFR, coronary angiography–derived fractional flow reserve; FFR, fractional flow reserve; QFR, quantitative flow ratio; uFR, Murray law-based quantitative flow reserve; VFAI, vessel fractional anatomy index; vFFR, vessel fractional flow reserve. Xu et al.,[16] 2017; Fearon et al.,[36] 2019; Yuasa et al.,[33] 2023; Morris et al.,[39] 2013; Westra et al.,[29] 2018; Echavarría-Pinto et al.,[31] 2022; Stähli et al.,[34] 2019; Omori et al.,[35] 2019; Westra et al.,[17] 2018; Li et al.,[18] 2020; Pellicano et al.,[14] 2017; Emori et al.,[25] 2018; Tu et al.,[15] 2014; Zuo et al.,[24] 2024; Tu et al.,[19] 2021; Omori et al.,[42] 2023; Hrakesh et al.,[32] 2020; Kornowski et al.,[37] 2016; Masdjedi et al.,[20] 2022; Tröbs et al.,[38] 2016; Yazaki et al.,[30] 2017; Smit et al.,[23] 2019; Daemen et al.,[43] 2022; and Papafaklis et al.,[41] 2014.

randomized (1:1) to QFR-guided or FFR-guided treatment of intermediate lesions. The results showed that the QFR-guided group had higher rates of mortality, myocardial infarction, and unplanned revascularization at 12 months.

Although these findings may initially seem discouraging, they do not contradict the results of our study, in which non-hyperemic indices demonstrated superior performance over conventional angiography in the functional classification of lesions. Therefore, their use remains valuable in clinical scenarios where invasive assessment with a pressure guidewire or the use of adenosine is not feasible or contraindicated.

Of note, while QFR is currently the most widely used non-hyperemic index, it is the only one that has been evaluated in clinical trials with hard clinical endpoints vs FFR. Other tools with promising results are still to be investigated in this context.

CONCLUSIONS

Substantial correlations and concordances have been demonstrated between ADPAT and FFR. These techniques have also shown accurate categorization of lesions deemed significant by the current gold standard (FFR). However, the results of the FAVOR III Europe study[1] indicate that QFR–guided revascularization, compared with FFR-guided revascularization, is associated with higher rates of mortality, myocardial infarction, and unplanned revascularization. Therefore, the current role of ADPAT requires re-evaluation.

In this context, the use of QFR may be most appropriate when invasive assessment using a pressure guidewire is not feasible or when adenosine is contraindicated. Additionally, due to the unique characteristics of other clinical scenarios, further reviews are warranted to evaluate the diagnostic accuracy of this index.

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ETHICAL CONSIDERATIONS

The present study was conducted in full compliance with the clinical practice guidelines set forth in the Declaration of Helsinki for clinical research and was approved by the ethics committees of the reference hospital (*Hospital Clínico Universitario de Valladolid*) and other participant centers. Possible sex- and gender-related biases were also taken into consideration according to the SAGER recommendations.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the writing of this text.

AUTHORS' CONTRIBUTIONS

J. Ruiz-Ruiz and C. Cortés-Villar participated in the study design, data analysis, manuscript drafting, and critical revision. C. Fernández-Cordón and M. García-Gómez contributed to data collection and results analysis. A. Lozano-Ibáñez and D. Carnicero-Martínez contributed to data gathering. S. Blasco-Turrión and M. Carrasco-Moraleja contributed to the statistical analysis. J.A. San Román-Calvar and I.J. Amat-Santos performed the final review and approved the version for publication.

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.M25000523.

REFERENCES

1. Andersen BK, Sejr-Hansen M, Maillard L, et al. Quantitative flow ratio versus fractional flow reserve for coronary revascularisation guidance (FAVOR III Europe): a multicentre, randomised, non-inferiority trial. *Lancet*. 2024;404:1835-1846.
2. Patil CV, Beyar R. Intermediate coronary artery stenosis: Evidence-based decisions in interventions to avoid the oculostenotic reflex. *Int J Cardiovasc Intervent*. 2000;3:195-206.
3. 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.
4. De Bruyne B, Paulus WJ, Vantrimpont PJ, Sys SU, Heyndrickx GR, Pijls NHJ. Transstenotic coronary pressure gradient measurement in humans: In vitro and in vivo evaluation of a new pressure monitoring angioplasty guide wire. *J Am Coll Cardiol*. 1993;22:119-126.
5. Sousa-Uva M, Neumann FJ, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur J Cardio-thoracic Surg*. 2019;55:4-90.
6. Tonino PAL, De Bruyne B, Pijls NHJ, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2011;365:213-224.
7. De Bruyne B, Pijls NHJ, Kalesan B, et al. Fractional Flow Reserve–Guided PCI versus Medical Therapy in Stable Coronary Disease. *N Engl J Med*. 2012;367:991-1001.
8. Johnson NP, Koo BK. Coronary Psychology: Do You Believe? *JACC Cardiovasc Interv*. 2018;11:1492-1494.
9. De Waard GA, Di Mario C, Lerman A, Serruys PW, Van Royen N. Instantaneous wave-free ratio to guide coronary revascularisation: Physiological framework, validation and differences from fractional flow reserve. *EuroIntervention*. 2017;13:450-458.
10. Svanerud J, Ahn JM, Jeremias A, et al. Validation of a novel non-hyperaemic index of coronary artery stenosis severity: The Resting Full-cycle Ratio (VALIDATE RFR) study. *EuroIntervention*. 2018;14:806-814.
11. Davies JE, Sen S, Dehbi H-M, et al. Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI. *N Engl J Med*. 2017;376:1824-1834.
12. Götberg M, Christiansen EH, Gudmundsdottir IJ, et al. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. *N Engl J Med*. 2017;376:1813-1823.
13. Min JK, Leipsic J, Pencina MJ, et al. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. *Jama*. 2012;308:1237-1245.
14. Pellicano M, Lavi I, De Bruyne B, et al. Validation study of image-based fractional flow reserve during coronary angiography. *Circ Cardiovasc Interv*. 2017;10:E005259.
15. Tu S, Barbato E, Köszegi Z, et al. Fractional flow reserve calculation from 3-dimensional quantitative coronary angiography and TIMI frame count: A fast computer model to quantify the functional significance of moderately obstructed coronary arteries. *JACC Cardiovasc Interv*. 2014;7:768-777.
16. Xu B, Tu S, Qiao S, et al. Diagnostic Accuracy of Angiography-Based Quantitative Flow Ratio Measurements for Online Assessment of Coronary Stenosis. *J Am Coll Cardiol*. 2017;70:3077-3087.
17. Westra J, Andersen BK, Campo G, et al. Diagnostic performance of in-procedure angiography-derived quantitative flow reserve compared to pressure-derived fractional flow reserve: The FAVOR II Europe-Japan study. *J Am Heart Assoc*. 2018;7:e009603.
18. Li J, Gong Y, Wang W, et al. Accuracy of Computational Pressure-Fluid Dynamics applied to Coronary Angiography to Derive Fractional Flow Reserve – FLASH FFR. *Cardiovasc Res*. 2020;116:1349-1356.
19. Tu S, Ding D, Chang Y, Li C, Wijns W, Xu B. Diagnostic accuracy of quantitative flow ratio for assessment of coronary stenosis significance from a single angiographic view: A novel method based on bifurcation fractal law. *Catheter Cardiovasc Interv*. 2021;97(S2):1040-1047.
20. Masdjedi K, Tanaka N, Van Belle E, et al. Vessel fractional flow reserve (vFFR) for the assessment of stenosis severity: the FAST II study. *EuroIntervention*. 2022;17:1498-1505.
21. Masdjedi K, van Zandvoort LJC, Balbi MM, et al. Validation of a three-dimensional quantitative coronary angiography-based software to calculate fractional flow reserve: The FAST study. *EuroIntervention*. 2021;16:591-599.
22. Ai H, Zheng N, Li L, et al. Agreement of Angiography-Derived and Wire-Based Fractional Flow Reserves in Percutaneous Coronary Intervention. *Front Cardiovasc Med*. 2021;8:654392.
23. Smit JM, El Mahdiui M, van Rosendael AR, et al. Comparison of Diagnostic Performance of Quantitative Flow Ratio in Patients With Versus Without Diabetes Mellitus. *Am J Cardiol*. 2019;123:1722-1728.
24. Zuo W, Sun R, Xu Y, et al. Impact of calcification on Murray law-based quantitative flow ratio for physiological assessment of intermediate coronary stenoses. *Cardiol J*. 2024;31:205-214.
25. Emori H, Kubo T, Kameyama T, et al. Diagnostic accuracy of quantitative flow ratio for assessing myocardial ischemia in prior myocardial infarction. *Circ J*. 2018;82:807-814.
26. Deeks JJ. Systematic reviews of evaluations of diagnostic and screening tests. *Bmj*. 2001;323:157.
27. Walter SD. Properties of the summary receiver operating characteristic (SROC) curve for diagnostic test data. *Stat Med*. 2002;21:1237-1256.
28. Whiting PF, Reitsma JB, Leeflang MMG, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;155:529-536.
29. Westra J, Tu S, Winther S, et al. Evaluation of Coronary Artery Stenosis by Quantitative Flow Ratio during Invasive Coronary Angiography: The WIFI II Study (Wire-Free Functional Imaging II). *Circ Cardiovasc Imaging*. 2018;11:1-8.
30. Yazaki K, Otsuka M, Kataoka S, et al. Applicability of 3-dimensional quantitative coronary angiography-derived computed fractional flow reserve for intermediate coronary stenosis. *Circ J*. 2017;81:988-992.
31. Echavarría-Pinto M, Van de Hoef TP, Pacheco-Beltran N, et al. Diagnostic agreement of quantitative flow ratio with fractional flow reserve in a Latin-American population. *Int J Cardiovasc Imaging*. 2022;38:1423-1430.
32. Hrakesh O, Hay M, Lim RY, et al. Comparison of diagnostic performance between quantitative flow ratio, non-hyperemic pressure indices and fractional flow reserve. *Cardiovasc Diagn Ther*. 2020;10:442-452.
33. Yuasa S, Lauri FM, Mejia-Renteria H, et al. Angiography-derived functional assessment of left main coronary stenoses. *Catheter Cardiovasc Interv*. 2023;101:1045-1052.
34. Stähli BE, Erbay A, Steiner J, et al. Comparison of resting distal to aortic coronary pressure with angiography-based quantitative flow ratio. *Int J Cardiol*. 2019;279:12-17.
35. Omori H, Witberg G, Kawase Y, et al. Angiogram based fractional flow reserve in patients with dual/triple vessel coronary artery disease. *Int J Cardiol*. 2019;283:17-22.

36. Fearon WF, Achenbach S, Engstrom T, et al. Accuracy of Fractional Flow Reserve Derived from Coronary Angiography. *Circulation*. 2019;139:477-484.
37. Kornowski R, Lavi I, Pellicano M, et al. Fractional Flow Reserve Derived From Routine Coronary Angiograms. *J Am Coll Cardiol*. 2016;68:2235-2237.
38. Tröbs M, Achenbach S, Röther J, et al. Comparison of Fractional Flow Reserve Based on Computational Fluid Dynamics Modeling Using Coronary Angiographic Vessel Morphology Versus Invasively Measured Fractional Flow Reserve. *Am J Cardiol*. 2016;117:29-35.
39. Morris PD, Ryan D, Morton AC, et al. Virtual fractional flow reserve from coronary angiography: Modeling the significance of coronary lesions. Results from the VIRTU-1 (VIRTUal fractional flow reserve from coronary angiography) study. *JACC Cardiovasc Interv*. 2013;6:149-157.
40. Neleman T, Masdjedi K, Van Zandvoort LJC, et al. Extended Validation of Novel 3D Quantitative Coronary Angiography-Based Software to Calculate vFFR: The FAST EXTEND Study. *JACC Cardiovasc Imaging*. 2021;14:504-506.
41. Papafaklis MI, Muramatsu T, Ishibashi Y, et al. Fast virtual functional assessment of intermediate coronary lesions using routine angiographic data and blood flow simulation in humans: Comparison with pressure wire - fractional flow reserve. *EuroIntervention*. 2014;10:574-583.
42. Omori H, Kawase Y, Mizukami T, et al. Diagnostic Accuracy of Artificial Intelligence-Based Angiography-Derived Fractional Flow Reserve Using Pressure Wire-Based Fractional Flow Reserve as a Reference. *Circ J*. 2023;87:783-790.
43. Scoccia A, Tomaniak M, Neleman T, Groenland FTW, Plantes ACZ des, Daemen J. Angiography-Based Fractional Flow Reserve: State of the Art. *Curr Cardiol Rep*. 2022;24:667-678.
44. Cortés C, Carrasco-Moraleja M, Aparisi A, et al. Quantitative flow ratio—Meta-analysis and systematic review. *Catheter Cardiovasc Interv*. 2021;97:807-814.
45. Faria D, Hennessey B, Shabbir A, et al. Functional coronary angiography for the assessment of the epicardial vessels and the microcirculation. *EuroIntervention*. 2023;19:203-221.
46. Leone AM, Campo G, Gallo F, et al. Adenosine-Free Indexes vs. Fractional Flow Reserve for Functional Assessment of Coronary Stenoses: Systematic Review and Meta-Analysis. *Int J Cardiol*. 2020;299:93-99.
47. Ninomiya K, Serruys PW, Kotoku N, et al. Anonymous Comparison of Various Angiography-Derived Fractional Flow Reserve Software With Pressure-Derived Physiological Assessment. *JACC Cardiovasc Interv*. 2023;16:1778-1790.

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Original article

Safety and efficacy profile of excimer laser coronary angioplasty for thrombus removal in STEMI

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ABSTRACT

Introduction and objectives: Thrombus removal in patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI) can be challenging in the presence of a large thrombus burden. Excimer laser coronary angioplasty (ELCA) is an adjuvant device capable of vaporizing thrombus. This study aimed to evaluate the safety and efficacy profile of ELCA in PCI.
Methods: Patients with STEMI undergoing PCI with concomitant use of ELCA for thrombus removal were retrospectively identified at our center. Data were collected on the device efficacy and its contribution to overall procedural success. Additionally, ELCA-related complications and major adverse cardiovascular events were recorded at a 2-year follow-up.
Results: ELCA was used in 130 STEMI patients, 124 (95.4%) of whom had a large thrombus burden. TIMI grade flow improved significantly after ELCA: before laser application, TIMI grade-0 flow was reported in 79 (60.8%) cases and TIMI grade-1 flow in 32 (24.6%) cases. After ELCA, TIMI grade-2 and 3 flows were achieved in 45 (34.6%) and 66 (50.8%) cases, respectively ($P < .001$). Technical and procedural success were achieved in 128 (98.5%) and 124 (95.4%) cases, respectively. The complications included 1 death at the cath lab (0.8%), 1 coronary perforation (0.8%), and 3 distal embolizations (2.3%). At the 2-years follow-up, major adverse cardiovascular events occurred in 18.3% of the population.
Conclusions: In the context of STEMI, ELCA seems to be an effective device for thrombus dissolution, with adequate technical and procedural success rates. In the present cohort, ELCA use was associated with a low complication rate and favorable long-term outcomes.

Keywords: Acute coronary syndrome. Thrombectomy. Excimer laser coronary angioplasty.

Perfil de eficacia y seguridad de la angioplastia con láser excímer para la eliminación de trombos en el IAMCEST

RESUMEN

Introducción y objetivos: La eliminación de trombos durante la intervención coronaria percutánea primaria (ICPp) en el infarto agudo de miocardio con elevación del segmento ST (IAMCEST) es un desafío en presencia de una carga trombótica elevada. La angioplastia coronaria con láser de excímeros (ELCA) es una técnica complementaria que permite vaporizar el trombo. Este estudio evaluó la eficacia y la seguridad de la ELCA en el contexto de la ICPp.
Métodos: Análisis retrospectivo unicéntrico de pacientes con IAMCEST sometidos a ICPp con ELCA. Se evaluaron la eficacia en la disolución del trombo, la mejoría del flujo, el éxito del procedimiento, las complicaciones asociadas y los eventos cardiovasculares adversos mayores durante un seguimiento de 2 años.
Resultados: Se realizó ELCA en 130 pacientes con IAMCEST, de los cuales 124 (95,4%) tenían carga trombótica elevada. El flujo TIMI mejoró significativamente tras la ELCA: previamente era 0 en 79 casos (60,8%) y 1 en 32 casos (24,6%), y se lograron flujos TIMI 2 y 3 en 45 casos (34,6%) y 66 casos (50,8%), respectivamente ($p < 0,001$). Las tasas de éxito técnico y del procedimiento fueron del 98,5% y el 95,4%, respectivamente. Las complicaciones incluyeron 1 muerte durante el (0,8%), 1 perforación coronaria (0,8%) y 3 embolizaciones distales (2,3%). A los 2 años, la tasa de eventos cardiovasculares adversos mayores fue del 18,3%.

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Conclusiones: La ELCA parece ser una técnica eficaz y segura en el IAMCEST para la disolución del trombo, con altas tasas de éxito técnico y procedimental, baja incidencia de complicaciones y resultados favorables a largo plazo.

Palabras clave: Síndrome coronario agudo. Trombectomía. Angioplastia coronaria con láser de excímeros.

Abbreviations

ELCA: excimer laser coronary angioplasty. **LTB:** large thrombus burden. **MACE:** major adverse cardiovascular events. **PCI:** percutaneous coronary intervention. **STEMI:** ST-segment elevation myocardial infarction. **TIMI:** Thrombolysis in Myocardial Infarction.

INTRODUCTION

In patients with ST-segment elevation myocardial infarction (STEMI), percutaneous coronary intervention (PCI) is the preferred reperfusion strategy, as long as it can be performed within 120 minutes of the electrocardiogram-based diagnosis.[1] Many patients with STEMI present with thrombotic occlusion of the infarct-related artery. Therefore, the use of devices aimed at reducing thrombus burden is a reasonable consideration to minimize distal embolization and no-reflow. Persistent no-reflow in patients with STEMI undergoing PCI is associated with the worst in-hospital outcomes and increased long-term mortality.[2]

While early studies on manual thrombus aspiration suggested benefits in terms of improved myocardial blush grades and ST-segment elevation resolution,[3] larger trials comparing manual thrombus aspiration with PCI alone showed no significant reduction in cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or a New York Heart Association FC IV heart failure within 180 days.[4] Consequently, routine aspiration thrombectomy is no longer recommended in patients with STEMI.[5]

Thrombus removal, particularly when dealing with a large thrombus burden (LTB) in the context of STEMI, remains a critical and sometimes challenging aspect of PCI. Excimer laser coronary angioplasty (ELCA Coronary Laser Atherectomy Catheter, Koninklijke Philips N.V., The Netherlands) is a well-established adjuvant therapy for coronary interventions. ELCA uses xenon-chloride gas as the lasing medium to produce UV light energy, which is delivered to the target site through an optical fiber. This energy has the ability to ablate inorganic material through photochemical, photothermal, and photomechanical mechanisms.[6,7] The microparticles released during laser ablation measure < 10 µm and are absorbed by the reticuloendothelial system, theoretically reducing the risk of microvasculature obstruction.[8] These unique characteristics of ELCA have facilitated its use as an adjuvant therapy in patients with STEMI to ablate and remove thrombus.

Although ELCA is part of the therapeutic armamentarium in some PCI-capable centers, literature data is limited on its safety and efficacy profile in this specific scenario. The aim of this study was to evaluate the contribution of ELCA, focusing on its safety and efficacy profile as an adjuvant therapy in patients with STEMI undergoing PCI in our center.

METHODS

Data from all patients undergoing PCI with the simultaneous use of ELCA as an adjuvant technique were retrospectively recorded in a dedicated database after each procedure, starting from the introduction of the device in our center. ELCA procedures were performed by 5 interventional cardiologists with dedicated training in the use of the device.

This study was approved by *Parque Sanitario Pere Virgili* ethics committee (Barcelona, Spain) (reference No.: CEIM 003/2025). For the purposes of this study, we selected the subgroup of patients with STEMI who underwent PCI in which ELCA was used to facilitate thrombus removal.

Thrombus burden was assessed using the thrombus grading classification[9] as defined by the Thrombolysis in Myocardial Infarction (TIMI) study group, ranging from 0 to 5. A LTB was defined as a thrombus score ≥ 3. According to our internal protocol, ELCA was considered in STEMI patients in the presence of angiographic evidence of LTB, defined as TIMI thrombus grade ≥ 3, particularly if TIMI grade-0–1 flow or, poor visualization of the distal vessel, or as a bailout strategy after unsuccessful manual thrombectomy. Clinical variables were meticulously refined, and follow-up details were obtained through a thorough review of the patients' health records. Following coronary angiography and successful guidewire crossing of the culprit lesion, ELCA was left at the operator's discretion. It was used either as a primary device for thrombus removal or as a bailout strategy when manual thrombus aspiration did not improve TIMI grade flow. The selection of catheter size was mainly based on the target vessel diameter and on the characteristics of the vessel and the lesion; a 0.9 mm ELCA catheter is usually used in tortuous anatomies due to its better navigability and in small-caliber vessels, whereas a 1.4 mm catheter is used in selected cases involving larger proximal vessels with straight segments. Catheter size (0.9 mm or 1.4 mm) was selected based on vessel diameter and lesion characteristics. Laser fluence (45-60 mJ/mm²) and pulse repetition rate (25-40 Hz) were chosen as per manufacturer's recommendations.

Before laser application, the target vessel was flushed with saline solution to prevent interaction between the laser and blood or contrast medium. In all cases, continuous saline infusion was administered during laser delivery to avoid coronary artery wall heating. Laser energy was delivered using an 'on-off' technique, consisting of 10-s laser activation cycles interspersed with 5-s pauses. The laser catheter was advanced at a rate of approximately 1 mm/s over a 0.014-in coronary guidewire through the target lesion, following the manufacturer's recommendations.[7,10] After 2–3 laser catheter passes, a follow-up coronary angiography was performed to evaluate the efficacy of laser application and assess the feasibility of stent implantation. TIMI grade flow was recorded after the ELCA procedure (Post-ELCA TIMI grade flow) and once the PCI would have been completed (final TIMI grade flow).

Technical success was defined as the ability to advance the laser catheter through the entire target lesion and deliver laser energy successfully. Procedural success was defined as achieving a final TIMI grade ≥ 2 flow without any major cath lab-related complications, such as death, coronary perforation, or emergency bypass surgery after PCI completion. All procedural complications, including death, coronary perforation,[11] emergency bypass surgery, distal embolization, ventricular arrhythmia, and no-reflow were carefully documented and reported. Follow-up was conducted via retrospective review of health records, and major adverse cardiovascular events (MACE) defined as a composite endpoint of all-cause mortality, new myocardial infarction, and target lesion revascularization were recorded at the follow-up.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation for normally distributed data or as the median (interquartile range) for non-normally distributed data. Inter-group comparisons were performed using an unpaired Student's *t*-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables are expressed as counts and percentages and were analyzed using the chi-square test or Fisher's exact test, as appropriate.

The composite endpoint of MACE was analyzed as time-to-event data at the follow-up. Kaplan–Meier survival analysis was performed to estimate the event-free survival rates. All statistical analyses were conducted using SPSS Statistics (version 23.0, IBM Corp., United States). A 2-tailed *P* value < .05 was considered statistically significant.

RESULTS

Between July 2015 and August 2024, a total of 130 PCI s were performed in patients with STEMI using ELCA as an adjuvant therapy for thrombus removal. The patients' mean age was 61.8 ± 11.7 years, with 18 (13.8%) being women and 18 (13.8%) diagnosed with diabetes mellitus. ELCA was employed as the primary device for thrombus dissolution in 66 cases (50.8%) and as a bailout strategy in 64 cases (49.2%). Within the bailout group, manual thrombus aspiration was performed in 47 cases (36.2%), balloon dilation in 6 cases (4.6%), and thrombus debulking using the dotter effect in 11 cases (8.5%).

In the overall cohort, 124 patients (95.4%) presented with culprit lesions with a LTB. Before laser energy application, TIMI grade-0 flow was reported in 79 (60.8%) cases TIMI grade-1 flow in 32 (24.6%). After ELCA, TIMI grade-2 and 3 flows were achieved in 45 (34.6%) and 66 (50.8%) cases, respectively; *P* < .001 (figure 1).

Technical success was achieved in 128 (98.5%) cases, and procedural success in 124 (95.4%) (table 1). Procedural success was significantly higher when ELCA was used as the initial strategy vs when it was used as the bailout strategy (100% vs 90.6%; *P* = .013). However, procedural time was significantly longer in the bailout vs the initial strategy group (69.81 vs 48.50 min, respectively) (table 2).

One case of type IV coronary perforation, according to the modified Ellis classification, occurred in an octogenarian patient with an ecstatic and tortuous right coronary artery. Perforation sealing was achieved with the implantation of a covered stent. One cath lab-related death occurred in a patient with an uncrossable mid-segment of a left anterior descending coronary artery lesion and initial TIMI grade-3 flow. Following balloon dilation and partial advancement of the laser probe, complete vessel occlusion and suspected left main coronary artery dissection resulted in cardiac arrest and cath lab-related death.

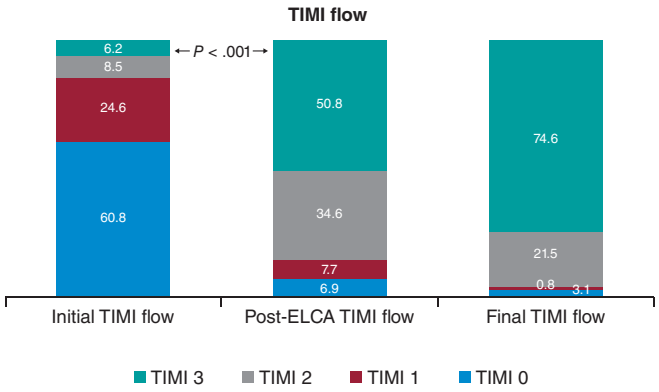

Figure 1. TIMI grade flow distribution before and after ELCA application. Stacked bar graph showing the distribution of TIMI grade 0-3 flows at 3 different time points: initial angiography, post-ELCA, and final angiographic result after PCI. A marked improvement in coronary flow is observed following ELCA, with a progressive increase in TIMI grade-3 flow from 6.2% to 74.6%. ELCA, excimer laser coronary angioplasty; TIMI, Thrombolysis in Myocardial Infarction.

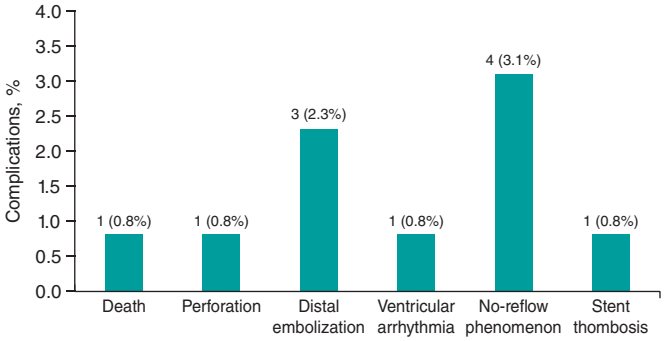

Figure 2. ELCA-related procedural complications. Bar chart showing the frequency and percentage of major complications during or immediately after ELCA. The most common was no-reflow (3.1%), followed by distal embolization (2.3%). Other events (death, perforation, ventricular arrhythmia, and stent thrombosis) were rare (0.8% each). ELCA, excimer laser coronary angioplasty.

Other procedural complications included distal embolization in 3 (2.3%) cases and slow flow or no-reflow in 4 (3.1%). Among the slow/no-reflow cases, 1 occurred after laser application, and 3 following stent implantation and/or post-dilation. All were successfully managed with optimal medical therapy, achieving final TIMI grade-2 flow. One episode of ventricular arrhythmia occurred during saline washout of the target vessel, requiring electrical cardioversion. Additionally, 1 case of stent thrombosis (0.8%) occurred intraoperatively (figure 2).

Long-term follow-up data were missing for 6 patients (4.6%). At the 2-year follow-up, the event-free rate for combined MACE was 0.80 (95%CI, 0.73–0.88) as determined by the Kaplan–Meier estimator (table 3 and figure 3).

DISCUSSION

The main finding of this single-center study is that coronary laser angioplasty is a feasible, safe, and effective adjuvant therapy in the

Table 1. Baseline characteristics of patients

Variable (n = 130)	Value
Age, yr	61.8 ± 11.7
Female *Hypertension* *Hypercholesterolemia* *Tobacco use*	18 (13.8) 59 (45,4%) 57 (43,8%) 78 (60%)
Diabetes mellitus	18 (13.8)
Killip classification	
I	98 (75.4)
II	18 (13.8)
III	3 (2.3)
IV	11 (8.5)
Radial access	118 (90,7%)
Femoral access	12 (9,3%)
Lesion localization	
LMCA	3 (2,3%)
LAD	55 (42,3%)
LCX	8 (6,2%)
RCA	64 (49,2 %)
Primary device	66 (50.8)
Bailout strategy	64 (49.2)
Large thrombus burden	124 (95.4)
Laser catheter size, Fr	
0.9	114 (87.7)
1.4	16 (12.3%)
Procedural time, min	60 (43–86)
Fluoroscopy time, min	22.2 ±12.2
Laser frequency, Hz	31 ± 10.4
Laser fluency, mJ/mm²	46.5 ± 9.17
Laser delivery time, s	125.9 ± 83.4
Technical success	128 (98.5)
Procedural success	124 (95.4)

LAD: left anterior descending coronary artery; LCX: left circumflex artery; LMCA: left main coronary artery; RCA: right coronary artery.
Categorical data are presented as absolute value and percentage, n (%); and continuous variables as mean ± standard deviation or first and third quartiles.

context of PCI (videos 1-4 of the supplementary data), demonstrating a low rate of complications and an acceptable long-term rate of MACE.

Data on the use of ELCA in acute myocardial infarction remain limited, with most evidence coming from non-randomized clinical trials. The CARMEL trial,[12] the largest multicenter study to date, evaluated the safety, feasibility, and acute outcomes of ELCA in patients with acute myocardial infarction within 24 h of symptom onset requiring urgent PCI. TIMI grade flow significantly improved after laser application, increasing from 1.2 to 2.8, with an overall procedural success rate of 91% and a low distal embolization rate of 2%, even though 65% of cases had a LTB. In our study, 95.4% of the patients had culprit lesions with a LTB, and laser delivery significantly improved the mean TIMI grade flow from 0.6 to 2.29, with a comparable distal embolization rate of 2.3%.

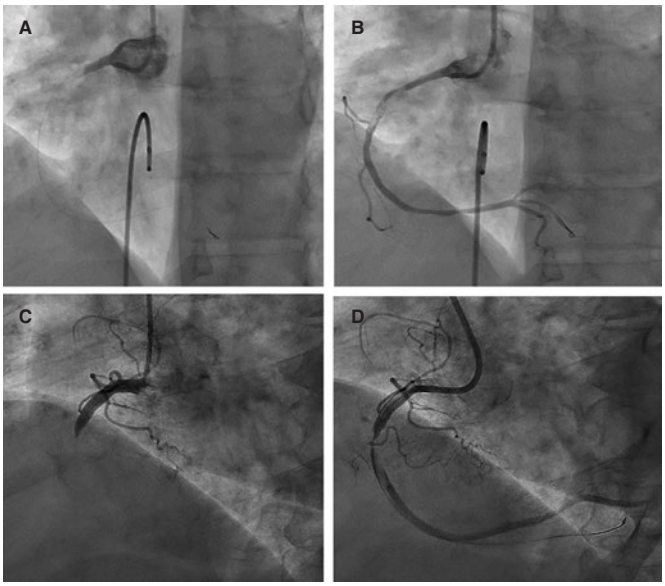

Figure 3. Pre- and post-ELCA findings in 2 typical cases of right coronary artery with large thrombus burden. ELCA, excimer laser coronary angioplasty.

Arai et al.[13] retrospectively analyzed 113 consecutive acute coronary syndrome cases undergoing PCI comparing an ELCA group (n = 48) with a thrombus aspiration group (n = 50). They found that ELCA was associated with a significantly shorter door-to-reperfusion time, a better myocardial blush grade, and fewer MACE vs thrombus aspiration. These favorable outcomes are likely attributable to ELCA's ability to vaporize thrombi through acoustic shockwave propagation and dissolution mechanisms,[12] as well as its capacity to suppress platelet aggregation kinetics (a phenomenon known as the 'stunned platelet' effect).[14]

Reperfusion injury to the coronary microcirculation is a critical concern during PCI in STEMI patients. While manual thrombus aspiration can reduce the rate of no-reflow in patients with a LTB, residual thrombi and decreased coronary flow following thrombectomy have been associated with a higher risk of no-reflow.[15] In a study of 812 patients with STEMI and a LTB undergoing PCI, Jeon et al.[16] reported that 34.4% experienced failed thrombus aspiration, defined as no thrombus retrieval, remnant thrombus grade ≥ 2, or distal embolization. This failure was associated with an increased risk of impaired myocardial perfusion and microvascular obstruction.

ELCA's ability to vaporize thrombi (with a low rate of distal embolization) and mitigate platelet activation, key cofactors in myocardial reperfusion damage,[17] can potentially reduce this undesirable effect. Although the direct impact of ELCA on coronary microcirculation in PCI has not been well documented, evidence from smaller studies suggests potential benefits. For example, Ambrosini et al.[18] investigated ELCA in 66 patients with acute myocardial infarction and complete thrombotic occlusion of the infarcted related artery, demonstrating excellent acute coronary and myocardial reperfusion outcomes (as assessed by the myocardial blush score and the corrected TIMI frame count), as well as a low rate of long-term left ventricular remodeling (8%). The significant

Table 2. Difference in variables between the initial and bailout strategy groups

Variable	ELCA as the initial strategy (n = 66)	ELCA as the bailout strategy (n = 64)	*P*-value
Complications	8 (12.1%)	3 (4.7%)	.100
Large thrombus burden	64 (97%)	60 (93.8%)	.440
Technical success	65 (98.5%)	63 (98.4%)	1.000
Procedural success	66 (100%)	58 (90.6%)	.013
Procedural time, median	48.50 (38.83–66.61)	69.81 (55.36–101)	< .001

ELCA, excimer laser coronary angioplasty.
Categorical data are presented as absolute value and percentage, n (%); and continuous variables as mean ± standard deviation or first and third quartiles.

Table 3. List of adverse clinical events

Patient No.	Event	Date
6	Death	1
13	Death	493
15	Death	148
23	Death	11
33	Death	170
36	Death	4
43	New myocardial infarction associated with TLR	39
50	New myocardial infarction	213
61	Death	16
77	Death	1
83	New myocardial infarction associated with TLR	119
84	Death	4
92	Death	1
98	Death	0
101	Death	37
110	Death	0
113	Death	12
118	Death	253
121	Death	139
124	New myocardial infarction associated with TLR	291
128	Death	10

TLR, target lesion revascularization.
Lost to follow-up: 6 patients (4.6%).

improvement in mean TIMI grade flow observed immediately after ELCA application in our cohort may indirectly suggest a protective effect of this technique on coronary microcirculation. However, the lack of large studies comparing ELCA with conventional STEMI treatment limits the ability to definitively confirm the benefits of coronary laser therapy in this setting. Shibata et al.[19] explored the impact of ELCA on myocardial salvage using nuclear scintigraphy in 72 STEMI patients and an onset-to-balloon time < 6 h, comparing ELCA (n = 32) and non-ELCA (n = 40) groups. Their findings indicated a trend towards a higher myocardial salvage index in the ELCA vs the non-ELCA group (57.6% vs 45.6%).

Limitations

This study has several limitations. It is a retrospective analysis, which inherently introduces biases related to data collection, interpretation and application of inclusion and exclusion criteria. Besides, the absence of a comparative group limits the ability to establish the definitive clinical benefit of ELCA and its potential superiority over other strategies in the context of STEMI patients undergoing PCI. Furthermore, while the significant improvement of TIMI grade flow observed after laser application suggests potential benefits for coronary microcirculation, we did not directly assess this effect or thrombus burden reduction since post-ELCA thrombus grading was not systematically recorded. Unfortunately, in our retrospective database, PCI details (segmental analysis of coronary arteries and classification), the use of intravascular imaging modalities, dual antiplatelet therapy regimens (aspirin in addition to a potent $P2Y_{12}$ inhibitor, or clopidogrel when prasugrel or ticagrelor were contraindicated, was routinely prescribed following current guidelines recommendations) or post-PCI echocardiography or cardiac magnetic resonance parameters were not systematically collected (unavailable in the health reports we revised) and follow-up data were missing for 4.6% of patients, all of which limited our ability to assess their potential impact on clinical outcomes. Last, our findings represent the experience of a single center, the percentage of women and patients with diabetes is relatively low, and procedures were performed by 5 trained operators, which may limit the external validity of the results.

CONCLUSIONS

ELCA seems to be an effective device for thrombus dissolution in the STEMI scenario, with excellent technical and procedural success rates. Besides, a low complication rate and favorable long-term outcomes with an acceptable event-free survival rate was observed in the present cohort.

DATA AVAILABILITY

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This study was approved by the center Ethics Committee (waiving the need for informed consent due to the retrospective nature of

the investigation) in full compliance with national legislation and the principles set forth in the Declaration of Helsinki. Sex was reported as per biological attributes (SAGER guidelines).

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

The authors state that no generative artificial intelligence technologies were used in the preparation or revision of this article.

AUTHORS' CONTRIBUTIONS

A. Pernigotti and M. Mohandes were responsible for the conceptualization and study design and contributed equally as co-first authors. M. Mohandes, A. Pernigotti, R. Bejarano, H. Coimbra, F. Fernández, C. Moreno, M. Torres, J. Guarinos were involved in data collection and statistical analysis. M. Mohandes, A. Pernigotti, and J.L. Ferreiro were involved in manuscript drafting and critical revision and were responsible for the supervision and final approval. All authors have accepted responsibility for the entire content of this manuscript and consented to its submission to the journal. Each author reviewed all results and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest related to this manuscript. J.L. Ferreiro declared having received speaker's fees from Eli Lilly Co, Daiichi Sankyo, Inc., AstraZeneca, Pfizer, Abbott, Boehringer Ingelheim, Bristol-Myers Squibb, Rovi, Terumo and Ferrer; consulting fees from AstraZeneca, Eli Lilly Co., Ferrer, Boston Scientific, Pfizer, Boehringer Ingelheim, Daiichi Sankyo, Inc., Bristol-Myers Squibb and Biotronik; and research grants from AstraZeneca, not related to this manuscript.

WHAT IS KNOWN ABOUT THE TOPIC?

- ELCA is a specialized technique used as adjuvant therapy during PCI for STEMI, particularly in patients with LTB.
- Although former studies have shown that ELCA can improve coronary flow and potentially reduce thrombotic material, data in the setting of acute myocardial infarction remain limited.
- ELCA is mostly used in high-volume centers by experienced operators, and standardized criteria for use in STEMI patients are not consistently reported in the literature.

WHAT DOES THIS STUDY ADD?

- This is one of the largest retrospective single-center series (130 patients) ever reported on the use of ELCA in STEMI patients with angiographically defined LTB.
- The study shows a high rate of technical and procedural success, significant improvement in TIMI flow, low rate of complication, and acceptable long-term outcomes.
- It provides detailed information on operator training, device selection, and laser settings, contributing to transparency and reproducibility.
- It also identifies current limitations in data reporting (eg, lack of systematic thrombus grading or dual antiplatelet therapy regimen documentation), underscoring the need for standardization in future studies.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000537.

REFERENCES

1. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC guidelines for the management of acute coronary syndromes. *Eur Heart J.* 2023;44:3720-3826.
2. Kim MC, Cho JY, Jeong HC, et al. Long-term clinical outcomes of transient and persistent no reflow phenomena following percutaneous coronary intervention in patients with acute myocardial infarction. *Korean Circ J.* 2016;46:490-498.
3. Sardella G, Mancone M, Bucciarelli-Ducci C, et al. Thrombus aspiration during primary percutaneous coronary intervention improves myocardial reperfusion and reduces infarct size: the EXPIRA prospective, randomized trial. *J Am Coll Cardiol.* 2009;53:309-315.
4. Jolly SS, Cairns JA, Yusuf S, et al. Randomized trial of primary PCI with or without routine manual thrombectomy. *N Engl J Med.* 2015;372:1389-1398.
5. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: Executive summary. *Circulation.* 2022;145:e4-e17.
6. Grundfest WS, Litvack F, Forrester JS, et al. Laser ablation of human atherosclerotic plaque without adjacent tissue injury. *J Am Coll Cardiol.* 1985;5:929-933.
7. Mohandes M, Fernández L, Rojas S, et al. Safety and efficacy of coronary laser ablation as an adjuvant therapy in percutaneous coronary intervention: a single-centre experience. *Coron Artery Dis.* 2021;32:241-246.
8. Rawlins J, Din JN, Talwar S, O'Kane P. Coronary intervention with the excimer laser: review of the technology and outcome data. *Interv Cardiol Rev.* 2016;11:27-32.
9. Gibson CM, de Lemos JA, Murphy SA, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. *Circulation.* 2001;103:2550-2554.
10. Topaz O, Das T, Dahm J, et al. Excimer laser revascularisation: current indications, applications and techniques. *Lasers Med Sci.* 2001;16:72-77.
11. Ellis SG, Ajluni S, Arnold AZ, et al. Increased coronary perforation in the new device era. Incidence, classification, management, and outcome. *Circulation.* 1994;90:2725-2730.
12. Topaz O, Ebersole D, Das T, et al. Excimer laser angioplasty in acute myocardial infarction (the CARMEL multicenter trial). *Am J Cardiol.* 2004;93:694-701.
13. Arai T, Tsuchiyama T, Inagaki D, et al. Benefits of excimer laser coronary angioplasty over thrombus aspiration therapy for patients with acute coronary syndrome and thrombolysis in myocardial infarction flow grade 0. *Lasers Med Sci.* 2022;38:13.
14. Topaz O, Minisi AJ, Bernardo NL, et al. Alterations of platelet aggregation kinetics with ultraviolet laser emission: the "stunned platelet" phenomenon. *Thromb Haemost.* 2001;86:1087-1093.
15. Ahn SG, Choi HH, Lee JH, et al. The impact of initial and residual thrombus burden on the no-reflow phenomenon in patients with ST-segment elevation myocardial infarction. *Coron Artery Dis.* 2015;26:245-253.
16. Jeon HS, Kim YI, Lee JH, et al. Failed thrombus aspiration and reduced myocardial perfusion in patients with STEMI and large thrombus burden. *JACC Cardiovasc Interv.* 2024;17:2216-2225.
17. Rezkalla SH, Kloner RA. No-reflow phenomenon. *Circulation.* 2002;105:656-662.
18. Ambrosini V, Cioppa A, Salemme L, et al. Excimer laser in acute myocardial infarction: single centre experience on 66 patients. *Int J Cardiol.* 2008;127:98-102.
19. Shibata N, Takagi K, Morishima I, et al. The impact of the excimer laser on myocardial salvage in ST-elevation acute myocardial infarction via nuclear scintigraphy. *Int J Cardiovasc Imaging.* 2020;36:161-170.

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Original article

Heart block after transcatheter septal defect closure in infants under 10 kg: clinical outcomes and management options

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ABSTRACT

Introduction and objectives: This study reviewed the management of heart block following transcatheter device closure of perimembranous ventricular septal defects in pediatric patients.
Methods: We evaluated the follow-up and treatment of 1 patient who developed complete atrioventricular block and 5 patients who developed left bundle branch block (LBBB) from January 2019 through December 2023 after transcatheter ventricular septal defect closure in our clinic.
Results: All patients who developed heart block weighed less than 10 kg. The only patient who developed complete atrioventricular block was successfully treated with temporary pacing, returning to sinus rhythm. In 2 of the 5 patients with LBBB, conduction disturbances were observed during the procedure, leading to termination without device release. One patient with postoperative LBBB returned to sinus rhythm following steroid therapy, and another one required surgical device removal. The patient with late-onset LBBB is still under close follow-up with serial ECG and echocardiography.
Conclusions: Heart block after transcatheter closure of perimembranous ventricular septal defect is a serious complication, particularly in young patients with low body weight. Early detection and appropriate management, including procedural interruption, steroid therapy, and surgery when necessary, can lead to favorable outcomes. Careful patient selection and close follow-up are essential to minimize the risk of conduction disturbances.

Keywords: Atrioventricular block. Left bundle branch block. Pediatric patients. Perimembranous ventricular septal defects. Transcatheter closure.

Bloqueo tras el cierre percutáneo de defectos septales en lactantes de menos de 10 kg: resultados y opciones de tratamiento

RESUMEN

Introducción y objetivos: En este estudio se revisó el tratamiento del bloqueo cardiaco después del cierre con dispositivo percutáneo de defectos del tabique ventricular perimembranoso en pacientes pediátricos.
Métodos: Se evaluó el seguimiento y el tratamiento de 1 paciente que desarrolló bloqueo auriculoventricular completo y de 5 pacientes que desarrollaron bloqueo de rama izquierda (BRI), entre enero de 2019 y diciembre de 2023, tras del cierre percutáneo de una comunicación interventricular en nuestro centro.
Resultados: Todos los pacientes que desarrollaron bloqueo cardiaco pesaban menos de 10 kg. El único paciente que desarrolló un bloqueo auriculoventricular completo respondió al tratamiento médico con estimulación temporal y recuperó el ritmo sinusal. En 2 de los 5 pacientes con BRI se observó una anomalía de conducción durante el procedimiento, lo que llevó a finalizarlo sin liberar el dispositivo. Un paciente con BRI después del procedimiento recuperó el ritmo sinusal tras recibir tratamiento con esteroides, mientras que otro requirió la retirada quirúrgica del dispositivo. El paciente con BRI de aparición tardía permanece bajo vigilancia estrecha con electrocardiogramas seriados y ecocardiografía.

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Conclusiones: El bloqueo que se desarrolla después del cierre percutáneo de una comunicación interventricular perimembranosa es una complicación grave, sobre todo en pacientes jóvenes con bajo peso corporal. La detección precoz y el tratamiento adecuado, incluida la interrupción del procedimiento, el tratamiento con esteroides y la intervención quirúrgica en caso necesario, pueden producir resultados favorables. La selección cuidadosa de los pacientes y un seguimiento estrecho son esenciales para minimizar el riesgo de alteraciones de la conducción.

Palabras clave: Bloqueo auriculoventricular. Bloqueo de rama izquierda. Pacientes pediátricos. Defectos septales ventriculares perimembranosos. Cierre percutáneo.

Abbreviations

CAVB: complete atrioventricular block. **LBBB:** left bundle branch block. **LV:** left ventricle. **RV:** right ventricle. **VSD:** ventricular septal defect.

INTRODUCTION

Transcatheter closure of ventricular septal defects (VSD) offers numerous advantages, including less trauma, faster recovery, and a reduced length of stay.[1] However, this technique has complications, such as device embolization, valve malfunction, and arrhythmias. One of the most concerning complications of transcatheter closure of perimembranous VSD is the development of complete atrioventricular block (CAVB).[2] Although this complication is more likely to occur when an inappropriate device is selected, pinpointing the exact cause of the block can sometimes be challenging. Factors significantly contributing to CAVB include young age, low body weight, device malapposition due to septal aneurysm, selection of an excessively large device, and direct device compression. Despite its rarity, CAVB remains a severe complication associated with this procedure.[3]

The atrioventricular node is located at the posterior superior area of the membranous ventricular septum and branches into the left and right bundles at the lower posterior edge. This close anatomical relationship increases the risk of developing heart block during the transcatheter closure of perimembranous VSD.[1,4,5] Left anterior fascicular block, a variant of left bundle branch block (LBBB), can result in ventricular asynchrony, which negatively impacts hemodynamics and left ventricular function.[6]

CAVB has been reported in 0-6.4% of cases after the transcatheter closure of VSD.[7] Recent publications indicate that this rate is gradually declining. A systematic review by Yang et al. found that 107 of 4394 patients, 107 (2.4%) required permanent pacemaker implantation after the interventional closure of VSD, with a higher incidence rate being reported in young children.[8] Additionally, Bergman et al. reported that CAVB was observed in 1 of 149 (0.7%) patients after the procedure involving various VSD devices at a 6-year follow-up.[7]

We evaluated a total of 180 patients, 42 of whom were under 10 kg, who underwent transcatheter closure of VSD in our center in the last 5 years, focusing on block development in young children. In this article we detail the treatment and follow-up of 1 patient who developed complete CAVB and 5 patients who developed LBBB.

METHODS

From January 2019 through December 2023, a total of 180 pediatric patients (42 of whom weighed less than 10 kg) underwent transcatheter closure of perimembranous ventricular septal defects (VSD) at our center.

The indications for closure included a left ventricular end-diastolic diameter Z score ≥ 2.0; Qp/Qs > 1.5, treatment-resistant heart failure, a cardiothoracic ratio ≥ 0.55 on chest radiography, and growth retardation unrelated to recurrent respiratory infections or malnutrition.

Patients with subaortic edge regurgitation, significant aortic regurgitation, ventricular outflow tract obstruction, mean pulmonary artery pressure > 20 mmHg, or associated surgical heart anomalies were excluded from the study.

The KONAR-MF VSD occluder (Lifetech, China) and Amplatzer Duct Occluder (ADO I and II, AGA Medical Corp., United States) devices were used in the procedures. The Konar MF was used more frequently due to its flexible design (Konar MF: 157, ADO I + ADO II: 23).

The device size was selected based on angiographic measurements, typically choosing a device 1–2 mm larger than the size of the left ventricular defect. In VSD with aneurysmal tissue, the left disc of the device was positioned inside the aneurysmal tissue.

All patients were continuously monitored with electrocardiography during the procedure and underwent serial electrocardiograms (ECG) and echocardiographic evaluations at the follow-up.

RESULTS

Heart block developed in 6 patients, all of whom weighed less than 10 kg: 1 CAVB and 5 LBBB.

Case 1

A 2-year-old female patient, weighing 9.9 kg (3rd to 10th percentile), was being followed by pediatric cardiology for a diagnosis of a VSD. She had a past medical history of failure to gain weight, growth retardation, and 2 hospitalizations due to lower respiratory tract infections. An echocardiogram revealed a perimembranous VSD, measuring 5 mm on the left ventricular (LV) side and 4 mm on the right ventricular (RV) one.

Due to the clinical and hemodynamic significance of the patient's VSD, a decision was made to perform a transcatheter closure. Prior to the procedure, the patient was administered cefazolin (50 mg/kg) and heparin (100 U/kg). The VSD was successfully closed using a Lifetech Konar MFO 6-4 device via antegrade access while the patient remained under general anesthesia. There were no signs of conduction disturbances in the ECG performed intra- and postoperatively. An ECG performed on postoperative day 2 confirmed that

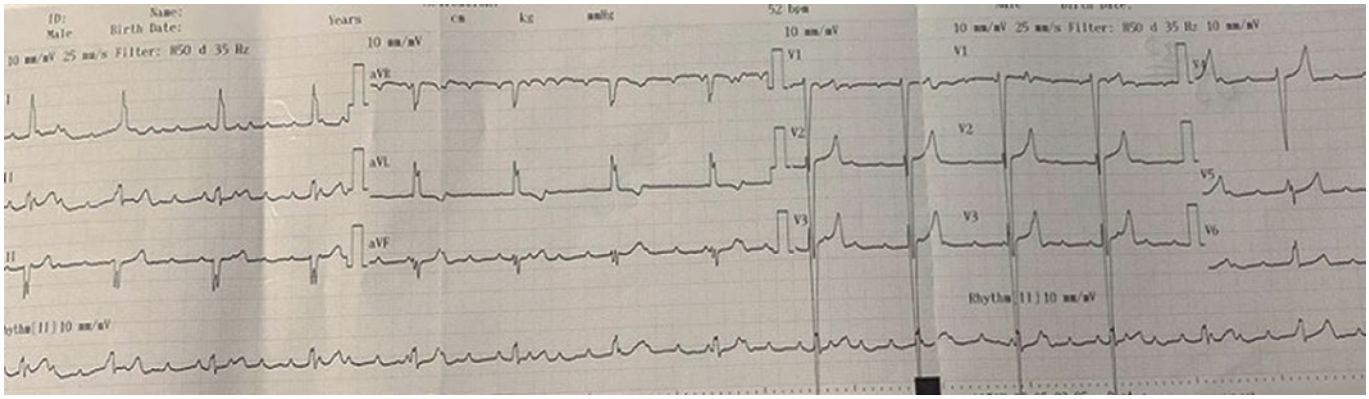

Figure 1. Case 1: electrocardiography of complete atrioventricular block after transcatheter closure of ventricular septal defect.

the device was correctly positioned in the absence of residual shunt. The patient was prescribed a 6-month regimen of aspirin at a dosage of 3 mg/kg/day and was discharged without any complications. Three days after discharge, the patient exhibited cyanosis. An ECG revealed the presence of CAVB (figure 1).

Atropine was administered twice at a dose of 0.02 mg/kg. The intervention successfully raised the peak heart rate to 135 beats per minute, and the patient's rhythm normalized to a junctional ectopic rhythm. However, as the CAVB persisted, a temporary transvenous pacemaker was implanted, and the patient was admitted to the pediatric intensive care unit under continuous follow-up. Dexamethasone was initiated at a dosage of 0.6 mg/kg per day.

On hospitalization day 3, the patient's ECG showed a return to sinus rhythm. After the temporary pacemaker was turned off, the patient underwent 24-hour Holter ECG monitoring. The Holter ECG showed a consistent sinus rhythm, meaning there was no evidence of CAVB or advanced second-degree block. On hospitalization day 5, the patient, whose ECG was still showing a consistent sinus rhythm, was discharged with a plan to complete a 10-day regimen of dexamethasone.

During the 3- and 6-month follow-up visits, the patient's ECG continued to show a normal sinus rhythm without the need for medication.

Case 2

A 15-month-old male patient, weighing 8 kg (which is below the 3rd percentile), presented with a VSD and a large patent ductus arteriosus who underwent transcatheter closure at 3.5 months of age due to symptoms of heart failure that remained unresponsive to optimal medical therapy. During follow-up, the patient showed signs of inadequate weight gain and fatigue during feeding. Due to these clinical and hemodynamic indicators, a decision was made to close the VSD at 15 months of age. Echocardiography revealed a defect measuring 5 mm on the LV side and 4 mm on the RV side in the perimembranous region. The defect was closed using a transcatheter approach via retrograde access with a Lifetech Konar MFO 6-4 device.

Postoperative follow-up revealed the widening of the QRS complex. An ECG showed that the patient had developed a LBBB. As a result, the device was removed without being released. The patient then began dexamethasone at a dosage of 0.6 mg/kg per day.

By the end of week 1 of postoperative follow-up, the patient's ECG showed a normal sinus rhythm with no evidence of LBBB.

Case 3

An 8-month-old patient, weighing 6.4 kg (below the 3rd percentile), was monitored for a VSD measuring 5 mm on the LV side and 4.5 mm on the RV side in the perimembranous region. Due to poor weight gain and left ventricular enlargement on the echocardiography, transcatheter closure was performed.

A Lifetech Konar MFO 6-4 device was successfully implanted under general anesthesia without immediate complications. However, 3 hours later, the patient developed a LBBB on the ECG (figure 2). Although dexamethasone was started at 0.6 mg/kg/day, the LBBB persisted by day 4, and the patient was discharged.

During the 1-week follow-up, an incomplete LBBB was noted on the ECG. Dexamethasone treatment went on for another 2 weeks, and at the 1-month follow-up, the LBBB had resolved, indicating successful treatment.

Case 4

A 14-month-old female patient, weighing 8 kg (which falls within the 3rd to 10th percentile), was being monitored for a VSD. The ECG indicated a 6 mm perimembranous VSD. A decision was made to perform the transcatheter closure of the defect. The procedure was performed with a Lifetech Konar MFO 8-6 device via retrograde access in the absence of immediate complications.

However, after the procedure, an ECG showed the development of LBBB. The patient began dexamethasone at a dosage of 0.6 mg/kg/day. After discharge, she was closely monitored through frequent outpatient follow-up. Despite ongoing treatment, LBBB persisted, and echocardiography performed at the 1-week follow-up showed onset of aortic regurgitation. At the 3-week follow-up, the device was surgically removed and the VSD repaired. This decision was made because her echocardiography showed increased aortic regurgitation, and the lLBBB persisted on her ECG.

Case 5

A 12-month-old male patient, weighing 7 kg (below the 3rd percentile), was admitted to the clinic with symptoms of growth retardation and evidence of left ventricular enlargement on echocardiography. The patient exhibited a perimembranous VSD measuring 6 mm on the LV side and 3.5 mm on the RV side. The defect was closed using a Lifetech Konar MFO 6-4 device, delivered through a transcatheter procedure, which went completed smoothly

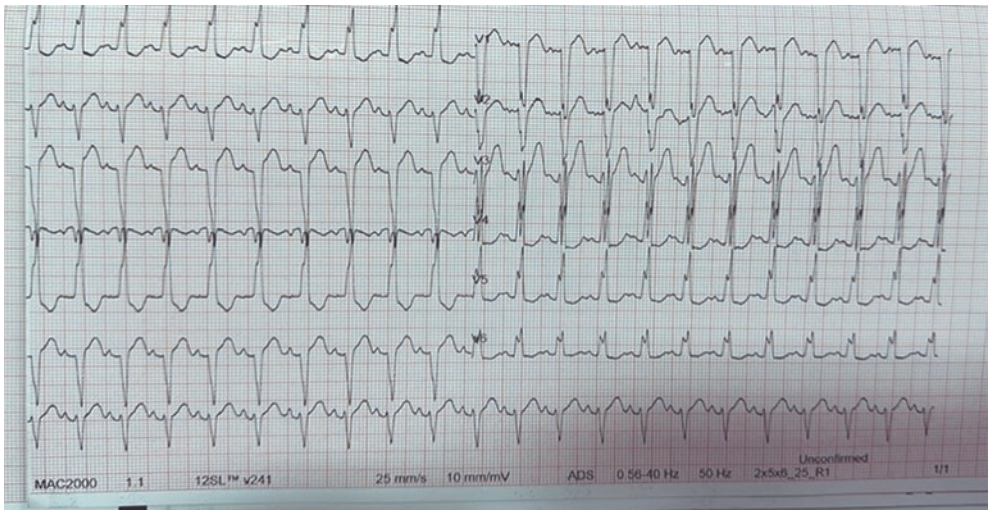

Figure 2. Case 3: electrocardiography of left bundle branch block after transcatheter closure of ventricular septal defect closure.

and without conduction disturbances being observed on the ECG at the follow-up. Echocardiography confirmed that the device had been implanted appropriately and in the absence of residual shunt. However, at the 4-year follow-up, LBBB was observed on the ECG. Since the left ventricular functions remained normal on echocardiography, the patient remained under close follow-up in the outpatient clinic without any additional treatment.

Case 6

A decision was made to perform a transcatheter closure of a VSD in an 11-month-old female patient who weighed 9 kg (falling within the 25th to 50th percentile). She had been on optimal medical therapy for heart failure and exhibited left ventricular dilatation on echocardiography. The defect measured 7 mm on the LV side and 4 mm on the RV side.

The procedure was performed via retrograde access using a Lifetech Konar MFO 7-5 device. After device implantation, QRS complex widening was observed on the monitor, and an ECG confirmed the development of LBBB. The device had to be removed without being released.

The patient began dexamethasone at a dose of 0.6 mg/kg/day. Four weeks after the procedure, the patient's ECG showed a return to sinus rhythm in the absence of LBBB.

The patients' demographic and clinical characteristics are shown in table 1.

DISCUSSION

Blocks that occur after transcatheter closure of perimembranous VSDs are primarily caused by the conduction bundle close proximity to the defect.[9,10] The edge of the perimembranous VSD is located in an area of fibrous continuity between the atrioventricular valves, which forms the posteroinferior border. In this region, the atrioventricular conduction bundle leaves the central fibrous body and runs just subendocardial. This position makes it vulnerable to damage from devices used to close perimembranous VSDs.[9]

AVB due to direct mechanical compression of the atrioventricular node typically occur immediately after performing the procedure or 2 to 7 days after percutaneous closure. Later onset AVB may result from inflammation and fibrosis.[2,9] CAVB are usually observed in the early postoperative period. In patients undergoing transcatheter closure, the timing of AVB formation can be unpredictable, with most cases being detected 2 to 7 days after the procedure.[7,10] However, late-onset AVBs have been reported as late as 2 to 4 weeks or even 10 to 20 months after the procedure. The need for permanent pacemaker implantation is greater in younger patients.[7] Although in our patient with complete AVB, symptoms developed 4 days after the procedure, there was no need for permanent pacemaker implantation.

After the perimembranous closure of VSD, bundle branch block is a more finding than CAVB. Right bundle branch block occurs more frequently than LBBB, likely because the right bundle branch is smaller and more prone to damage. While bundle branch blocks usually develop within 1 week after transcatheter closure, cases have been reported up to 3 years after the procedure.[11] Most bundle branch blocks may resolve spontaneously or with steroid treatment, such as IV dexamethasone at 1 mg/kg/day or oral prednisone at 1-2 mg/kg/day.[2,9] Close follow-up of patients is essential within the first 7 days after the procedure.[10] LBBB has been reported to lead to abnormal left ventricular remodeling and heart failure.[11]

If CAVB occurs intraoperatively while crossing the defect, it is advisable to abandon the procedure. For postoperative CAVB, high doses of IV steroids followed by a 2-week regimen of oral steroids are recommended.[9] The decision to remove the device is complex and depends on the patient's symptoms, parental preference, and the experience of the clinic.[9]

If AVB resolves with steroid therapy, leaving the device in place is recommended. In symptomatic patients, a temporary pacemaker should be implanted, and response to steroid treatment should be monitored.[9] In our patient with complete AVB, and in the 2 patients who developed postoperative LBBB, these blocks resolved after 2 weeks of steroid treatment, and sinus rhythm was restored. These patients have been closely monitored for any potential recurrence of the block.

For those patients who developed intraoperative bundle branch blocks, the devices were removed without release, as suggested in the literature.

Table 1. Demographic and clinical characteristics

Case	Age, months	Body weight, kg	VSD LV side (mm)	VSD RV side (mm)	Device	VSA	Approach	Time of block developing	Block	Administration	Follow-up
1	25	9.9	5	4	6-4	No	Antegrade	Day 4	CAVB	Transient pacemaker	Sinus
2	15	8	5	4	6-4	No	Retrograde	Intraoperatively	LBBB	Not released	Sinus
3	8	6.4	5	4.5	6-4	No	Antegrade	Hour 2	LBBB	Dexamethasone	Sinus
4	14	8	6	5.5	8-6	Yes	Retrograde	Hour 3	LBBB	Surgery	Sinus
5	11	7	6	3.5	6-4	No	Retrograde	Year 4	LBBB	Follow-up	LBBB
6	11	9	7	4	7-5	No	Antegrade	On the Intraoperatively	LBBB	Not released	Sinus

CAVB, complete atrioventricular block; LBBB, left bundle branch block; LV, left ventricle; RV, right ventricle; VSA, ventricular septal aneurysm; VSD, ventricular septal defect.

In the patient who developed postoperative LBBB, which did not regress during follow-up, the device was surgically removed, and the VSD was repaired. The LBBB regressed with the removal of pressure on the left bundle branch.

Factors such as young age, low body weight, improper device positioning according to septal aneurysm and the choice of a large device have been identified as significant contributors to the development of conduction block.[3] In our 5-year review, we observed that 5 of 180 cases of LBBB occurred in children weighing under 10 kg, which underscores the importance of age and body weight in the risk of developing LBBB.

To minimize the risk of a heart block, it is essential to prevent trauma and inflammation to the heart conduction tissue.[4,7] This means an experienced operator should perform the procedure, using appropriately sized and flexible devices for the defect, and avoiding large carrier sheaths.[7,9] The KONAR-MF VSD occluder, or KONAR-MFO, has become the primary choice in recent years for device selection due to its procedural flexibility, soft structure, and defect compatibility. We prefer to use KONAR-MFO in patients with low body weight and young age.[3,12] While keeping septal aneurysmal tissue within the device during device implantation increases the risk of block, placing the left disc of the device inside the aneurysm may reduce the risk of block by removing it from the conduction system.[13] Additionally, it is important to note that optimal medical therapy may be effective in cases without complete AVB basing the final treatment decision on the patient's response.[9]

The reported rate of complete heart block after the surgical closure of VSD is < 2%. While the risk of CAVB (1-5%) in interventional closure of VSD raises concern, recent publications indicate a decreasing trend in the rates of CAVB.[2,9,10] In our series, CAVB developed in only 1 patient (0.5%) and resolved with steroids after temporary transvenous pacing. Yang et al. (2012) reported that 8 of 228 patients (3.5%) developed postoperative LBBB.[14] In a retrospective study of 2349 patients published in 2019, Wang et al. reported LBBB in 57 patients (2.4%) after the transcatheter closure of perimembranous VSD.[11] In our center, LBBB developed in 5 of 180 transcatheter closures of VSD (2.7%), and the device was not implanted in 2 patients due to the development of intraoperative LBBB. Follow-up continues for our patient who developed late-onset LBBB.

Limitations

This study was conducted at a single center and retrospectively. Although patients were regularly monitored, longer follow-up periods are required, especially to detect conduction disturbance that may arise in the late period. Results may vary depending on the use of different devices or results obtained from different centers.

Considering these limitations, the findings should be interpreted with caution, particularly on the development of conduction block in low-birth-weight children. Further studies with larger sample groups, multicenter designs, and prospective follow-up data are required.

CONCLUSIONS

The risk of heart block in transcatheter procedures performed at experienced centers is lower than anticipated. Interventional closure of VSD has emerged as a viable alternative to surgery, providing benefits such as less trauma, faster recovery, and a reduced length of stay. With the arrival of newly developed devices, the risk of heart block in the transcatheter closure of VSD is steadily decreasing. Additionally, treatment often restores sinus rhythm in patients, and any heart block that may occur typically does not persist.

DATA AVAILABILITY

The raw data supporting the conclusions of this article will be made available by the authors upon request to any qualified researcher.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

The study protocol was approved by the SBU Tepecik Training and Research Hospital ethics committee in full compliance with national rules and regulations and the ethical principles outlined in the revised Declaration of Helsinki (2008). Prior written informed consent and assent was obtained to participate in this study from each patient or caregiver. Furthermore, the authors confirm that sex and gender variables were considered in full compliance with the SAGER guidelines.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence technologies were utilized in the conception, data analysis, writing, or revision of this manuscript.

AUTHORS' CONTRIBUTIONS

S. Oksuz and K. Yildiz designed the study protocol, analyzed the integrity of clinical data, and revised it. N. Narin and R. Aktas contributed to the conception and design, acquisition, and critically revised the manuscript, gave final approval, and agreed to be accountable for all aspects of work, ensuring integrity and accuracy. M.A. Atlan and S. Oksuz critically reviewed the article. R. Aktas and E. Gerceker contributed to the design, collected clinical data, and interpreted the results. C. Karadeniz provided editing and supervision. S. Oksuz took the lead in writing and reviewing the entire draft. All authors critically discussed the results and read and approved the final draft.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- The transcatheter closure of perimembranous VSD offers advantages such as less trauma, faster recovery, and a reduced length of stay vs surgical procedures.
- One of the most serious complications of transcatheter closure is CAVB and LBBB, which can develop, particularly in small and low-weight children.
- The development of heart block may be associated with factors such as the anatomical proximity of the device to the conduction system, inappropriate and large device selection, and device malapposition relative to the septal aneurysm.
- The rate of CAVB has been reported between 0% and 6.4%. This rate, however, has been decreasing in recent years with the use of newly developed devices.
- Although CAVB and LBBB usually occur within the first week after the procedure, they can occur later as well.
- Early diagnosis, steroid therapy, temporary pacemaker implantation, and device removal if necessary can restore sinus rhythm in most cases.

WHAT DOES THIS STUDY ADD?

- This study presents original data on the development of conduction block following transcatheter perimembranous closure of VSD in underweight children.
- In particular, the use of new-generation, flexible, and small-sized devices (eg, Konar-MF) has demonstrated that procedural success and safety can be improved.
- The study highlights that serious complications, such as conduction block primarily emerge in the early stages; however, with appropriate patient selection, close follow-up, and prompt intervention, these complications can be largely reversed.
- By emphasizing the importance of patient selection and device selection in low-weight and small children, the study supports the transcatheter closure of VSD as a safe and effective option for this patient group.
- The study contributes to the literature, particularly in terms of complication management and device selection in high-risk patient groups.

REFERENCES

1. Schubert S. Current and new perspectives for interventional closure of ventricular septal defect. *Kardiol Pol.* 2021;79:378-379.
2. Bai Y, Xu X-D, Li C-Y, et al. Complete atrioventricular block after percutaneous device closure of perimembranous ventricular septal defect: A single-center experience on 1046 cases. *Heart Rhythm.* 2015;12:2132-2140.
3. Yildiz K, Narin N, Oksuz S, et al. Safety and efficacy of Amplatzer duct occluder II and Konar-MF™ VSD occluder in the closure of perimembranous ventricular septal defects in children weighing less than 10 kg. *Front Cardiovasc Med.* 2023;10:1255808.
4. Landman G, Kipps A, Moore P, Teitel D, Meadows J. Outcomes of a modified approach to transcatheter closure of perimembranous ventricular septal defects. *Catheter Cardiovasc Interv.* 2013;82:143-149.
5. Saurav A, Kaushik M, Alla VM, et al. Comparison of percutaneous device closure versus surgical closure of peri-membranous ventricular septal defects: A systematic review and meta-analysis. *Catheter Cardiovasc Interv.* 2015;86:1048-1056.
6. Wu Z, Yang P, Xiang P, Ji X, Tian J, Li M. Left anterior fascicular block after transcatheter closure of ventricular septal defect in children. *Front Cardiovasc Med.* 2021;8:609531.
7. Bergmann M, Germann CP, Nordmeyer J, Peters B, Berger F, Schubert S. Short- and long-term outcome after interventional VSD closure: A single-center experience in pediatric and adult patients. *Pediatr Cardiol.* 2021;42:78-88.
8. Yang L, Tai BC, Khin LW, Quek SC. A systematic review on the efficacy and safety of transcatheter device closure of ventricular septal defects (VSD). *J Interv Cardiol.* 2014;27:260-272.
9. Walsh MA, Bialkowski J, Szkutnik M, Pawelec-Wojtalik M, Bobkowski W, Walsh KP. Atrioventricular block after transcatheter closure of perimembranous ventricular septal defects. *Heart.* 2006;92:1295-1297.
10. Butera G, Carminati M, Chessa M, et al. Transcatheter closure of perimembranous ventricular septal defects: Early and long-term results. *J Am Coll Cardiol.* 2007;50:1189-1195.
11. Wang C, Zhou K, Luo C, et al. Complete left bundle branch block after transcatheter closure of perimembranous ventricular septal defect. *JACC Cardiovasc Interv.* 2019;12:1625-1633.
12. Haddad RN, Houeijeh A, Odemis E, et al. MIOS-MFO, a multicenter international observational study of the Lifetech KONAR-MF ventricular septal defect occluder in treating perimembranous ventricular septal defects. *Rev Esp Cardiol.* 2025. https://doi.org/10.1016/j.rec.2025.02.010.
13. Jiang D, Zhang S, Zhang Y, et al. Predictors and long-term outcomes of heart block after transcatheter device closure of perimembranous ventricular septal defect. *Front Cardiovasc Med.* 2022;9:1041852.
14. Yang R, Kong X-Q, Sheng Y-H, et al. Risk factors and outcomes of post-procedure heart blocks after transcatheter device closure of perimembranous ventricular septal defect. *JACC Cardiovasc Interv.* 2012;5:422-427.

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Original article

Access to transcatheter aortic valve implantation: interregional variability and expert evaluation

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ABSTRACT

Introduction and objectives: Transcatheter aortic valve implantation (TAVI) has revolutionised the treatment of severe symptomatic aortic stenosis, providing an alternative to surgical valve aortic replacement, especially in high-risk patients. Despite its benefits, significant interregional variability in TAVI access persists within Spain. This study aimed to analyse disparities in TAVI implementation across different autonomous communities, identifying the key factors underlying this variability.
Methods: We conducted a retrospective observational study using data from the Spanish National Registry of Specialized Care Activity Minimum Basic Data Set for 2016–2023, including all TAVI performed in Spain. Additionally, a survey was distributed among specialists from 123 centres to assess the factors influencing clinical decision-making, barriers to access, and resource availability.
Results: Although the number of TAVI increased across all regions, significant differences were observed in the implantation rates (between 0.63 and 2.28 per 10 000 inhabitants). Survey responses indicated that the primary determinants for TAVI indication were heart team judgment (40.0%) and patient risk stratification (36.5%). The main barriers to expanding TAVI access included rigid patient stratification (25.6%), insufficient early detection (17.8%), and resource limitations (13.3%). Participants emphasized the need for better coordination among health care levels and establishing uniform access criteria.
Conclusions: Although TAVI adoption has increased in Spain, significant regional disparities remain, suggesting factors beyond economics contribute to access variability. Addressing these inequalities requires enhanced coordination across different health care levels, optimized resource allocation, and refined patient selection strategies.

Keywords: Transcatheter aortic valve implantation. Aortic valve stenosis. Health inequities. Health services accessibility. Delivery of health care.

Acceso al implante percutáneo de válvula aórtica: variabilidad interregional y valoración de expertos

ABSTRACT

Introducción y objetivos: El implante percutáneo de válvula aórtica (TAVI) ha revolucionado el tratamiento de la estenosis aórtica grave sintomática, ofreciendo una alternativa al reemplazo quirúrgico, en especial en pacientes de alto riesgo. A pesar de sus beneficios, persiste una significativa variabilidad interregional en el acceso al TAVI en España. Este estudio tuvo como objetivo analizar las disparidades en la implementación del TAVI entre las distintas comunidades autónomas, e identificar los factores determinantes de la variabilidad.
Métodos: Se realizó un estudio observacional retrospectivo con datos del Registro de Actividad de Atención Especializada Conjunto Mínimo Básico de Datos para el periodo 2016-2023, abarcando todos los procedimientos de TAVI realizados en España. Además, se distribuyó una encuesta entre especialistas de 123 centros para evaluar los factores que pueden influir en la toma de decisiones clínicas, las barreras de acceso y la disponibilidad de recursos.

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Resultados: El número de procedimientos de TAVI aumentó en todas las regiones, pero se observaron diferencias significativas en las tasas de implantación, que se situaron entre 0,63 y 2,28 por 10.000 habitantes. Las respuestas de la encuesta indicaron que los principales determinantes para la indicación de TAVI fueron el criterio del equipo médico (40,0%) y la estratificación del riesgo del paciente (36,5%). Las principales barreras para incrementar el acceso al TAVI incluyeron la estratificación rígida de los pacientes (25,6%), la detección temprana insuficiente (17,8%) y las limitaciones de recursos (13,3%). Los participantes subrayaron la necesidad de mejorar la coordinación entre los niveles asistenciales y la estandarización de los criterios de acceso.
Conclusiones: Aunque la adopción del TAVI en España ha crecido, persisten importantes disparidades regionales que no pueden explicarse únicamente por factores económicos. Para abordar estas desigualdades es necesario mejorar la coordinación entre niveles asistenciales, optimizar la asignación de recursos y perfeccionar las estrategias de selección de pacientes.

Palabras clave: Implante percutáneo de válvula aórtica. Estenosis de válvula aórtica. Inequidades en salud. Accesibilidad de los servicios de salud. Atención a la salud.

Abbreviations

AC.: autonomous communities. **AS:** aortic stenosis. **SNS:** Spanish National Health Service. **TAVI:** transcatheter aortic valve implantation.

INTRODUCTION

Aortic stenosis (AS) is the most common valvular heart disease, with a prevalence of 3% in individuals older than 65 years and 7.4% in those older than 85 years. AS is more common in men.[1,2] It is the leading cause of valve surgery in the adult population,[3] and is associated with risk factors such as advanced age.[4,5] Although aortic stenosis typically develops after age 60, symptoms usually present between ages 70 and 80; once symptoms occur, the mortality rate may reach 50% within the next few years.[4,6]

Transcatheter aortic valve implantation (TAVI), initially reserved for patients deemed ineligible for surgical aortic valve replacement,[7-11] was subsequently expanded to include those at intermediate risk and, more recently, patients at low risk.[5,12-14]

In Spain, the use of TAVI has increased,[5] reflecting its growing acceptance within the Spanish National Health System (SNS), largely attributable to improved clinical and economic outcomes.[5,15] Multiple studies have demonstrated the benefits of TAVI, including significant improvements in quality of life,[16,17] lower rates of major complications,[18] and reduced mortality.[5,19,20]

Nationwide, improvements in TAVI outcomes, shorter lengths of stay, and lower mortality rates have been reported. Furthermore, autonomous communities (AC) with higher implant volumes have a better safety and efficacy profile, lower risks of infection, reduced need for permanent pacemaker implantation, and shorter lengths of stay.[5] However, the distribution of TAVI reveals notable interregional disparities, with procedural rates varying considerably according to hospital resources and volumes.[21]

Despite these advances, in Spain, TAVI use remains significantly lower compared with other European countries.[22] Furthermore, Spain exhibits one of the highest variations in access and utilization rates among its AC (42%), which cannot be explained solely by economic differences, hospital utilization, or observed mortality.[21] An analysis by de la Torre Hernández et al.[21] described the need for strategies to promote equity in TAVI access across Spain.

This study analyzed heterogeneity in the use of TAVI across AC (2016–2023) and identified the factors associated with this inequality.

METHODS

TAVI data in Spain from 2016 through 2023

Data on TAVI performed from 2016 to 2023 were obtained from the Specialized Care Activity Minimum Basic Data Set[23-25] using the International Classification of Diseases, 10th revision for Spain (ICD-10-ES) (supplementary data 1). This mandatory registry, which includes all specialized care centers, is managed by the Spanish Ministry of Health and ensures strict compliance with privacy and data protection standards. The analysis included all TAVI performed in public and private hospitals across AC.

Survey

Simultaneously, we designed a survey to gather information on therapeutic decision-making in patients with AS to identify possible factors influencing TAVI implementation and interregional variability previously observed. This survey was distributed to department heads of the 123 medical centers affiliated with the Interventional Cardiology Association of the Spanish Society of Cardiology. Respondents were asked to extend the invitation to other department members to ensure representative and diverse responses.

The survey (supplementary data 2) covered clinical, structural, organizational, and patient-related aspects relevant to clinical practice during the study period, and was structured into 3 thematic blocks:

- Center and participant characteristics (questions A1–C3): evaluation of institutional context and department composition, including variables such as the respondent's specialty and annual budget allocation.
- Patient selection and decision-making (questions C4–E2): identification of key clinical and demographic factors influencing therapeutic choice, as well as barriers and determinants shaping clinical team decisions.
- Center evaluation and TAVI use (questions E3–F9): assessment of clinician perception and satisfaction regarding TAVI, and exploration of adoption, implementation, and geographic distribution of this strategy.

Responses were analyzed descriptive and qualitatively, allowing a comprehensive interpretation of factors influencing TAVI implementation and interregional heterogeneity.

RESULTS

TAVI in 2016–2023

The results of TAVI interventions, expressed as the number of cases and intervention rates per 10 000 inhabitants, are shown in figure 1. All AC experienced an increase in procedures during the study period (figure 1A), with the greatest growth observed in the Canary Islands (33 cases in 2016 and 368 in 2023) and La Rioja (2 cases in 2016 and 28 in 2023), corresponding to increases of 1.115% and 1.400%, respectively. The AC with the highest number of TAVI performed in 2023 were Andalusia (n = 1392), Catalonia (n = 1245), and the Community of Madrid (n = 1257). La Rioja had the fewest (2 cases in 2016, 28 in 2023).

Procedure rates (figure 1B) indicated that, in 2023, the AC with the highest per capita TAVI volumes were Galicia (2.82 per 10 000 inhabitants), Asturias (2.18 per 10 000), Cantabria (2.00 per 10 000), Castile and León (2.00 per 10 000), and Madrid (1.82 per 10 000), all above the national average (1.65 per 10 000). The lowest per capita TAVI volumes were found in Extremadura (1.24 per 10 000), the Balearic Islands (1.13 per 10 000), Aragón (1.12 per 10 000), La Rioja (0.87 per 10 000), and Castile-La Mancha (0.63 per 10 000).

The mean in-hospital mortality rate during the study period was 3.07% (figure 1C).

Survey

Center and participant characteristics

The survey was completed by 26 specialists with different TAVI-related profiles: 18 in interventional cardiology, 7 in clinical cardiology, and 1 in cardiac imaging, including 4 heads of cardiac surgery departments and 18 cath lab directors. The respondents' mean professional experience was 26.5 years (range, 9–41 years) and worked in hospitals with a mean TAVI experience of 10.6 years (range, 1–16 years). Responses were obtained from hospitals in 11 of the 17 AC (64.7% of the national territory). Team composition by professional profile is provided in supplementary data 3.

Teams performed a mean of 76 TAVI (range, 0–148) in 2021 and 95 (range, 0–254) in 2022, with marked variation across hospitals. Annual budgets allocated to units ranged from €474 765 to €25 111 709, reflecting wide disparities in resource availability. Despite these differences, most respondents reported being satisfied with the extent to which purchasing committees allocated budgets to meet their teams' clinical needs (19.2%, very satisfied; 42.3%, quite satisfied; 34.6%, moderately satisfied; 3.9%, unsatisfied).

Most participants rated continuity of care across different settings as good or improvable (54.9% and 38.5%, respectively) and gave examples of best practices as well as areas for improvement. Best practices included teleconsultation, specialized programs such as TAVI Nurse,[26] periodic cross-level meetings, and shared protocols between primary and hospital care. Suggested improvements included insufficient coordination between primary and specialized care, overloaded schedules, and the need to improve clinical information systems such as integrating joint activities.

Patient selection and decision-making

The clinical indication for TAVI was determined primarily by heart team judgment (40.0%) and patient stratification (36.5%), followed by patient preference (12.5%) and resource availability (10.4%). Barriers to expanding TAVI included rigid patient stratification (25.6%), insufficient early detection (17.8%), intra-team discrepancies (14.2%), insufficient budget (13.3%) and technology (11.8%), and obstacles to multidisciplinary team integration (7.4%).

Most centers had decision-support tools for TAVI (76.9%) and specific training programs (65.4%). Tools included decision algorithms, clinical practice guidelines, consensus protocols, and software for anatomical, feasibility, and comorbidity assessment. Specific training and periodic multidisciplinary meetings were also in place.

Most centers (76.9%) conducted periodic evaluations of outcomes—described as continuous process evaluation—to optimize procedures, including registries, internal audits, analysis of complications, in-hospital mortality, and readmissions. Annual and monthly clinical meetings allowed protocol adjustments and improved care processes, with high adherence to international clinical practice guidelines.

On the other hand, respondents indicated limited satisfaction with information exchange among departments and specialists involved in TAVI decision-making (figure 2A).

The survey on patient profiles treated with TAVI, which is performed primarily in intermediate- and high-risk patients, showed that 96.2% of centers treat high-risk patients; 76.9%, intermediate-risk patients; and only 30.8%, low-risk patients. In general, although no major barriers to treatment based on risk profile were reported (69.3% responded negatively), some resistance from cardiac surgery (n = 5), disagreement with institutional protocols (n = 4), and infrastructure limitations expressed as restricted availability of cath labs (n = 3) were noted.

Similarly, respondents perceived that the professional background of team members influences clinical decision-making for TAVI (63.6% strongly agreed and 27.3% moderately agreed; n = 11), highlighting the importance of training, experience, and individual performance. Multidisciplinary, consensus-based decisions among specialists in clinical cardiology, imaging, interventional cardiology, and cardiac surgery allow for the consideration of specific anatomic and clinical factors. Although such multidisciplinary teams promote more objective decision-making, participation from cardiac surgery may affect the indication in low-risk patients.

Therefore, participants considered the heart team's judgment on additional factors in the indication for TAVI to be relevant, rating it as fairly (50%) or very relevant (50%). Similarly, respondents reported overall satisfaction with the process by which clinical decisions were made within the team: 53.8% found it fairly satisfactory; 38.5%, very satisfactory; 7.7%, moderately satisfactory.

There was near-unanimous agreement (96%) on the importance of incorporating the patient's opinion into the decision-making process for TAVI indication. When ranking the key factors guiding clinical decision-making, comorbidity and age stratification were rated as the most relevant (figure 3).

The leading criteria for inclusion on the TAVI waiting list were the presence of comorbidities (n = 22), clinical status or overall risk (n = 20), followed by the minimum (n = 17) and maximum age threshold (n = 2).

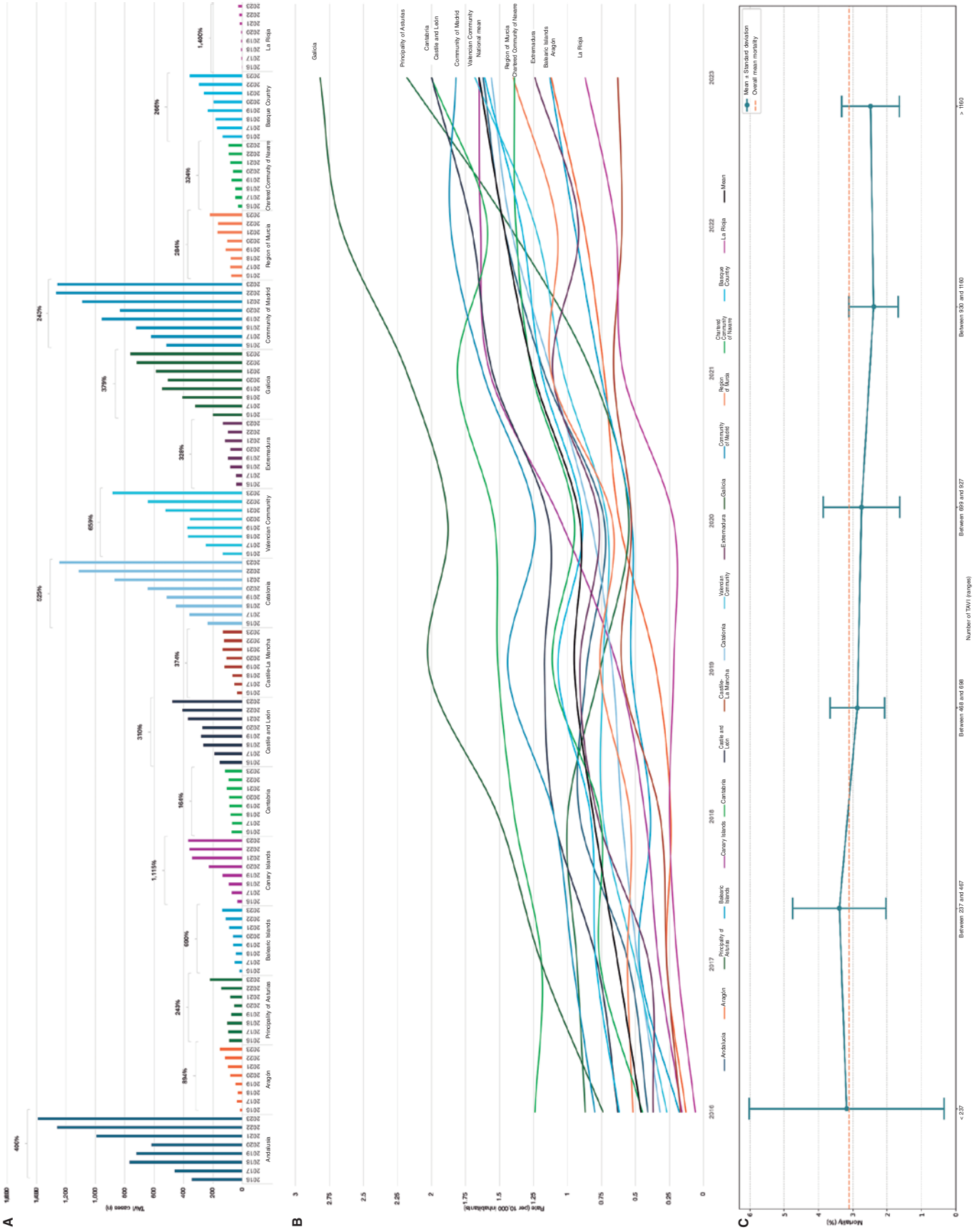

Figure 1. **A:** total number of transcatheter aortic valve implantation (TAVI) cases by autonomous community and year (2016–2023). **B:** population-adjusted procedural rates adjusted (per 10 000 inhabitants) by autonomous community and year (2016–2023). **C:** mean and dispersion of mortality based on the number of TAVI.

Figure 2. A: respondents' evaluation of information exchange across departments, committees, and professionals involved in decision-making for aortic valve replacement. **B:** respondents' evaluation of information exchange and best practices across centers performing transcatheter aortic valve implantation in Spain.

The mean waiting time for the procedure was approximately 2 months (mean, 1.92 months; range, 0–4 months). Compared with surgical aortic valve replacement, the waiting list was generally perceived as shorter (50.0%) or equivalent (26.9%).

The primary factors influencing waiting time for TAVI were the need for computed tomography (n = 7) and cath lab availability (n = 5). Other factors included computed tomography availability (n = 3), anesthesia availability (n = 3), and waiting list length (n = 2). In line with this, respondents indicated that most patients (88.5%) undergo TAVI as scheduled procedures

Center evaluation and TAVI use

Most respondents considered the number of centers performing TAVI in Spain sufficient (n = 18, 24 respondents) and highlighted the importance of ensuring adequate procedural volume per center to optimize outcomes and minimize complications. Strengthening infrastructure, human resources, and networking was considered essential, prioritizing quality and safety over opening new centers.

Likewise, participants were generally satisfied with the exchange of information and best practices among TAVI centers in Spain (figure 2B).

There was consensus that improving the early detection of AS would, in turn, improve outcomes and patient experience (91.7%; n = 24). Conversely, most considered that regulatory thresholds for accrediting centers would not substantially affect total TAVI volume (62.5%; n = 24).

Finally, participants shared additional considerations. They emphasized prioritizing safety and clinical outcomes in TAVI programs beyond simply increasing the number of available centers. Although concentration of procedures in high-volume centers was suggested to improve health outcomes, it could also reduce the total number of procedures. The need for audits and dissemination of risk-adjusted results was highlighted to ensure transparency and care quality. Lastly, concern was expressed about the impact of health system fragmentation on equity of access.

DISCUSSION

The present study confirms the upward trend in TAVI implantation in Spain, which is consistent with previous research.[5,22] From 2016 through 2023, the number of procedures increased in all AC, reflecting broader acceptance of this technique within the SNS. This trend is attributed to the consolidation of TAVI as a reference therapeutic alternative for the treatment of severe symptomatic AS, progressively expanding from high-risk to intermediate- and low-risk patients.[12-14]

Despite this generalized increase, results show notable interregional variability in TAVI rates. In 2023, some AC reported procedural rates well above the national average, while others were considerably lower. This inequality has been documented previously and suggests a key role for organizational factors in determining access to the procedure.[21] Of note, in regions such as La Rioja, the absence of local cardiac surgery centers may partly explain the low number of TAVI. However, this does not mean that patients are not treated; rather procedures are performed in neighboring AC.

From a clinical perspective, multiple studies have shown that TAVI reduces in-hospital mortality, improves quality of life, and decreases the rate of major complications.[16-20] Although these outcomes were not directly assessed in the present study, former studies have identified a relationship between higher procedural volume and improved outcomes, including reduced infection risk, decreased pacemaker need, and a shorter length of stay.[5] Our analysis does not allow a direct correlation to be established between procedural volume and quality of care in Spain. This suggests that, although cumulative experience is a determinant of improved outcomes, other organizational and resource-management factors may also contribute to the observed discrepancies. Nonetheless, our findings

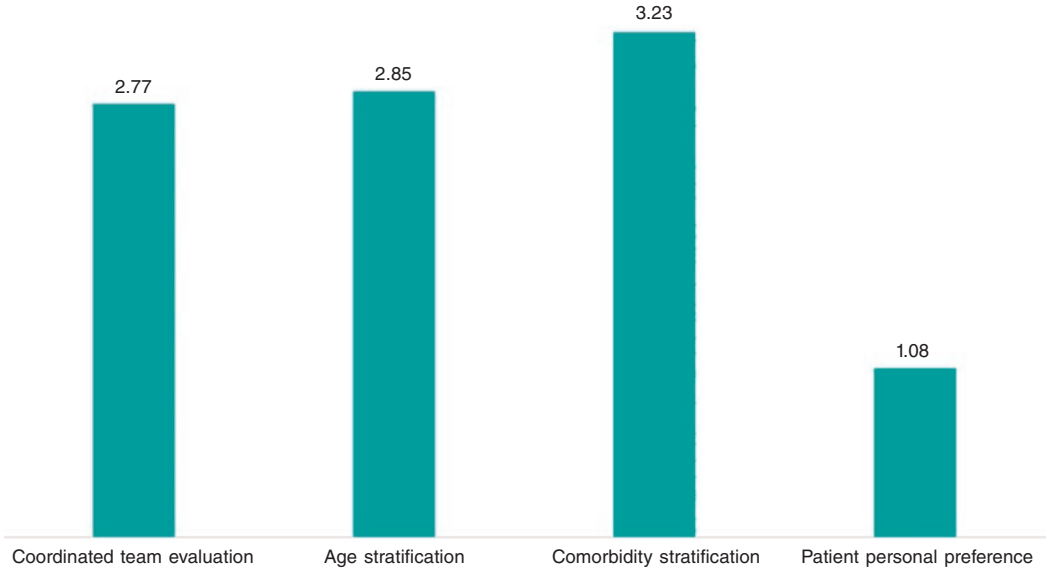

Figure 3. Weighted average of responses ranking factors by relevance in the clinical decision to indicate transcatheter aortic valve implantation.

indicate that as TAVI volume increases, the variability in mortality outcomes tends to diminish, suggesting greater standardization of practice and reduced variability across more experienced centers.

The survey analysis revealed that TAVI indication in Spain continues to depend primarily on physician judgment and patient risk stratification, with less influence from patient preference or resource availability. These findings are consistent with former studies underscoring the importance of multidisciplinary clinical judgment in decision-making, which results in patient selection aligned with clinical practice guidelines and safety criteria.[27] However, organizational barriers hindering the expansion of TAVI were identified, including rigid patient stratification, insufficient identification of candidates, and difficulties integrating heart teams. Such limitations have previously been recognized as determinants of inequality in TAVI access in Spain,[21] reinforcing the need for strategies to optimize care.

From a financial perspective, TAVI has been shown to be cost-effective compared with conventional surgical aortic valve replacement across various clinical scenarios.[15,28] In our study, however, participants did not identify financing as a major barrier to expansion. This finding is consistent with prior Spanish investigations, which found no clear correlation between regional health spending and TAVI rates,[5,21] suggesting that variability is more strongly influenced by organizational rather than economic factors.

The perception of infrastructure is relevant too, as most respondents considered the number of centers performing TAVI in Spain sufficient, while emphasizing the importance of guaranteeing a minimum procedural volume per center to optimize outcomes and minimize complications. Former studies have highlighted that cumulative team experience can improve clinical outcomes.[27] However, no consensus was reached in this study on whether concentrating procedures in a smaller number of centers would favor equity of access or, conversely, limit availability in regions with restricted supply.

With respect to continuity of care, both advances and opportunities for improvement were identified. While > 90% of specialists positively evaluated the implementation of teleconsultation, specialized nursing programs (TAVI Nurse[26]), and shared protocols across levels of care, participants also emphasized the need to strengthen coordination between primary and specialized care, improve clinical information systems, and optimize scheduling management. These aspects have previously been highlighted as important for improving the efficiency of TAVI care processes[5] and identified as cross-cutting priorities in the 2022 report of the SNS, *Estrategia en Salud Cardiovascular*.[29]

Limitations

This study has certain limitations. First, although the analysis of the Specialized Care Activity Minimum Basic Data provides information on overall TAVI trends, the Spanish Ministry of Health's statistical portal does not include detailed patient-level clinical data, thus preventing assessment of outcomes such as complications.

Second, although the survey was designed to achieve representation from all AC, responses were obtained from only 11 of them (26 of 123 [21%] affiliated centers of the Interventional Cardiology Association), meaning that the perceptions and experiences reflected are drawn from a subset of regions, which may influence interpretation of certain findings. Nevertheless, this limitation is inherent to survey-based research, as participation greatly depends on availability and willingness of respondents. Despite this, the sample offers a representative perspective on organizational and clinical factors influencing variability in TAVI access within the SNS.

Finally, sex and gender variables were not considered in accordance with the SAGER guidelines, as the focus was on regional differences across AC. Future studies should explore sex- and gender-related influences on TAVI implementation.

CONCLUSIONS

Our findings reflect sustained growth in TAVI implementation in Spain, alongside marked interregional variability in procedural rates. Patient selection is driven primarily by physician judgment and clinical risk, while barriers to expansion are more organizational than financial. Key strategies are suggested to reduce regional variability and ensure equitable TAVI access within the SNS, including improved coordination across different levels of care, standardization of selection criteria, and strengthened resource management.

FUNDING

This work was funded by Edwards Lifesciences.

ETHICAL CONSIDERATIONS

Approval from the study ethics committee was deemed unnecessary, as it used administrative data from the Spanish Ministry of Health without accessing patient-level data. Similarly, informed consent was deemed unnecessary. Sex and gender variables were not analyzed in accordance with the SAGER guidelines, as the study focused on regional differences across AC.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used in this study.

AUTHORS' CONTRIBUTIONS

All authors were involved in the study design. A. Morán-Aja, O. Martínez-Pérez, M. Cerezales, and J. Cuervo requested the data and implemented the web-based survey. O. Martínez-Pérez conducted data analysis. All authors reviewed and validated the results. A. Morán-Aja, O. Martínez-Pérez, M. Cerezales, and J. Cuervo drafted the manuscript. All authors reviewed and approved the final version.

CONFLICTS OF INTEREST

J.M. de la Torre-Hernández is editor-in-chief of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure impartial handling of the manuscript. A. Morán-Aja, O. Martínez-Pérez, M. Cerezales, and J. Cuervo work for Axentiva Solutions S.L., a consultancy providing services to various pharmaceutical and medical device companies.

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WHAT IS KNOWN ABOUT THE TOPIC?

- TAVI has revolutionized the treatment of severe AS, becoming a first-line option in high- and intermediate-risk patients. It has demonstrated advantages over conventional surgery, including reduced mortality, a shorter length of stay, and improved quality of life. In Spain, TAVI use has grown unevenly across AC, influenced not only by economic factors but also by organizational and structural differences in patient selection criteria and resource availability. However, the impact of this variability on clinical outcomes and equity of access remains unclear.

WHAT DOES THIS STUDY ADD?

- This study provides a comprehensive analysis of interregional variability in TAVI implementation in Spain, combining the Specialized Care Activity Minimum Basic Data Set with a specialist survey. Compared with former studies, it not only identifies differences in implementation rates across AC but also organizational, structural, and care-related barriers influencing access. Furthermore, it evaluates professional perceptions of team composition in clinical decision-making and challenges in continuity of care. These findings improve understanding of the determinants of heterogeneity in TAVI access and offer recommendations to enhance equity of implementation within the SNS. Results may be key for health policy planning and the design of strategies to optimize resource allocation and ensure more uniform access to this technology.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at: https://doi.org/10.24875/RECICE.M25000533.

REFERENCES

1. Ferreira-González I, Pinar-Sopena J, Ribera A, et al. Prevalence of calcific aortic valve disease in the elderly and associated risk factors: a population-based study in a Mediterranean area. *Eur J Prev Cardiol*. 2013;20:1022-1030.
2. Stewart BF, Siscovick D, Lind BK, et al. Clinical Factors Associated With Calcific Aortic Valve Disease. *J Am Coll Cardiol*. 1997;29:630-634.
3. Salinas P, Moreno R, Calvo L, et al. Long-term Follow-up After Transcatheter Aortic Valve Implantation for Severe Aortic Stenosis. *Rev Esp Cardiol*. 2016;69:37-44.
4. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of Aortic-Valve Sclerosis with Cardiovascular Mortality and Morbidity in the Elderly. *New Engl J Med*. 1999;341:142-147.
5. Íñiguez-Romo A, Zueco-Gil JJ, Álvarez-Bartolomé M, et al. Outcomes of transcatheter aortic valve implantation in Spain through the Activity Registry of Specialized Health Care. *REC Interv Cardiol*. 2022;4:123-131.
6. Ramaraj R, Sorrell VL. Degenerative aortic stenosis. *BMJ*. 2008;336:550-555.
7. Van Hemelrijck M, Taramasso M, De Carlo C, et al. Recent advances in understanding and managing aortic stenosis. *F1000Res*. 2018;7:58.
8. Maldonado Y, Baisden J, Villablanca PA, Weiner MM, Ramakrishna H. General Anesthesia Versus Conscious Sedation for Transcatheter Aortic Valve Replacement — An Analysis of Current Outcome Data. *J Cardiothorac Vasc Anesth*. 2018;32:1081-1086.
9. Perrin N, Frei A, Noble S. Transcatheter aortic valve implantation: Update in 2018. *Eur J Intern Med*. 2018;55:12-19.
10. Leon MB, Smith CR, Mack M, et al. Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. *New Engl J Med*. 2010;363:1597-1607.
11. Duncan A, Ludman P, Banya W, et al. Long-Term Outcomes After Transcatheter Aortic Valve Replacement in High-Risk Patients With Severe Aortic Stenosis. *JACC Cardiovasc Interv*. 2015;8:645-653.
12. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;43:561-632.
13. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *New Engl J Med*. 2019;380:1695-1705.
14. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *New Engl J Med*. 2019;380:1706-1715.

15. Pinar E, de Lara JG, Hurtado J, et al. Cost-effectiveness analysis of the SAPIEN 3 transcatheter aortic valve implant in patients with symptomatic severe aortic stenosis. *Rev Esp Cardiol*. 2022;75:325-333.
16. Tamm AR, Jobst ML, Geyer M, et al. Quality of life in patients with transcatheter aortic valve implantation: an analysis from the INTERVENT project. *Front Cardiovasc Med*. 2023;10:181771.
17. van Nuland PJA, van Ginkel DJ, Overduin DC, et al. The impact of stroke and bleeding on mortality and quality of life during the first year after TAVI: A POPular TAVI subanalysis. *Catheter Cardiovasc Interv*. 2024;104: 1107-1118.
18. Zhang S, Kolominsky-Rabas PL. How TAVI registries report clinical outcomes — A systematic review of endpoints based on VARC-2 definitions. *PLoS One*. 2017;12:e0180815.
19. Gargiulo G, Sannino A, Capodanno D, et al. Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement. *Ann Intern Med*. 2016;165:334.
20. Sehatzadeh S, Doble B, Xie F, et al. Transcatheter aortic valve implantation (TAVI) for treatment of aortic valve stenosis: an evidence update. *Ont Health Technol Assess Ser*. 2013;13:1-40.
21. de la Torre Hernández JM, Lozano González M, García Camarero T, et al. Interregional variability in the use of cardiovascular technologies (2011-2019). Correlation with economic indicators, admissions, and in-hospital mortality. *Rev Esp Cardiol*. 2022;75:805-815.
22. Biagioni C, Tirado-Conte G, Nombela-Franco L, et al. Situación actual del implante transcatéter de válvula aórtica en España. *Rev Esp Cardiol*. 2017; 70(Supl 1):477.
23. Ministerio de Sanidad. Registro de Actividad de Atención Especializada, Conjunto Mínimo Básico de Datos. Available at: https://www.sanidad. gob. es/estadEstudios/estadisticas/cmbdhome.htm. Accessed 8 Apr 2024.
24. Ministerio de Sanidad. Registro de Actividad de Atención Sanitaria Especializada (RAE-CMBD). Actividad y resultados de la hospitalización en el SNS. Año 2022. Madrid: Ministerio de Sanidad; 2024. Available at: https://www.sanidad.gob.es/estadEstudios/estadisticas/docs/RAE-CMBD_Informe_Hospitalizacion_2022.pdf. Accessed 29 May 2025.
25. Ministerio de Sanidad. Registro de Atención Sanitaria Especializada RAE-CMBD. Manual de Usuario y Glosario de Términos. Portal Estadístico; 2023. Available at: https://pestadistico.inteligenciadegestion.sanidad.gob. es/publicoSNS/D/rae-cmbd/rae-cmbd/manual-de-usuario/manual-de-usuario-rae. Accessed 29 May 2025.
26. González Cebrián M, Valverde Bernal J, Bajo Arambarri E, et al. Documento de consenso de la figura TAVI Nurse del Grupo de Trabajo de Hemodinámica de la Asociación Española de Enfermería en Cardiología. *Enfermería en Cardiología*. 2022;24:5-13.
27. Carnero-Alcázar M, Maroto-Castellanos LC, Hernández-Vaquero D, et al. Isolated aortic valve replacement in Spain: national trends in risks, valve types, and mortality from 1998 to 2017. *Rev Esp Cardiol*. 2021;74: 700-707.
28. Baron SJ, Magnuson EA, Lu M, et al. Health Status After Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients With Aortic Stenosis. *J Am Coll Cardiol*. 2019;74:2833-2842.
29. Ministerio de Sanidad. Estrategia en Salud Cardiovascular del Sistema Nacional de Salud (ESCAV). 2022. Available at: https://www.sanidad.gob.es/areas/calidadAsistencial/estrategias/saludCardiovascular/docs/Estrategia_de_salud_cardiovascular_SNS.pdf. Accessed 29 May 2025.

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Review article

Embolization of left atrial appendage occluders: review of the current evidence

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ABSTRACT

Percutaneous left atrial appendage closure has emerged as a promising procedure for patients with non-valvular atrial fibrillation with a very high or prohibitive bleeding risk. It is a safe technique, with a low rate of complications; however, complications, such as device embolization can be potentially serious, and decision-making as well as selecting the most appropriate strategy may be challenging due to the limited evidence available in this context. This review provides an overview of the most critical aspects of left atrial appendage closure device embolization focusing on its prevalence, management strategies, and treatment options.

Keywords: Left atrial appendage closure. Embolization. Devices.

Embolización de dispositivos de cierre de la orejuela izquierda: revisión de la evidencia disponible

RESUMEN

El cierre percutáneo de la orejuela izquierda ha ido emergiendo como un procedimiento cada vez más prometedor para pacientes con fibrilación auricular no valvular y riesgo hemorrágico muy alto o prohibitivo. Se trata de una técnica segura, con un porcentaje de complicaciones bajo; sin embargo, algunas de ellas, como la embolización del dispositivo, pueden ser graves, y la toma de decisiones y la estrategia más adecuada pueden ser difíciles debido a la escasa evidencia disponible. La presente revisión proporciona un resumen de los aspectos más importantes sobre la embolización de dispositivos de cierre de la orejuela izquierda, tanto en su prevalencia como en su abordaje y las opciones de tratamiento.

Palabras clave: Cierre de orejuela. Embolización. Dispositivos.

Abbreviations

LAA: left atrial appendage. **LV:** left ventricle. **TEE:** transesophageal echocardiogram.

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INTRODUCTION

Atrial fibrillation has become the most common arrhythmia of our time. Its estimated prevalence in the Spanish population is 4.4% among individuals older than 40 years, which, in absolute numbers, translates into > 1 million Spaniards living with this rhythm disorder.[1] There has been solid evidence for years regarding its association with an increased rate of stroke and cardiovascular mortality in both sexes,[2,3] which is why therapeutic-dose anticoagulation a fundamental pillar in the treatment of these patients. However, in patients with high or prohibitive bleeding risk, percutaneous left atrial appendage closure has emerged as a reasonable and noninferior alternative to anticoagulation regarding cardioembolic events, cardiovascular mortality, and clinically relevant hemorrhage.[4]

Although intraoperative and post-implantation complication rates remain low, the increasing global use of these devices has led to a current embolization rate of approximately 0%–1.5% of all procedures.[5]

This review summarizes the available evidence on embolization of percutaneous left atrial appendage closure devices, including a description of currently available devices, potential predictors of embolization, and recommended management strategies.

TYPES OF DEVICES

Below is a brief description of the 3 device families currently available in our setting.

WATCHMAN family

WATCHMAN devices (Boston Scientific, United States) are single-lobe occlusion systems implanted approximately 10 mm from the left atrial appendage coronary ostium, leaving the ostial opening uncovered.

In 2020, Boston Scientific released the next-generation WATCHMAN FLX, which in a meta-analysis of 54 727 patients demonstrated superiority over its predecessor, WATCHMAN 2.5, in cardiovascular mortality, major hemorrhage, pericardial effusion, and device embolization.[6,7] These advantages are partly attributed to its smaller metal surface—reducing the risk of thrombosis—and its greater number of anchors (18 vs 10), which enhance adaptation to the ostium and reduce residual leaks.[6,7] It is available in 5 sizes, covering ostial diameters from 14 mm to 31.5 mm.

In 2024, the U.S. Food and Drug Administration approved the WATCHMAN FLX Pro device, which features a fluoropolymer-coated fabric membrane designed to enhance thromboresistance and promote endothelialization, potentially allowing shorter postoperative antithrombotic regimens. It has shown promising results in published case reports.[8] A single-center study, the WATCHMAN FLX PRO CT trial (NCT05567172), is currently underway to evaluate the morphology and tissue coverage of the device surface 90 days after implantation. The device has not yet received CE (Conformité Européenne) marking for commercialization in Europe.

Amplatzer family

In 2013, the second-generation Amplatzer Amulet (Abbott, United States) received the CE marking (figure 1A). It features a closure lobe—usually implanted 10 mm to 15 mm away from the coronary ostium—and a disc that fully covers the ostial opening. The 2 components are connected by a central waist. Device sizing is based on the appendage landing zone, the region where the lobe rests. Sizes range from 16 mm to 34 mm to accommodate landing zones from 11 mm to 31 mm.[9]

The Amulet IDE trial[10], which compared the Amplatzer Amulet with the first-generation WATCHMAN device, found a higher rate of left atrial appendage occlusion with the dual-seal device. Furthermore, the study demonstrated the noninferiority of the Amulet regarding its safety and efficacy profile in stroke reduction among patients with nonvalvular atrial fibrillation. However, the rate of adverse events, such as pericardial effusion and device embolization, was nearly twice as high, a finding likely influenced by the greater operator experience at the time with WATCHMAN devices, which may have contributed to higher complication rates with the Amplatzer system.[10] Noninferiority findings remained consistent at 5 years, with a significantly higher proportion of patients free from prescribed anticoagulation in the Amulet group (94% vs 91%; $P = .009$) and a very low annual stroke rate in the 2 groups (1.6% per year), although the rate of fatal stroke was higher in the WATCHMAN group (1.9% vs 1.2%; $P = .03$).[11]

A study comparing the 2 generations of Abbott devices concluded that the second-generation system exhibited a lower rate of residual peridevice leaks, with no significant differences in major complications, mortality, or implantation success.[12]

LAmbre

LAmbre (Lifetech Scientific Corporation, China) is a dual-seal (lobe and disc) occluder (figure 1B). It is available in 15 different sizes (from 16 mm to 36 mm) and is made of a nitinol mesh and polyester membrane. Its design includes 8 distal hooks and 8 U-shaped hooks that enhance stabilization by improving anchoring within the trabeculations. It received the CE marking in 2016.

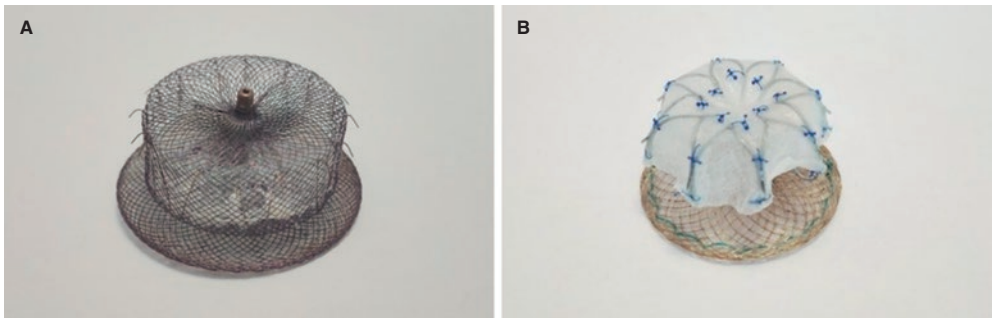

Figure 1. A: Amplatzer device. **B:** LAmbre device.

In a prospective multicenter Chinese study of 103 patients, the LAmbre device achieved a 98.05% implantation success rate. Postoperative pericardial effusion within the first 7 days was reported in 4.95% of patients, none requiring intervention. One patient experienced a stroke at 2 months in the context of reduced anticoagulant dosing. Although there was no device-related thrombosis, mean follow-up was only 12.2 months.[13]

A unique advantage of this device is the possibility of custom manufacturing for anatomically complex or out-of-range appendages.

INCIDENCE RATE OF EMBOLIZATION

Left atrial appendage embolization—whether into a cardiac chamber, a great vessel, or a peripheral artery—is a rare but potentially life-threatening complication, with reported mortality rates of up to 10.2% in published registries. The experience of interventional cardiologists or electrophysiologists performing device implantation, as well as the number of procedures performed annually at each hospital, has been significantly associated with differences in the incidence rate of embolization (0.6% in high-volume centers vs 1.5% in low-volume centers).[5]

The relationship between device type and the rate of embolization is still to be elucidated. The WATCHMAN FLX has demonstrated a lower rate vs its predecessor, the WATCHMAN 2.5 (odds ratio, 0.35; 95%CI, 0.18-0.70; $P < .02$), as shown in a 2023 meta-analysis including 54 727 patients,[6] and an embolization rate of 0% in the PINNACLE FLX study.[7]

For the Amulet device, the Amulet IDE trial—which compared the Amulet with the first-generation WATCHMAN—reported embolization rates of 0.6% and 0.2%, respectively. Nonetheless, the authors suggested that this difference was partly attributable to the lower operator experience with Amulet at that time.[10] In the 2021 SWISS-APERO trial comparing Amulet with WATCHMAN FLX, the embolization rate reached 0.9% of patients in each group.[14]

A 2020 systematic review of 403 patients reported zero embolization events with the LAmbre device.[15] In contrast, a 2024 German study including 118 patients reported an embolization rate of 1.7%; however, procedures were performed without contrast, representing an important limitation when interpreting this higher rate of complications.[16] Spanish series have reported embolization rates close to 0%,[17-18] while an initial Brazilian experience reported an embolization rate of 2% (1 of 51 patients).[19]

Therefore, taken together, these data suggest that the overall rate of device embolization is approximately 1%, with no consistent, clinically meaningful differences among the various devices.

Of note, not only device-related characteristics but also the anatomic and morphologic features of the appendage are among the factors influencing embolization. Cactus-type appendages—those with a dominant central lobe giving rise to numerous small secondary lobes—have been associated with a higher risk of embolization. Similarly, shallow appendages and those with wide necks have been associated with a higher risk of device embolization.[20-21]

Although the patient cardiac rhythm has been proposed as a potential contributor to the risk of embolization, its role is not fully understood. It has been suggested in published case reports[22] that a contractile appendage—that is, one in sinus rhythm—may have a higher risk of device migration or embolization due to greater contractile force vs atrial fibrillation. Furthermore, rhythm conversion, whether from sinus rhythm to atrial fibrillation or vice versa, has been proposed as a mechanism that could facilitate embolization.

A retrospective analysis of WATCHMAN device embolizations using data from the NCDR LAAO registry[23] concluded that patients in sinus rhythm at the time of implantation seemed to have a higher risk of late embolization (within the first 45 days after discharge), possibly because active appendage contraction in sinus rhythm may lead to underestimating the ostial size. If the patient subsequently transitions to atrial fibrillation, a state in which the appendage is typically more dilated, the device may become undersized predisposing migration.[23]

Regarding timing, the review by Eppinger et al.[5] showed that device embolization occurred more commonly in the acute period (within the first 24 hours after implantation), except in peripheral arteries, where late embolization (> 45 days) was a more prevalent finding.

Table 1, figure 2, and figure 3 illustrate the characteristics of all devices and their rates of embolization.

TECHNIQUES TO REDUCE THE RISK OF DEVICE EMBOLIZATION

Multiple factors related to left atrial and appendage anatomy, the procedural technique being used, and device selection may increase the risk of embolization. In May 2023, a consensus document from the Society for Cardiovascular Angiography & Interventions and the Heart Rhythm Society reviewed key considerations for left atrial appendage closure and associated complications.[32] Table 2 illustrates the most relevant points. Selecting the correct device size is essential, as both over- and undersizing increase the risk of embolization. Additionally, operators should be well trained and familiar with the implantation technique (at least 25 transseptal punctures and, at least, of 10 appendage closures as primary operator are recommended), and retrieval techniques (requiring expertise with large-bore introducer sheaths and snare systems). Various imaging modalities can be used throughout the procedure.

- A targeted transesophageal echocardiogram (TEE) should be performed, acquiring bidimensional images in 0°, 45°, 90°, and 135°. Three-dimensional TEE should be used on a routine basis because it provides more accurate sizing. Cardiac CT is increasingly recognized as superior to TEE for procedural planning due to its better spatial resolution and more precise identification of maximal landing zone diameter. Furthermore, three-dimensional reconstructions provide volumetric visualization of the appendage, enhance device-size prediction, and in some cases allow virtual implantation and planning of access routes and transseptal puncture sites.[20]

- In the intraoperative period, the procedure should be guided by fluoroscopy and bidimensional/tridimensional TEE. Although three-dimensional intracardiac echocardiography is emerging as another available imaging modality, it is currently more expensive and complex than TEE, requiring placement of the probe within the left atrium (LA). LA pressure should be measured during the procedure, as underfilled atria tend to produce inaccurate measurements. An important aspect is measuring LA pressure during the procedure, as markedly depleted atria have been shown to produce inaccurate measurements. In general, a LA pressure ≥ 12 mmHg is recommended for correct interpretation. In cases of low atrial pressure, IV fluids may be administered until appropriate parameters are achieved.[32]

- In the immediate postoperative period proper device positioning must be confirmed, and pericardial effusion or other complications must be excluded.

Table 1. Characteristics and embolization rates of CE-marked devices

Device	CE year	Specific characteristics	Embolization rates
WATCHMAN FLX, Boston Scientific	2019	Umbrella-shaped design Smaller metallic surface than its predecessor 18 fixation hooks	PINNACLE FLX,[7] 2021: 0 % SWISS-APERO,[14] 2021: 0.9% SEAL-FLX,[24] 2022: 0% Della Rocca et al.,[25] 2022: 0% SURPASS FLX,[26] 2024: 0.04%
Amplatzer Amulet, Abbott	2013	Proximal disc and distal lobe Proximal disc independent of the lobe, without screw 10 pairs of hooks on the distal disc Waist length up to 20 mm (greater adaptability) Disc diameter 40% larger than the lobe	Kleinecke et al.,[12] 2020: 0.9% AMULET IDE,[10] 2021: 0.6% SWISS-APERO,[14] 2021: 0.9% SEAL-FLX,[24] 2022: 0.7% Della Rocca,[25] 2022: 0.1%
LAmbre, Lifetech	2016	Adjustable umbrella + polyester cover 8 radial U-shaped hook pairs Wide size range (up to 40 mm)	Cruz-González et al.,[18] 2018: 0% Li et al.,[27] 2018: 0% Park et al.,[28] 2018: 0% Huang et al.,[29] 2019: 0% Ali et al.,[15] 2020: 0% Llagostera-Martín et al.,[17] 2021: 0% Wang et al.,[30] 2021: 0% Chamié et al.,[19] 2022: 2% Chen et al.,[31] 2022: 0% Vij et al.,[16] 2024: 1.7% (non-contrast protocol)

Figure 2. Bar chart showing the percentage of embolizations for each device.

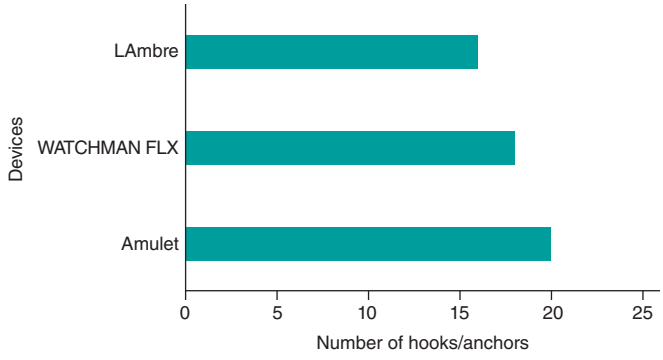

Figure 3. Devices and number of hooks and anchors they incorporate.

- Before discharge, a transthoracic echocardiogram is essential because most embolizations occur within the first 24 hours after implantation.[33,34]

- During follow-up, a TEE or cardiac CT is recommended at 45–90 days.

Manufacturers of the WATCHMAN and Amplatzer devices recommend a series of intraoperative steps to ensure proper device implantation; all criteria must be met before the device is released.

WATCHMAN devices follow the PASS (position, anchor, size, seal) acronym, while Amplatzer devices follow CLOSE (circumflex, lobe, orientation, separation, elliptical), outlined in table 3.

An important aspect of the intraoperative performance of the "tug test," which is used to assess the stability of the implanted device. This maneuver consists of applying controlled traction to the device once it has been deployed within the appendage, with the aim of confirming that it is securely anchored and will not migrate. Its use is widespread worldwide and it is now performed routinely. However, in 2020, a study evaluated its efficacy profile by implanting a device in the primary introducer sheath equipped to measure the traction force in Newtons.[35] The device used was the Amulet, and the investigators found that the force applied by the operator while releasing the device exceeded the force applied during the subsequent tug test, both for larger devices (2.96 ± 0.57 vs 1.04 ± 0.24 N; $P < .001$) and for devices < 25 mm (1.72 ± 0.43 vs 1.01 ± 0.59 N; $P = .049$). Thus, the authors concluded that the tug test was redundant. Notably, all 23 implants in the study fulfilled the manufacturer-recommended CLOSE criteria.

MANAGEMENT OF DEVICE EMBOLIZATION

The approach and management of embolizations fundamentally depend on 3 factors: the size of the embolized device, the site to which it has migrated, and the patient's hemodynamic status. In the review conducted by Eppinger et al.,[5] the most frequent migration site was the aorta (37%), followed by the left ventricle (LV) (33.3%), the LA (24.3%), and peripheral arteries (4.6%). Moreover, the authors concluded that embolization into the LV or the mitral subvalvular apparatus was associated with the highest degree of complications and the greatest need for surgery (44.4%). In the systematic review conducted by Aminian et al.,[34] the predominant site of embolization was split between the aorta and the LV (30% each), with the WATCHMAN device showing a predilection for the aorta (7 out of 9 cases) and the Amplatzer Cardiac Plug (Abbott, United States; no longer marketed in Spain) for the LV (6 out of 9

Table 2. Prevention of embolization across the different phases of the procedure

Preoperative	Intraoperative	Postoperative
Correct device sizing (avoid over- and undersizing)	Intraoperative guidance using 2D/3D TEE and fluoroscopy	Immediate postoperative verification with TTE for early detection of embolization
Adequate operator training (at least 25 transseptal punctures and 10 LAA closures)	Proper performance of the tug test (although its utility is still under discussion)	Pre-discharge evaluation with TTE
Use of preoperative imaging: 2D/3D TEE at multiple angles or CT	Fulfillment of PASS (WATCHMAN) or CLOSE criteria (Amplatzer) before releasing the device	Follow-up imaging at 45–90 days with TEE or CT
3D CT is superior to TEE for procedural planning		
	Avoid markedly depleted atria (< 12 mmHg)	

2D, bidimensional; 3D, tridimensional; CT, computed tomography; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

Table 3. PASS and CLOSE criteria for WATCHMAN and Amplatzer devices

Criteria	PASS (WATCHMAN)	CLOSE (Amplatzer)
1	Position: adequate coverage of the ostium, immediately distal to or at the ostium	Circumflex: the device lobe should be positioned one-third to two-thirds distal to the left circumflex artery
2	Anchoring: gentle traction test without displacement of the device	Lobe: "tyre-like" appearance when compressed
3	Size: device compression between 8% and 20% of its original size	Orientation: the device lobe must be coaxial with the left atrial appendage wall
4	Seal: residual leak < 5 mm; all lobes fully covered	Adequate separation between the lobe and the disc
5		Elliptical: the disc should be under tension, showing a concave appearance

cases). In this review, all devices > 25 mm were lodged in the LA or the LV. In the LAAODE trial,[33] the most frequent site of embolization remained the aorta (30%), followed by the LA (24%) and the LV (20%)."

Once embolization occurs, 2 main approaches exist:

- Percutaneous retrieval: via transarterial or transseptal access. Although single or multiple snares are widely used, myocardial biopsy forceps have been described.[36] Technique depends on device size, location, and anatomy. Alkhouli et al.[36] give a series of recommendations: single snares work best for large devices; the introducer sheath should be 2-Fr - 4-Fr larger than the size of the sheath required for device implantation; nitinol devices (eg, Amplatzer) can be folded and withdrawn into the introducer sheath, whereas non-nitinol devices (eg, WATCHMAN) require greater deformation for extraction. Table 4, table 5, and table 6 list snares, forceps, biotomes, and catheters useful for percutaneous retrieval according to the European Device Guide.[37] Figure 4 illustrates examples of single- and triple-loop snares.

- Surgical retrieval: more invasive, with longer hospitalization and higher mortality rates.[36] Indicated in cases of severe valvular damage or need for ventricular repair.

In percutaneous retrieval, Fahmy et al.,[38] in their ex vivo experience, required larger introducer sheaths to retrieve WATCHMAN devices than those used to retrieve Amplatzer Cardiac Plug–type devices. They emphasized the need for a larger "gooseneck" snare (preferably 15 mm–20 mm) to facilitate engagement of the WATCHMAN anchors, as well as a larger sheath (ideally 18-Fr) to allow easier retraction of the device. Other options include capturing the device centrally or laterally, although substantially greater traction force is required to withdraw the WATCHMAN into the sheath. Two operators should participate in the retrieval attempt: one to stabilize the sheath and the other to firmly pull the captured device into it.[38]

As mentioned above, device embolization into the LV can cause hemodynamic instability and often requires surgical retrieval. Percutaneous retrieval is especially challenging due to the risk of damaging the aortic and mitral valves. Stabilizing guidewires, especially when the device has been released, may become entangled in surrounding structures and cause tissue damage. Abbadi et al.[39] reported a case of Amulet embolization into the LV entrapping the mitral subvalvular apparatus and causing severe mitral regurgitation. Retrieval was achieved using a 35-mm Amplatz snare inserted through a 24-Fr MitraClip system (Abbott, United States), allowing the device to be captured by its central waist, pulled into the LA, and withdrawn into the MitraClip catheter. The patient remained stable with mild mitral regurgitation.

Research is currently underway on specific materials and systems designed to facilitate the capture, repositioning, and retrieval of devices. One of these is the ŌNŌ device (B. Braun, Germany), which consists of a 35-mm self-expanding nitinol basket attached to a 12-Fr catheter with a 7.5-Fr internal lumen. In a 3-case series published in 2024 (2 with migration to the LA and 1 to the LVOT beneath the aortic valve), the ŌNŌ device achieved a 100% retrieval success rate, with no complications[40].

Figure 5 and figure 6 illustrate examples of left atrial appendage device embolization.

TREATMENT ALGORITHMS

Several algorithms have been published with the aim of providing guidance and helping the operator in the decision-making process. In all of them, it is considered that if the patient is

Table 4. Snares useful for recapturing an embolized device

Snare	Manufacturer	Introducer sheath (Fr)	Loop length (cm)	Catheter length (cm)	Usable loop diameter (mm)	Characteristics
GooseNeck MicroSnare	Medtronic	2.3-3	175; 200	150	2; 4; 7	Single 90° loop; gold-plated tungsten coils
GooseNeck Snare	Medtronic	4; 6	120	102	5; 10; 15; 20; 25; 30; 35	Similar to MicroSnare
EN Snare standard	Merit Medical	6; 7	120	100	6-10; 9-15; 12-20; 18-30; 27-45	3 intertwined loops
EN Snare Mini	Merit Medical	3.2	175	150	2-4; 4-8	Similar to the EN Snare Standard
One Snare standard	Merit Medical	4; 6	120	100	5; 10; 15; 20; 25; 30; 35	Capture loop with a single 90° angle, gold-plated tungsten coating
One Snare Micro	Merit Medical	2.3-3	175; 200	150; 175	2; 4; 7	Similar to the One Snare standard
Atrieve Snare	Argon Medical Devices, Inc.	3.2; 6; 7	120; 175	100; 150	2-4; 4-8; 6-10; 9-15; 12-20; 18-30; 27-45	3 superimposed, non-intertwined loops
Bard Snare Kit	BD Interventional	9; 11	120	63; 58	20	Radiopaque 90° capture loop
CloverSnare 4-Loop Vascular Retrieval System	Cook Medical	6	90	85	32	4-loop nitinol snare with tantalum core
Multi-Snare	PFM Medical	3; 4; 5; 6	125; 175	105; 150	2-3; 4-6; 5-8; 10-15; 15-20; 20-30; 30-40	Dual-plane retrieval system

Table 5. Forceps and bioptomes useful for recapturing embolized devices

Forceps / Bioptome	Manufacturer	Introducer sheath (Fr)	Length (cm)	Characteristics
Standard biopsy forceps	Cordis	5.5; 7	50; 104	Available in straight and curved jaws
Procure endomyocardial biopsy forceps	Abbott	5.4–7	50; 105	Available in straight and curved jaws
Raptor* grasping device	US Endoscopy	7	230	360° rotation
Needle's Eye retrieval system	Cook Medical	16	54; 94	Stainless-steel/nitinol guidewire; widely used for cardiac lead extraction
Adjustable Lasso catheter	Biosense Webster	7	115	Mapping catheter used in electrophysiology
ŌNŌ retrieval device	B. Braun Interventional Systems, Inc.	7.5	100	35-mm self-expanding nitinol basket
Cardiology grasping forceps with 3 plate claws	H + H Maslanka	5.4	120	3 retractable claws

* Intravascular use of this device is considered off-label.

Table 6. Catheters and introducer sheaths useful for recapturing embolized devices

Catheter / Introducer sheath	Manufacturer	Size (Fr)	Length (cm)	Shape	Guidewire compatibility (inches)
Extra-large Check-Flo	Cook Medical	20-24	25; 40; 65	Rigid	0.038
Gore DrySeal Flex introducer sheath	Gore & Associates	10; 12; 14; 15; 16; 18; 20; 22; 24; 26	33; 45; 65	Flexible	0.035
MitraClip delivery system	Abbott	24	80	Flexible	0.035
Keller–Timmermans	Cook Medical	18-24	65; 85	Available straight and curved	0.038
Destino bidirectional guiding catheter with hemostatic valve	Oscor Inc.	8.5; 10; 12	67; 71; 73; 75; 77	Available straight and curved	0.038

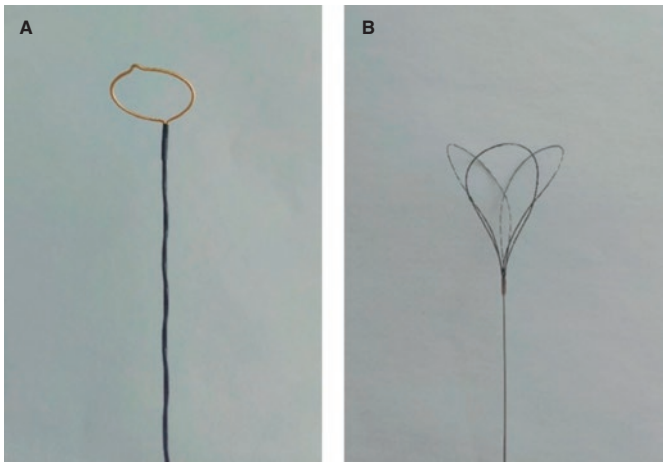

Figure 4. A: Amplatz gooseneck snare as an example of a single-loop retrieval device. **B:** EN Snare device showing its 3 interlaced loops.

hemodynamically stable and there is no significant vascular or valvular damage, the percutaneous retrieval technique should be the first-line approach (76.4% vs 21.7% of patients who required open cardiac surgery as an initial strategy in the series by Eppinger et al.[5], of whom 60% exhibited embolization to the LV), always taking into account that embolization into a cardiac chamber carries higher risk than embolization into a large or peripheral vessel.[36] If the first attempt is successful, it is acceptable to either try to reposition the device in its correct location or remove it from the patient and schedule a new implant.

If the first percutaneous attempt is unsuccessful—something that occurs in approximately one-third of the patients—a second percutaneous attempt may be performed, or the operator may proceed directly to open cardiac surgery, while bearing in mind that a failed first attempt increases mortality rate from 2.9% to 21.4%.[5]

If the second attempt fails too, and the patient is ineligible for surgery, Alkhouli et al.[36] propose several options, such as trying to disimpact the device and reposition it in a less anatomically compromised area, inflating a balloon distal to the device to apply traction and facilitate its mobilization to a safer position, and even using 2 snares simultaneously.

Finally, in patients with prohibitive surgical risk who remain asymptomatic, and only when the device is lodged in the descending aorta, conservative management with periodic follow-up is an option, although it is unclear how often follow-up should be performed or what antithrombotic or anticoagulant therapy should be administered.

Figure 7 proposes a management and treatment algorithm according to the latest evidence available, summarizing the information presented above.

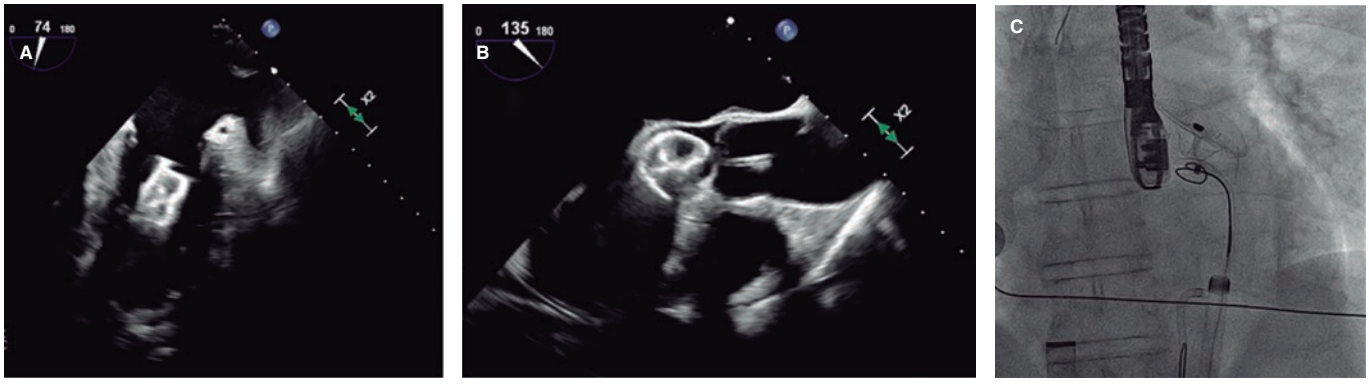

Figure 5. Intraoperative transesophageal echocardiography (TEE) and fluoroscopy of left atrial appendage closure with a 25-mm Amulet device. **A:** the device migrated to the left ventricle (LV). **B:** an 8-Fr JR4 guiding catheter with a 20-mm snare was introduced via left femoral access, capturing the device by the distal lobe screw and allowing it to be pulled into the descending aorta. **C:** afterwards, the right femoral artery was cannulated with a 16-Fr introducer sheath; using a guiding catheter and a 30-mm snare, the device was again captured by the distal lobe screw, pulled back, and finally extracted.

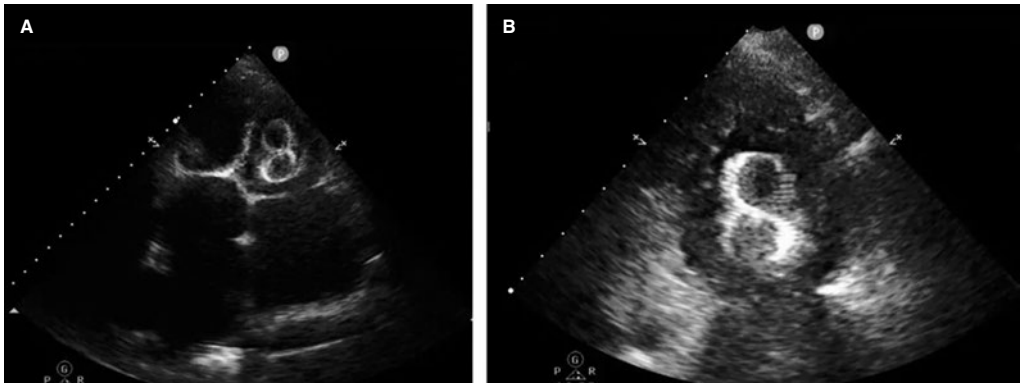

Figure 6. Transthoracic echocardiogram (TTE) performed 24 hours after implantation of a 38-mm LAmbre device. **A:** migration to the left ventricle (LV), with entrapment in the mitral subvalvular apparatus. **B:** magnified image.

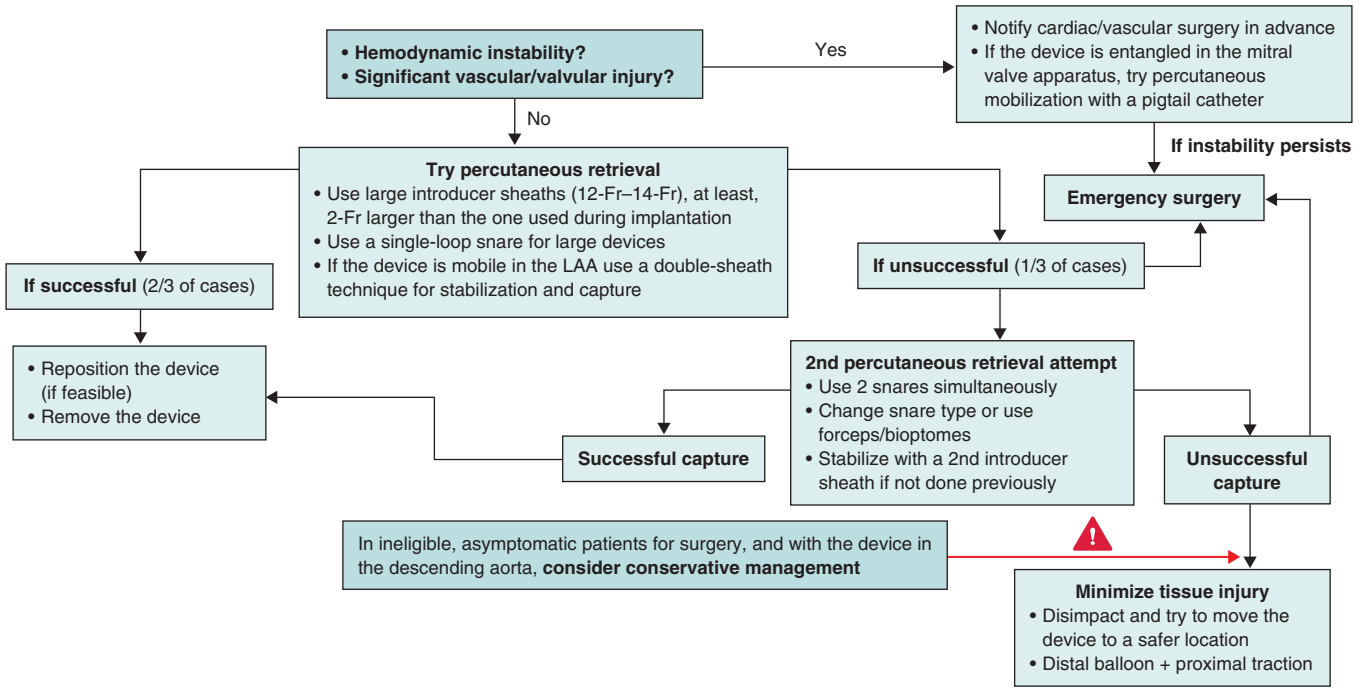

Figure 7. Proposed treatment algorithm for the embolization of a left atrial appendage (LAA) closure device.

CONCLUSIONS

Left atrial appendage occlusion device embolization is a rare but potentially fatal complication in a procedure that has proven safe and effective for stroke prevention in patients with nonvalvular atrial fibrillation who cannot take anticoagulation. Although device designs have evolved over the past few years, appropriate patient selection, meticulous preprocedural planning, and precise procedural execution remain essential to minimize the risks. This review highlights the multifactorial complexity and numerous contributing factors involved. When embolization occurs, percutaneous retrieval should be the initial approach when feasible, reserving surgery for specific cases, such as valvular disruption, hemodynamic instability, or failed percutaneous attempt. Development of specialized retrieval tools and standardized management algorithms will help optimize the outcomes. Future research should focus on identifying more precise anatomical and technical predictors and validating universal preventive strategies.

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None declared.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used in preparing this review.

AUTHORS' CONTRIBUTIONS

M.Á. Martín-Arena and G. Galeote-García conducted the literature search, collected data, and drafted the initial and final versions of the manuscript. A. Lara-García, A. Jurado-Román, S. Jiménez-Valero, A. Gonzálvez-García, D. Tébar-Márquez, B. Rivero-Santana, J. Zubiaur, M. Basile, S. Valbuena-López, L. Fernández-Gassó, R. Dalmau González-Gallarza, and R. Moreno provided images, figures, and data, critically reviewed the text, and contributed to the final manuscript. All authors approved the final version.

CONFLICTS OF INTEREST

R. Moreno is associate editor of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed; additionally, he has received speaker and consultant fees from Abbott, Medtronic, and Boston Scientific. A. Gonzálvez declared to have received speaker fees from Abbott. G. Galeote declared to have received honoraria from Abbott, Boston Scientific, and M.A. Jurado is a proctor for Abbott and Boston Scientific and declared to have received speaker fees from both. M. Basile declared to have received conference attendance fees from Abbott.

REFERENCES

1. Gómez-Doblas JJ, Muñiz J, Martin JJA, et al. Prevalence of Atrial Fibrillation in Spain. OFRECE Study Results. *Rev Esp Cardiol*. 2014;67:259-269.
2. Wolf PA, Abbott RD, Kannel WB. Atrial Fibrillation: A Major Contributor to Stroke in the Elderly: The Framingham Study. *Arch Intern Med*. 1987; 147:1561-1564.
3. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates 1. *Am J Cardiol*. 1998;82(7, Suppl 1):2N-9N.
4. Osmancik P, Herman D, Neuzil P, et al. 4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation. *J Am Coll Cardiol*. 2022;79:1-14.
5. Eppinger S, Piayda K, Rodes-Cabau J, et al. Embolization of percutaneous left atrial appendage closure devices: timing, management and associated clinical outcomes. *Eur Heart J*. 2023;44(Suppl 2):ehad655.2276.
6. Najim M, Reda Mostafa M, Eid MM, et al. Efficacy and safety of the new generation Watchman FLX device compared to the Watchman 2.5: a systematic review and meta-analysis. *Am J Cardiovasc Dis*. 2023;13:291-299.
7. Kar S, Doshi SK, Sadhu A, et al. Primary Outcome Evaluation of a Next-Generation Left Atrial Appendage Closure Device. *Circulation*. 2021;143:1754-1762.
8. Nielsen-Kudsk JE, Kramer A, Andersen A, Kim WY, Korsholm K. First-in-human left atrial appendage closure using the WATCHMAN FLX Pro device: a case report. *Eur Heart J Case Rep*. 2024;8:ytae135.

9. Bavishi C. Transcatheter Left Atrial Appendage Closure: Devices Available, Pitfalls, Advantages, and Future Directions. *US Cardiol Rev*. 2023;17:e05.
10. Lakkireddy D, Thaler D, Ellis CR, et al. Amplatzer Amulet Left Atrial Appendage Occluder Versus Watchman Device for Stroke Prophylaxis (Amulet IDE): A Randomized, Controlled Trial. *Circulation*. 2021;144: 1543-1552.
11. Lakkireddy D, Ellis CR, Thaler D, et al. 5-Year Results From the AMPLATZER Amulet Left Atrial Appendage Occluder Randomized Controlled Trial. *J Am Coll Cardiol*. 2025;85:1141-1153.
12. Kleinecke C, Cheikh-Ibrahim M, Schnupp S, et al. Long-term clinical outcomes of Amplatzer cardiac plug versus Amulet occluders for left atrial appendage closure. *Catheter Cardiovasc Interv*. 2020;96:E324-E331.
13. Bangash AB, Li Y, Huang W, et al. Left atrial appendage occlusion using the LAmbre device in atrial fibrillation patients with a history of ischemic stroke: 1-Year outcomes from a multicenter study in China. *Pacing Clin Electrophysiol*. 2023;46:1478-1483.
14. Galea R, De Marco F, Meneveau N, et al. Amulet or Watchman Device for Percutaneous Left Atrial Appendage Closure: Primary Results of the SWISS-APERO Randomized Clinical Trial. *Circulation*. 2022;145:724-738.
15. Ali M, Rigopoulos AG, Mammadov M, et al. Systematic review on left atrial appendage closure with the LAmbre device in patients with non-valvular atrial fibrillation. *BMC Cardiovasc Disord*. 2020;20:78.
16. Vij V, Ruf TF, Thambo JB, et al. Contrast-free left atrial appendage occlusion in patients using the LAMBRE™ device. *Int J Cardiol*. 2024;405:131939.
17. Llagostera-Martín M, Cubero-Gallego H, Mas-Stachurska A, et al. Left Atrial Appendage Closure with a New Occluder Device: Efficacy, Safety and Mid-Term Performance. *J Clin Med*. 2021;10:1421.
18. Cruz-González I, Freixa X, Fernández-Díaz JA, Moreno-Samos JC, Martín-Yuste V, Goicolea J. Left Atrial Appendage Occlusion With the LAmbre Device: Initial Experience. *Rev Esp Cardiol*. 2018;71:755-756.
19. Chamié F, Guerios E, Silva DP, Fuks V, Torres R. Oclusão do Apêndice Atrial Esquerdo com a Prótese Lambre: Experiência Multicêntrica Inicial no Brasil. *Arq Bras Cardiol*. 2022;119:48-56.
20. Holmes DR, Korsholm K, Rodés-Cabau J, Saw J, Berti S, Alkhouli MA. Left atrial appendage occlusion. *EuroIntervention*. 2023;18:e1038-e1065.
21. Garg J, Kabra R, Gopinathannair R, et al. State of the Art in Left Atrial Appendage Occlusion. *JACC Clin Electrophysiol*. 2025;11:602-641.
22. Bhagat A, Gier C, Kim P, Diggs P, Gursoy E. Delayed embolization of next-generation left atrial appendage closure device in an asymptomatic patient. *Hear Case Rep*. 2023;9:598-601.
23. Friedman DJ, Freeman JV, Zimmerman S, et al. Watchman device migration and embolization: A report from the NCDR LAAO Registry. *J Cardiovasc Electrophysiol*. 2023;34:1192-1195.
24. Korsholm K, Kramer A, Andersen A, et al. Left atrial appendage sealing performance of the Amplatzer Amulet and Watchman FLX device. *J Interv Card Electrophysiol*. 2023;66:391-401.
25. Rocca DGD, Magnocavallo M, Gianni C, et al. Procedural and short-term follow-up outcomes of Amplatzer Amulet occluder versus Watchman FLX device: A meta-analysis. *Heart Rhythm*. 2022;19:1017-1018.
26. Kapadia SR, Yeh RW, Price MJ, et al. Outcomes With the WATCHMAN FLX in Everyday Clinical Practice From the NCDR Left Atrial Appendage Occlusion Registry. *Circ Cardiovasc Interv*. 2024;17:e013750.
27. Li S, Zhang J, Zhang J, et al. GW29-e1803 LAmbre Occluder in Patients with Atrial Fibrillation: a Prospective single-center registry. *J Am Coll Cardiol*. 2018;72(16, Suppl):C150.
28. Park JW, Sievert H, Kleinecke C, et al. Left atrial appendage occlusion with lambre in atrial fibrillation: Initial European experience. *Int J Cardiol*. 2018;265:97-102.
29. Huang H, Liu Y, Xu Y, et al. Percutaneous Left Atrial Appendage Closure With the LAmbre Device for Stroke Prevention in Atrial Fibrillation: A Prospective, Multicenter Clinical Study. *JACC Cardiovasc Interv*. 2017;10: 2188-2194.
30. Wang B, Wang Z, He B, et al. Percutaneous Left Atrial Appendage Closure Confirmed by Intra-Procedural Transesophageal Echocardiography under Local Anesthesia: Safety and Clinical Efficacy. *Acta Cardiol Sin*. 2021;37: 146-154.
31. Chen YH, Wang LG, Zhou XD, et al. Outcome and safety of intracardiac echocardiography guided left atrial appendage closure within zero-fluoroscopy atrial fibrillation ablation procedures. *J Cardiovasc Electrophysiol*. 2022; 33:667-676.
32. Saw J, Holmes DR, Cavalcante JL, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. *Heart Rhythm*. 2023;20:e1-e16.
33. Murtaza G, Turagam MK, Dar T, et al. Left Atrial Appendage Occlusion Device Embolization (The LAAODE Study): Understanding the Timing and Clinical Consequences from a Worldwide Experience. *J Atr Fibrillation*. 2021;13:2516.
34. Aminian A, Lalmand J, Tzikas A, Budts W, Benit E, Kefer J. Embolization of left atrial appendage closure devices: A systematic review of cases reported with the watchman device and the amplatzer cardiac plug. *Catheter Cardiovasc Interv*. 2015;86:128-135.
35. Salmon MK, Hammer KE, Nygaard JV, Korsholm K, Johansen P, Nielsen-Kudsk JE. Left atrial appendage occlusion with the Amulet device: to tug or not to tug? *J Interv Card Electrophysiol*. 2021;61:199-206.
36. Alkhouli M, Sievert H, Rihal CS. Device Embolization in Structural Heart Interventions: Incidence, Outcomes, and Retrieval Techniques. *JACC Cardiovasc Interv*. 2019;12:113-126.
37. European Device Guide. Cardiac Interventions Today. Available at: https://citoday.com/device-guide/european. Accessed 2 Jul 2025.
38. Fahmy P, Eng L, Saw J. Retrieval of embolized left atrial appendage devices. *Catheter Cardiovasc Interv*. 2018;91:E75-E80.
39. Abbadi AB, Akodad M, Horvilleur J, Neylon A. Retrieval of a left appendage device from the left ventricle using a large bore steerable catheter. *Catheter Cardiovasc Interv*. 2024;104:365-367.
40. Hermann D, Khan Z, Khan Z, Abreu J, Loyalka P, Qureshi AM. First-in-Human Percutaneous Removal of Left Atrial Appendage Occlusion Devices With a Novel Retrieval System. *JACC Clin Electrophysiol*. 2024;10: 1004-1009.

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Scientific letter

Usability and accuracy of a cloud-based sizing software for left atrial appendage closure

Utilidad y precisión de un software basado en la nube para cierre de la orejuela izquierda

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To the Editor,

The complex and highly variable 3D anatomy of the left atrial appendage (LAA) makes it challenging for planning and device sizing for left atrial appendage closure (LAAC).[1] Echocardiography and multi-slice computed tomography (CT) are widely used imaging modalities for this purpose. 3Mensio Structural Heart (Pie Medical Imaging BV, The Netherlands) is the most widely used software for CT evaluation of LAA providing automatic segmentation of the heart. TribusConnect (TribusMed Beheer BV, The Netherlands) is a novel cloud-based Digital Imaging and Communications in Medicine (DICOM) viewer that can also be used to securely access, review, interpret, manipulate, measure and visualize images with automatic cardiac segmentation for LAA evaluation. Furthermore, TribusConnect allows for manual correction or adjustment of the automatically generated measurements or segmentation which could be crucial for centers with varying image quality, or challenging anatomies. This study aimed to investigate the feasibility, accuracy and reproducibility of evaluating the LAA in TribusConnect compared with the 3Mensio for preprocedural planning of LAAC.

Seventeen patients who underwent LAAC at *Hospital Clínico Universitario de Valladolid* (Valladolid, Spain) were included in our study. A total of 52.9% (9 patients) of these patients underwent LAAC by Amplatzer Amulet (Abbott, United States) while 17.6% (3 patients) and 29.4% (5 patients) received the Watchman (Boston Scientific, United States) and Omega (Vascular Innovations, Thailand) left atrial appendage occlude devices, respectively. The device size used varied from 18 mm to 35 mm. Only 1 of the 17 patients had mild peridevice leak (< 3 mm) due to device malapposition while 0 patients had device embolization or need for changing the device size or device type during the procedure. All patients underwent preoperative contrast-enhanced, electrocardiogram-gated high-pitch spiral acquisition mode CT. Images were obtained at 30%-60% of the R-R interval with a delayed scan after contrast injection in full compliance with LAA-specific expert recommendations on CT acquisition.[2] All datasets were saved as DICOM files and processed with dedicated software (3mensio Structural Heart) and novel TribusConnect. In the presence of inadequate delineation of the endocardial border due to incomplete contrast opacification of the LAA, the images were considered insufficient and excluded from the study. All datasets were evaluated, and measurements were performed by 2 independent cardiologists. Conventional measurements of LAA sizes (ostium, landing zone, depth, and working depth) were compared. The landing zone (LZ) was defined at a location 10 mm from the ostium into the LAA after adjusting the angle. The working depth was measured as a perpendicular line drawn from ostium to the LAA roof.

The intraclass correlation coefficients (ICC) between TribusConnect and 3Mensio for minimum, maximum, and mean diameters were, respectively, 0.912 (95%CI, 0.780-0.967), 0.826 (95%CI, 0.592-0.933), and 0.944 (95%CI, 0.852-0.979) at the ostium, and 0.667 (95%CI, 0.058-0.887), 0.806 (95%CI, 0.548-0.925), and 0.835 (95%CI, 0.371-0.948) at the LZ. This showed a good intraclass correlation. The Bland Altman plot for the measurements of ostium and LZ using the 2 software applications is shown in figure 1. ICC were 0.666 (95%CI, 0.286-0.865) for LAA depth and 0.753 (95%CI, 0.451-0.902) for working depth.

The ICC for the interobserver analysis for TribusConnect at the ostium (minimum, maximum, mean diameters) was 0.941 (0.846-0.978), 0.978 (0.941-0.992) and 0.973 (0.928-0.990) vs 0.901 (0.753-0.963), 0.815 (0.526-0.931) and 0.861 (0.662-0.947) for 3Mensio. Similarly, at the LZ, the ICC for TribusConnect (minimum, maximum, mean diameters) was 0.887 (0.719-0.957), 0.873 (0.689-0.952) and 0.941 (0.849-0.978) vs 0.736 (0.404-0.896), 0.718 (0.390-0.887) and 0.831 (0.602-0.935) for 3Mensio reflecting a better reproducibility of results across different operators with TribusConnect.

ICC for depth and working depth measurements was high for both systems. For TribusConnect, ICCs were 0.813 (95%CI, 0.445-0.935) for depth and 0.828 (95%CI, 0.467-0.941) for working depth. For 3Mensio, ICCs were 0.761 (95%CI, 0.348-0.914) for depth and 0.845 (95%CI, 0.629-0.941) for working depth.

TribusConnect was deemed by the operators to have better accessibility (video 1 of the supplementary data). Since it is a cloud-based

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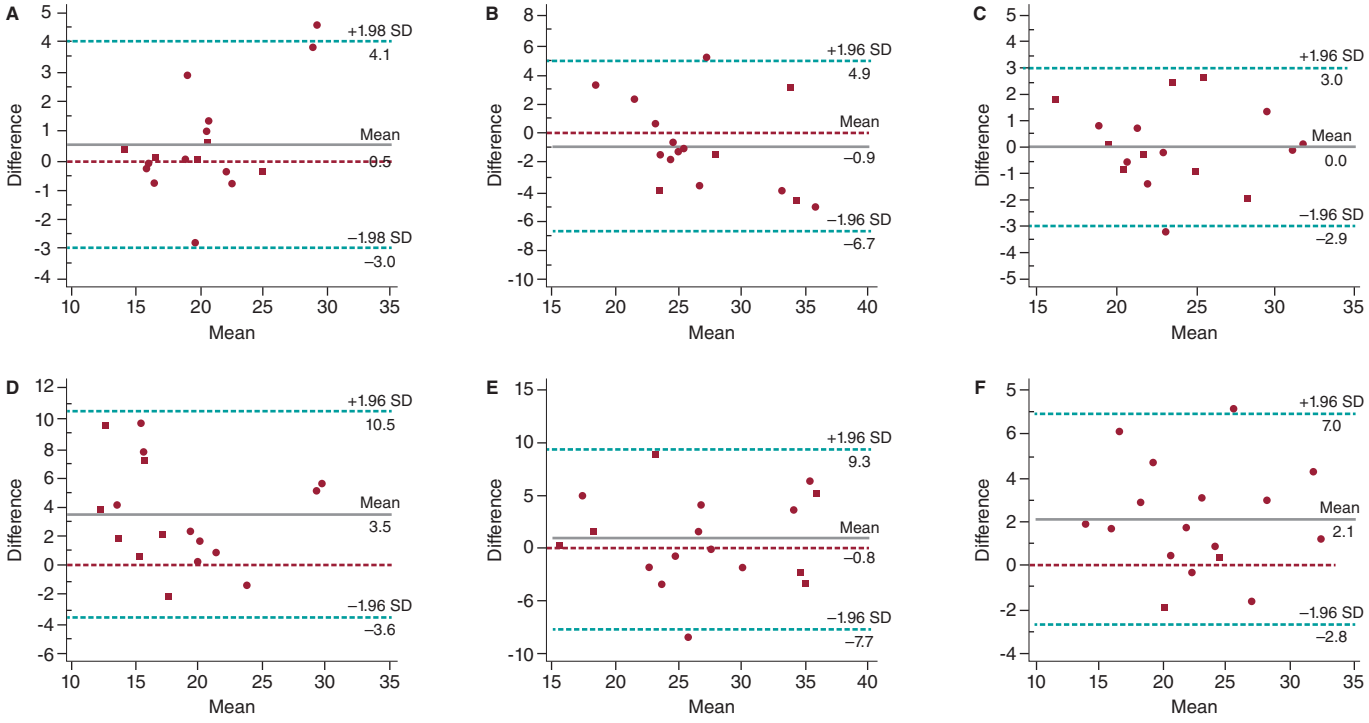

Figure 1. Bland Altman Plot showing the difference in measurement of minimum, maximum and mean diameter at ostium (A,B,C) and landing zone (D,E,F) between TribusConnect and 3Mensio. SD, standard deviation.

software with no need for any licensing or software installation into a device, CT images can be retrieved from any device and location across the globe. Secondly, TribusConnect has a workflow agnostic approach, bringing the user directly into the LAA without the need for restrictive steps in a workflow. Thirdly, TribusConnect ensures better data safety as no patient data is downloaded and the CT is anonymised by the software. Fourthly, all results are automatically saved, and the analysed results can be shared wherein multiple users can view, edit or improve the analysis. This was a retrospective study with a small number of patients with potential influence of unknown confounders. Further progressive studies might be needed to assess the impact of usability of this novel software on LAA device sizing and eventually clinical outcomes.

The study demonstrates a strong ICC between TribusConnect and 3Mensio in the CT assessment of the LAA for LAAC. TribusConnect exhibited lower interobserver variability and provided the added benefit of remote access to patient data.

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None declared.

ETHICAL CONSIDERATIONS

This study did not involve patient participants or animals, which is why ethical clearance was deemed unnecessary. Although this study included male and female patients alike, sex disaggregated analyses were not performed due to lack of expected sex related differences.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence tools were used in the writing of this study.

AUTHORS' CONTRIBUTIONS

A. Jain and I.J. Amat-Santos conducted the study and wrote the draft. The remaining authors helped to collect the data. All authors approved the final version.

CONFLICTS OF INTEREST

L. Verstraaeten and J. Vogelaar are shareholders and employees of TribusMed. The remaining authors declared no conflicts of interest whatsoever.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000536.

REFERENCES

1. Heidari H, Kanschik D, Erkens R, et al. Left atrial appendage sizing for percutaneous closure in virtual reality-a feasibility study. *Front Cardiovasc Med.* 2023;10:1188571.
2. Korsholm K, Berti S, Iriart X, et al. Expert Recommendations on Cardiac Computed Tomography for Planning Transcatheter Left Atrial Appendage Occlusion. *JACC Cardiovasc Interv.* 2020;13:277-292.

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Scientific letter

Clinical clustering of TAVI patients: multivariate profiling and outcome associations using two-step cluster analysis

Clasificación clínica de pacientes con TAVI: análisis multivariante y correlación con resultados mediante agrupamiento en dos fases

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To the Editor,

Transcatheter aortic valve implantation (TAVI) has revolutionized the management of severe aortic stenosis (AS).[1] Despite increasing TAVI experience and procedural improvement, outcomes remain hard to foresee.[1] Several clinical and anatomical risk factors have been well established as independent predictors of adverse events.[2] Nonetheless, the macro-level interactions between them are complex and challenging to quantify with traditional models, particularly given the dynamic clinical trajectory of AS.

Although standardized risk scores, such as the Society of Thoracic Surgeons (STS) score and the EuroSCORE II offer estimates of procedural risk[3] they miss the broader clinical profile and interactions. Advanced statistical techniques, such as multivariate cluster analysis, can identify subgroups, potentially uncovering patterns overlooked by conventional risk stratification. This study aimed to stratify TAVI patients using a 2-step cluster analysis based on clinical and risk factor variables and evaluate the association between these clusters and procedural timing and clinical outcomes.

We conducted a retrospective, single-center study with 300 patients undergoing TAVI from 2020 through 2023, without immediate cardiac surgery back-up. Data were retrospectively analyzed. Procedural and outcome definitions followed the Valve Academic Research Consortium-3 criteria.[4] A 2-step cluster analysis was performed, incorporating variables such as age, sex, New York Heart Association (NYHA) functional class, significant mitral regurgitation, pulmonary hypertension, and relevant comorbidities, including chronic kidney disease and atrial fibrillation.

Clusters were compared regarding baseline characteristics, procedural variables, and outcomes. The primary composite endpoint was 30-day mortality, stroke, and 1-year hospital readmission. Secondary endpoints included 1-year mortality, stroke, hospital readmission, permanent pacemaker implantation, and vascular complications. Statistical analyses were performed using IBM SPSS Statistics, Version 30.0 (IBM Corp., Armonk, NY, USA).

Two clusters were identified: Cluster 1 (n = 182) and Cluster 2 (n = 32) (silhouette coefficient, 0.69). The remaining patients had incomplete data for clustering variables. Baseline demographic and comorbidity profiles were similar between clusters. Mean age (82 ± 5 vs 83 ± 5 years; $P = .6$), female sex (54% vs 50%; $P = .7$), and comorbidities did not differ significantly (table 1). Additionally, echocardiographic and computed tomography parameters were similar between the 2 clusters (table 1).

Differences emerged in clinical presentation and procedural timing. Cluster 1 had a higher proportion of NYHA III/IV patients (52% vs 25%; $P = .005$), previous hospitalization for AS (28% vs 3%; $P = .03$), significant mitral regurgitation (30% vs 12%; $P = .05$), and pulmonary hypertension (64% vs 43%; $P = .03$) at baseline initial assessment. Notably, these patients had a significantly shorter median TAVI waiting time (48 [24-72] vs 93 [47-139] days; $P = .03$), suggesting a prioritization based on symptomatic burden and perceived procedural urgency.

Despite patients from Cluster 1 being more symptomatic, their outcomes were better vs those from Cluster 2. The primary composite endpoint of death, stroke, and hospital readmission occurred in 12% of Cluster 1 patients vs 100% of Cluster 2 patients (risk ratio [RR], 8.3; 95% confidence interval [95%CI], 5.2-13.3; $P < .001$). The 30-day all-cause mortality rate was 1% in Cluster 1 vs 6% in Cluster 2 (RR ,5.7; 95%CI, 0.8-38.9; $P = .05$). The 1-year mortality rate remained significantly lower in Cluster 1 at 7% vs 29% in Cluster 2 (RR, 4.1; 95%CI, 1.9-8.6; $P < .001$). Similarly, stroke occurred in only 0.5% of patients from Cluster 1 while 16% of the patients from Cluster 2 experienced this complication (RR, 33.3; 95%CI, 4.5-247.7; $P < .001$). The 1-year rate of hospital readmissions was also less common in Cluster 1, occurring in 13% of patients vs 88% in Cluster 2 (RR, 6.77; 95%CI, 3.7-12.5; $P < .01$). Rates of vascular complications and permanent pacemaker implantation were similar between the clusters (5.5% vs 9.4%, RR, 1.7; 95%CI, 0.5-5.7; $P = .4$ and 21% vs 23%, RR, 1.10; 95%CI, 0.6-2.2; $P = .9$, respectively).

This study demonstrates that multivariate clustering can identify distinct clinical profiles within a TAVI cohort, revealing paradoxical but clinically meaningful outcome patterns. Patients with advanced symptoms (NYHA III/IV) and prior AS-related hospitalizations, typically considered higher risk, achieved better survival and lower complication rates vs less symptomatic patients.

Procedural timing and patient surveillance intensity might contribute to the different outcomes reported. More symptomatic

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Table 1. Baseline characteristics, procedural data, and clinical outcomes according to cluster analysis in patients undergoing TAVI

Variable	Total (n = 300)	Cluster 1 (n = 182)	Cluster 2 (n = 32)	*P*-value
Baseline				
Age				
Mean, SD	82 ± 5	82 ± 6	83 ± 5	.6
Median, IQR	82 [78-86]	82 [78-86]	84 [79-87]	
Female, (%)	54%	54%	50%	.7
Katz score > 4 (%)	96%	97%	94%	.6
STS score				
Mean, SD	5.2 ± 4.5	4.9 ± 4.2	5.8 ± 4.3	.3
Median, IQR	3.8 [2.8-6.9]	3.7 [2.7-6.6]	4.0 [2.8-7.8]	
STS score high risk (> 8)	17%	13%	22%	.2
EuroSCORE	2.32-2.4	2.2-2	2.6-2	.5
Hospital admission due to AS	22%	28%	3%	.03
NYHA > 2	51%	52%	25%	.005
Comorbidities				
HTN	86%	85%	88%	.7
DM	35%	36%	41%	.6
CAD	21%	16%	25%	.2
COPD/OSA	11%	10%	16%	.3
GFR < 30 mL/kg/m^2	11%	11%	16%	.5
Atrial fibrillation	22%	24%	19%	.5
MI	9%	9%	13%	.5
PCI	14%	12%	22%	.1
Stroke	8%	8%	18%	.07
ECG				
1st AV block	12%	11%	13%	.8
LBBB	9%	8%	7%	.8
RBBB	7%	6%	16%	.05
TTE				
Mean gradient (mmHg)	48 ± 14	49 ± 13	46 ± 15	.2
AVA (cm^2)	0.7 ± 0.2	0.7 ± 0.2	0.8 ± 0.2	.08
LVEF (%)	56 ± 11	55 ± 10	57 ± 10	.7
LVEF < 40%	13%	10%	10%	.9
SPAP > 40mmHg	54%	64%	43%	.03
Significant MR	30%	30%	12%	.05
CT				
Aortic calcium score	721 ± 88			.3
Min femoral diameter (mm)	7.3-1.8	7.0-1.9	7.3-1.6	.3
Laboratory findings				
Hemoglobin	12.2 ± 1.9	12.3 ± 1.8	12.1 ± 2.2	.8
Serum creatinine	1.2, 0.6	1.0, 0.6	1.0, 0.8	.9
NT-proBNP	526 ± 284	510 ± 269	657 ± 291	.09
TAVI waiting time (days)	60-101	48-98	93-92	.03
Outcomes				
Death, stroke and hospital readmission	25%	12%	100%	< .001
30-day mortality rate	3.7%	1%	6%	.05
1-year mortality rate	12%	7%	29%	< .001
Stroke	2.8%	0.5%	16%	< .001
Hospital admission	17%	13%	88%	< .01
Pacemaker implantation	20%	21%	23%	.9
Vascular complication	7.8%	5.5%	9.4%	.4

AS, aortic stenosis; AV, atrioventricular; AVA, aortic valve area; CAD, coronary artery disease; CT, computed tomography; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; ECG, electrocardiogram; GFR, glomerular filtration rate; HTN, hypertension; IQR, interquartile range; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; OSA, obstructive sleep apnea; PCI, percutaneous coronary intervention; RBBB, right bundle branch block; SD, standard deviation; SPAP, systolic pulmonary artery pressure; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation; TTE, transthoracic echocardiogram.
Data are expressed as no. (%), mean ± standard deviation or median [interquartile range].

patients tend to undergo closer clinical follow-up and prioritized TAVI scheduling, as reflected by the significantly shorter waiting times observed in Cluster 1. Conversely, patients with less severe symptoms are often deprioritized, experiencing procedural delays during which subclinical deterioration or decline in functional status can be significant. AS is a progressive condition, with substantial mortality on the waiting list. Moreover, a history of unplanned hospital admission for AS should be considered a significant warning sign to anticipate intervention, given its association with increased risk of subsequent events. Former studies have shown that delayed intervention is associated with higher rates of adverse outcomes,[5] thus supporting the notion that waiting time is a critical modifiable risk factor. Moreover, current risk prediction models inadequately account for dynamic clinical evolution and complex factor interactions. STS and EuroSCORE II values were comparable between clusters, yet outcomes differed substantially. The higher outcome rate from Cluster 2 raises concerns about unrecognized vulnerability and cumulative procedural risk aggravated by disease progression during the waiting period. These findings suggest that, beyond baseline comorbidities, procedural timing and dynamic clinical follow-up should be part of risk stratification and procedural prioritization strategies in TAVI programs.

This study has several limitations. Its retrospective single-center design may limit external validity. Small sample size, especially in Cluster 2, limits power. Unmeasured factors, such as frailty may have influenced outcomes. The 2-step cluster model, while robust, is sensitive to the included variables and missing data, potentially

affecting cluster assignment and interpretation. Additionally, our conclusions may not be applicable to centers with short waiting lists.

This clustering method allows a macroscopic view and the identification of potential interactions between multiple clinical variables by organizing patients into groups. However, further studies with larger sample sizes are needed to validate this risk assessment approach. These findings highlight the importance of minimizing waiting times and ensuring close follow-up in managing AS. Multidimensional clinical profiling and dynamic procedural scheduling should be considered when optimizing TAVI care pathways to improve patient outcomes.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request

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None declared.

ETHICAL CONSIDERATIONS

This study was conducted in full compliance with the Declaration of Helsinki and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines on clinical research. As a retrospective analysis of anonymized data, formal ethical approval and informed consent were waived. This study was conducted in full compliance with the SAGER (Sex and Gender Equity in Research) guidelines. Sex and gender considerations were addressed appropriately, and any potential sex- or gender-related differences were assessed and reported where relevant.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence tools were used in the preparation of this manuscript.

AUTHORS' CONTRIBUTIONS

A. Rocha de Almeida: conceptualization, methodology, data curation, formal analysis, investigation, writing – original draft, writing – review and editing. R. Viana: writing – original draft, writing – review and editing. R. Fernandes: writing – review and editing. Â. Bento: writing – review and editing. L. Patrício: conceptualization, supervision, writing – review and editing, validation.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;43:561-632.
2. Carroll JD, Mack MJ, Vemulapalli S, et al. STS-ACC TVT Registry of Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol*. 2020;76:2492-2516.
3. Wendler O, Schymik G, Treede H, et al. SOURCE 3 Registry. *Circulation*. 2017;135:1123-1132.
4. Généreux P, Piazza N, Alu MC, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *Eur Heart J*. 2021;42:1825-1857.
5. Bhattacharyya S, Lloyd G. Mortality whilst waiting for intervention in symptomatic severe aortic stenosis. *Eur Heart J Qual Care Clin Outcomes*. 2020;6:89-90.

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The clover sign. A predictor of optimal plaque modification after orbital atherectomy

El signo del trébol. Un predictor de modificación óptima de la placa tras aterectomía orbital

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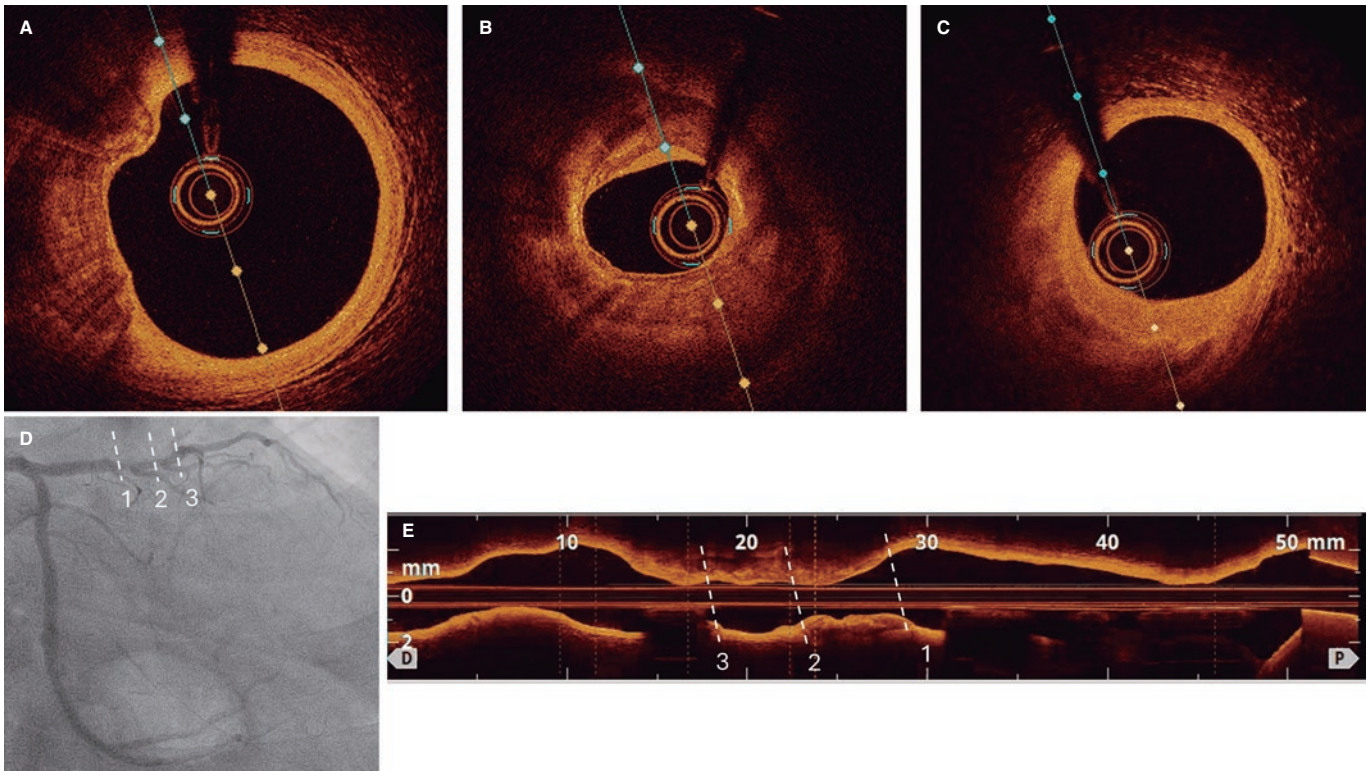

Figure 1.

A 72-year-old man with stable angina underwent coronary angiography, which revealed the presence of severe, calcified stenosis in the proximal left anterior descending coronary artery. Optical coherence tomography (OCT) confirmed the presence of a thick calcified lesion of eccentric and concentric distribution (figure 1, video 1 of the supplementary data). Orbital atherectomy (OA) using the Diamondback 360 system (Abbott Vascular, United States) was advanced initially at low speed (80 000 rpm) and, then, at high-speed backward ablation (120 000 rpm). Post-OA OCT revealed significant plaque modifications. Firstly, the sanding effect on the superficial calcium revealed a notable finding that could resemble a clover morphology (figure 2B,E, dashed red lines, asterisks). This "clover sign" consisted of 3 symmetrically distributed ablation pathways due to the combination of the antegrade and retrograde ablations that modify the plaque in different axes. Additionally, pulsatile forces of the OA induced deep calcium fractures (figure 2C). After predilation, a drug eluting stent was implanted with excellent results (figure 2D,F; video 2 of the supplementary data).

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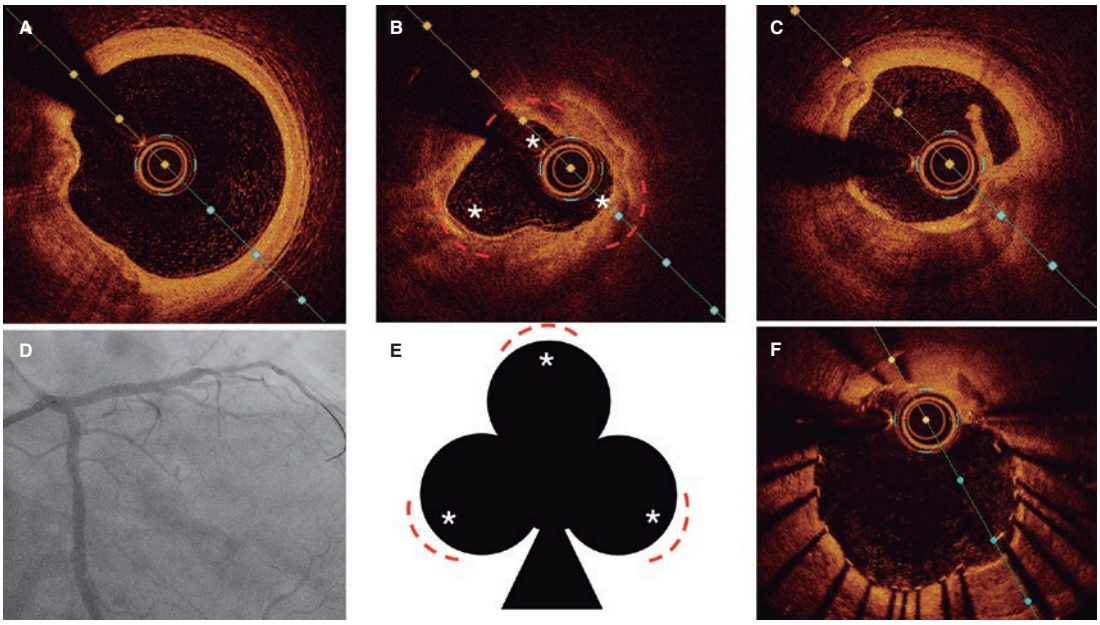

Figure 2.

We believe that this case adequately illustrates the effect of OA in calcified plaques and defines the specific features of the "clover sign". In deep, concentric calcified plaques, OA shows its double effect: the sanding effect reduces plaque volume by ablating the superficial calcium while pulsatile forces of crown rotation act on the deeper and thicker calcium layers, thus contributing to plaque fracture.

The "clover sign" resembles the unique effect of bidirectional sanding on the calcium surface of OA, which increases with multiple directions and velocities. Furthermore, OA is the only plaque modification device that can ablate forward and backwards taking advantage of a "favorable wire-bias" and, consequently, producing 2 or 3 ablation pathways, thus revealing this characteristic finding in intracoronary imaging. Therefore, the "clover sign" could be a predictor of better plaque modification by significant debulking while facilitating stent apposition and expansion.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This case report was conducted in full compliance with the ethical principles set forth in the Declaration of Helsinki. Prior written informed consent was obtained from the patient for the publication of this report and accompanying images. Additionally, the authors have adhered to the Sex and Gender Equity in Research (SAGER) guidelines. No sex/gender bias was identified in the interpretation of this case.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

The authors declare that no artificial intelligence software has been used in the creation of this manuscript.

AUTHORS' CONTRIBUTIONS

J. Zubiaur and A. Jurado-Román conceptualized the case report, performed the literature review, and drafted the manuscript. A. Gonzálvez García, S. Jiménez-Valero, G. Galeote and R. Moreno contributed to manuscript revision, provided clinical insights, and conducted a critical review of the manuscript. All authors read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

R. Moreno is associate editor of *REC: Interventional Cardiology;* the journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The authors declared no financial conflicts on the content herein.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000506.

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Ten-year follow-up of coronary artery vasculitis

Diez años de seguimiento de enfermedad coronaria por vasculitis

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Coronary artery vasculitis is a cause of coronary artery disease especially in young patients. Certain inflammatory conditions, such as Kawasaki disease, can trigger this entity. Histological confirmation is challenging, as coronary artery biopsy is not feasible. However, tissue characterization can be achieved using optical coherence tomography (OCT).

In 2014, a 25-years-old male with a past medical history of hypereosinophilic syndrome was referred to our center after an incidental finding of right coronary artery calcification on a computed tomography scan. A coronary angiography revealed the presence of aneurysmal lesions in the right coronary artery (RCA) (figure 1). OCT imaging showed mixed arterial wall abnormalities: a calcified aneurysm (figure 1A), fibrotic intimal thickening with medial disruption and prominent vasa vasorum (figure 1B), calcification (figure 1C), and a less diseased distal vessel (figure 1D). Treatment with acetylsalicylic acid 100 mg daily was initiated.

In 2024, repeat coronary angiography for exertional angina showed RCA disease progression with larger mid-RCA calcification, confirmed by OCT of the same artery segment. Furthermore, the distal segment showed disease progression with intima thickening and medial disruption (figure 1; figure 1E-1H). A new critical stenosis was found in the left anterior descending coronary artery. Furthermore, a biopsy was obtained from an aneurysmal segment of the temporal artery (figure 2). Histopathological findings were similar to those seen on the OCT of coronary arteries. The thickened arterial wall was characterized by fibrous/myofibroblastic intimal hyperplasia, acute inflammatory infiltrate, necrosis, and fibrinoid changes (figure 2A-arrow). Moreover, a loss of the internal elastic lamina (figure 2B-arrow and figure 2A-asterisk) and adventitial vessels confirmed the presence of perivascular chronic inflammation.

Based on the symptoms and left anterior descending coronary artery findings (intimal thickening and medial disruption, suggestive of vasculitis; figure 3A, asterisk and arrow), with a healthy distal vessel (figure 3A, double asterisk). A transcatheter coronary intervention with drug-coated balloon was performed (figure 3B).

FUNDING

This was an investigator-initiated study with no funding.

ETHICAL CONSIDERATIONS

The Ethics Committee approval was deemed unnecessary. The patient's prior written informed consent was obtained for publication of this case report and accompanying images. Variables of sex and gender have been taken into consideration in full compliance with the SAGER guidelines.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used in the present manuscript.

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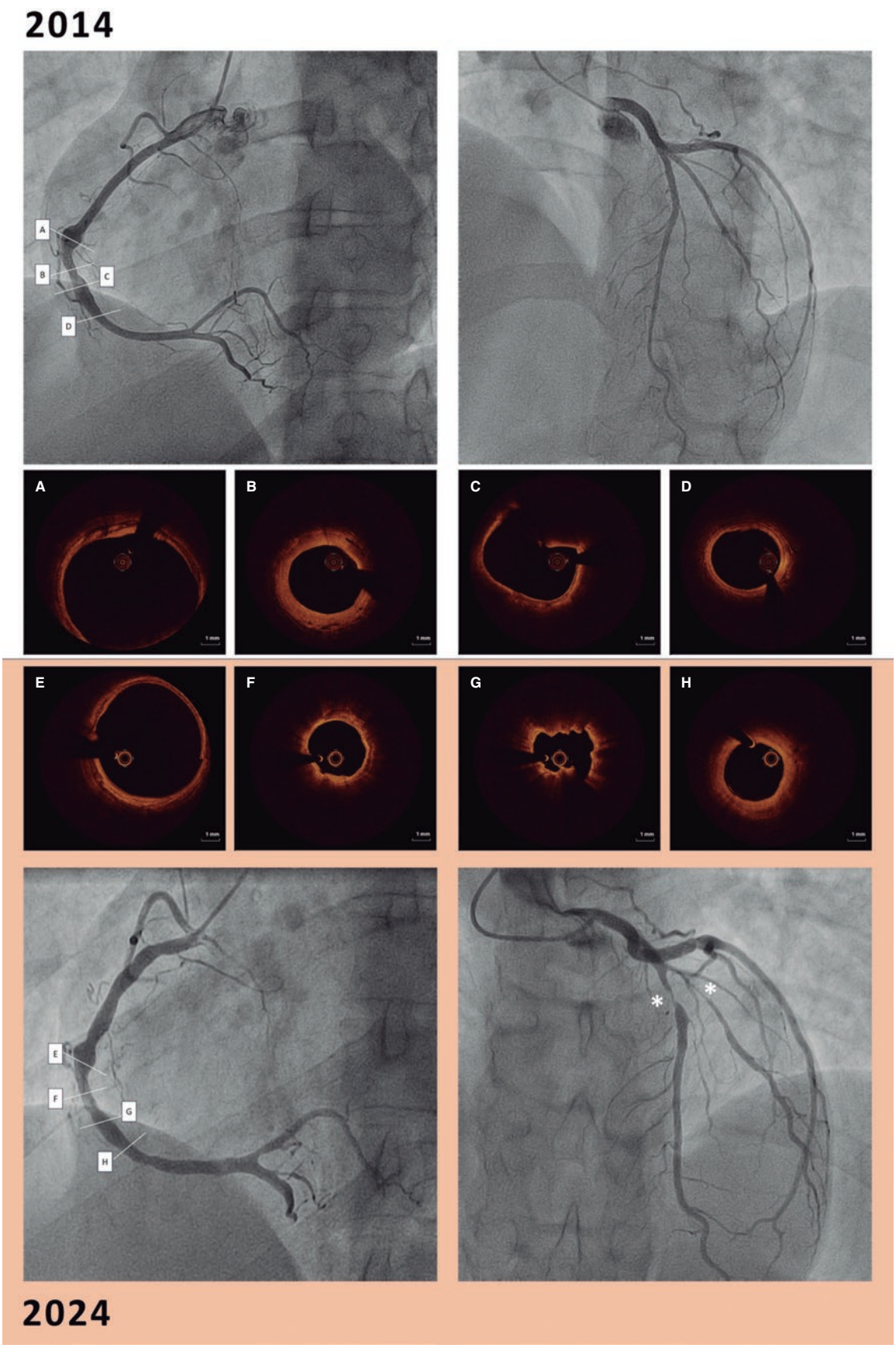

Figure 1.

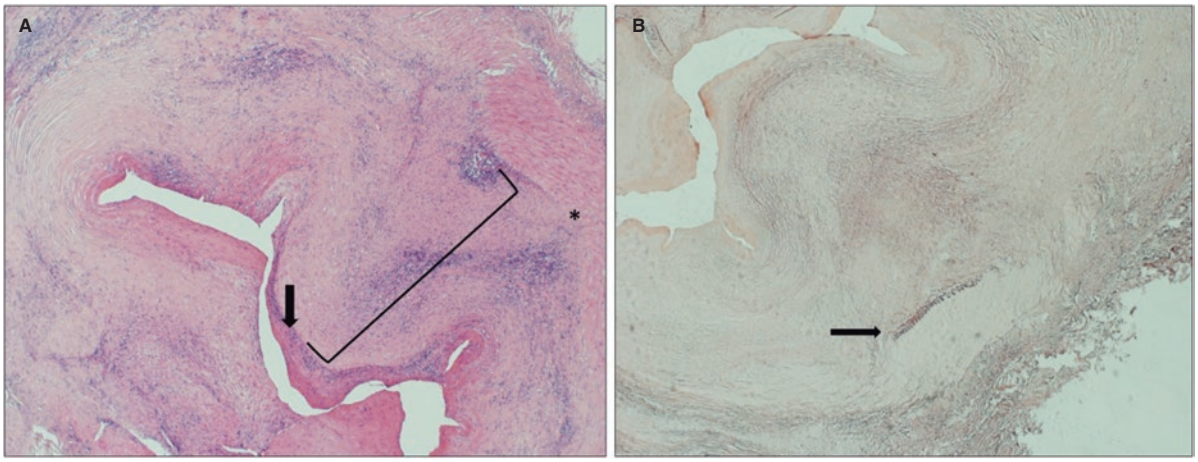

Figure 2.

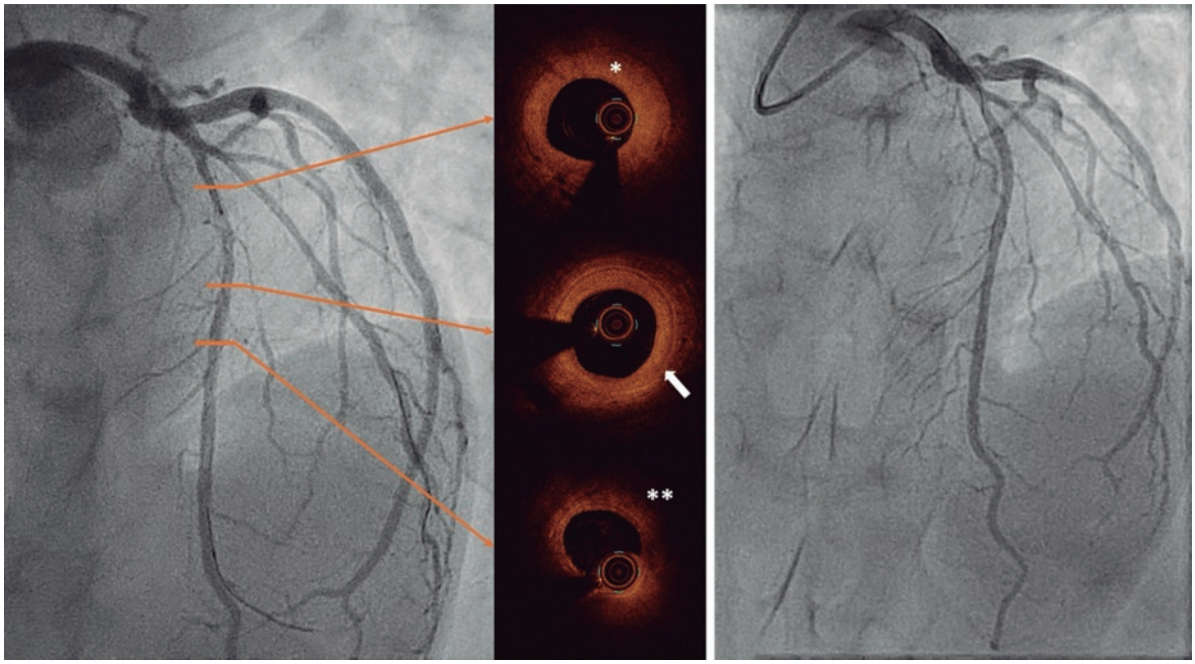

Figure 3.

AUTHORS' CONTRIBUTIONS

C. Tejada and J.M. de Alba were the patient's treating physicians. C. Real, P. Salinas and J.F. Chávez-Solsol were the interventional cardiologists who performed the procedures. Y. Castro analyzed the pathological findings. C. Tejada and C. Real drafted the initial version of this manuscript, which was subsequently revised by P. Salinas. All the authors critically reviewed and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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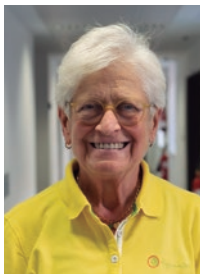
Interview



An interview with Camino Bañuelos

Una entrevista con Camino Bañuelos

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Camino Bañuelos (Puebla de Alcocer, Badajoz, 1947) belongs to the pioneering generation of women physicians who transformed interventional cardiology in Spain. Her vocation was kindled in adolescence, inspired by her father's stories, a health care worker during the Spanish Civil War. After overcoming academic and social barriers in an era when few women studied medicine, she began her career in the Madrid mountain range, where she is still remembered for her warmth and dedication. She soon entered the emerging field of interventional cardiology at Hospital Clínico San Carlos (Madrid, Spain) becoming a reference in cardiac catheterizations, valvuloplasties, and as a teacher of future specialists.

In the first place, could you give us a brief overview of your biography?

I was born in Extremadura (Spain) in 1947, into a family of public servants. I was the youngest of 3 siblings. My life seemed destined for a different path, but a failed exam opened the door to what would become my true vocation: medicine. When I was 14, my parents offered me a job at a bank in Toledo (Spain), provided that I passed the *reválida*—Spain's national secondary school exam required for university admission—which ended up shaping my future. I failed it, but after retaking it, I was able to continue studying. That "failure" ended up shaping my future.

Why did you decide to study medicine?

My inspiration came from home: my father, who had worked as a nurse during the Civil War, passed his passion for medicine over to me through the stories he told from that time. That was how my dream of becoming a doctor was born, at a time when very few women dared to take that step.

A student against convention… Did you face difficulties because of that?

In my class at the School of Medicine of Complutense University of Madrid (Madrid, Spain), less than 10% of students were women, and discrimination was evident. I remember one day when a professor said: *"Ladies, what are you doing here and not at home waiting for a good husband to come your way?"* The entire classroom fell completely silent, and the session resumed as though nothing had occurred. My school years were also marked by student uprisings that even led to the faculty's closure for a year. To reopen, we had to apologize to the government!

You began your career in rural medicine. How were your first steps as a doctor?

After graduating, I began working in several small towns in the Madrid mountains—Cabanillas, Venturada, Valdemanco, and Redueña. There were no health centers there, so I held consultations at the town hall. My work focused on vaccination campaigns and prevention of rheumatic fever, which meant diagnosing childhood tonsillitis early and treating it with penicillin. Even today, some neighbors remember those times! When I walk through Cabanillas, some dads tell their children: *"That doctor used to chase me with a syringe when I was little."*

From primary care to interventional cardiology—how did that transition happen?

While working in the Madrid mountains, I began my cardiology training under the mentorship of Pedro Zarco and Luis Martínez Elbal. With them, I learned to perform diagnostic catheterizations, coronary angiographies, and ventriculograms via femoral access and humeral surgical dissection—techniques that, in the 1980s, were essential to refer patients for surgery. I also entered the emerging field of echocardiography, then performed in M-mode. In the cath lab, I also met Ester de Marco Guilarte, another pioneering cardiologist who, after participating in diagnostic cardiac catheterizations, later specialized in pediatric cardiology.

In 1982, I joined the Cardiopulmonary Exploration Unit at Hospital Clínico San Carlos (Madrid, Spain) where I conducted consultations, cardiac catheterizations, and echocardiograms. In the afternoons, I worked at a clinic in Torrejón de Ardoz. Things were not as they are now; I remember driving patients with arrhythmias to Madrid in my own car for hospitalization.

You witnessed major advances in interventional cardiology firsthand. What do you remember from that time?

The arrival of Carlos Macaya at Hospital Clínico in 1985 marked a turning point: he brought plain old balloon angioplasty, and a few years later, stenting. In 1989, we both learned the mitral valvuloplasty

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technique directly from Masami Inoue, who developed it. Because of that experience, I was able to teach the procedure to colleagues such as Rosana Hernández Antolín and specialists from hospitals across the country. That teaching role took me abroad; I fondly remember my time in Cuba, where I performed a valvuloplasty on a pregnant patient, and in Romania too.

At the end of the 1980s, together with Carlos Macaya and under the direction of Alain Cribier, I learned balloon dilation for severe aortic stenosis, a procedure later discontinued because of its limited efficacy, yet one that marked a milestone in the history of cardiology.

After an alert in the cath lab at Hospital Clínico San Carlos in 2008. Camino Bañuelos (second from left) with Tamara Gorgadze (fellow), Vera Rodríguez (nurse), and María José Morales (nurse).

In the 1990s, Hospital Clínico became an international training hub. You were recognized not only as a cardiologist but also as a teacher. How do you remember that time?

During those years, with the consolidation of the stent, Hospital Clínico attracted physicians from across Latin America to train in interventional techniques. I have always believed that properly training young doctors is a fundamental responsibility: the better we prepare them today, the better they will care for us when we grow old. I still remember those long afternoons of complex cardiac catheterizations and angioplasties with fellows, often late into the night, while the nursing staff, exhausted, joked about closing the lab.

Did you face obstacles because of being woman?

Honestly, I never felt any significant barriers from my colleagues for being a woman. What I did notice, especially in the early years, was a certain disbelief from patients, who would call me "Miss" or address me informally, not realizing I was the doctor.

Would you like to leave a message for new generations?

I would tell them that although medicine demands effort and commitment, it gives back much more than it takes. Do not be afraid to make mistakes or to fight for your place; every step you take today will open the door for those who will come after you.

Camino Bañuelos at the tribute paid to her by her colleagues during the 16th Annual Meeting of the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC), held in Santiago de Compostela in June 2025. With her, from left to right: Ana Belén Cid Álvarez, Pilar Jiménez Quevedo, and Nieves Gonzalo.

FUNDING

None declared.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

None used.

CONFLICTS OF INTEREST

None declared.

ABOUT THE AUTHORS

Pilar Jiménez Quevedo is an interventional cardiologist at Hospital Clínico San Carlos. Ana Belén Cid Álvarez is an interventional cardiologist at Hospital Clínico Universitario de Santiago de Compostela (Galicia, Spain) and president of the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC).

The ACI-SEC honored Camino Bañuelos at its 36th Annual Meeting in gratitude for her legacy—that of a woman who forged a path in a field where few, at that time, succeeded, and who helped transform cardiology in Spain.