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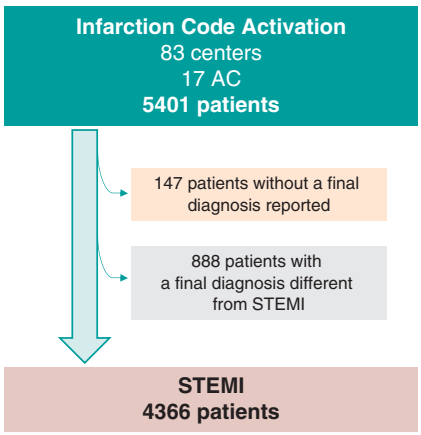

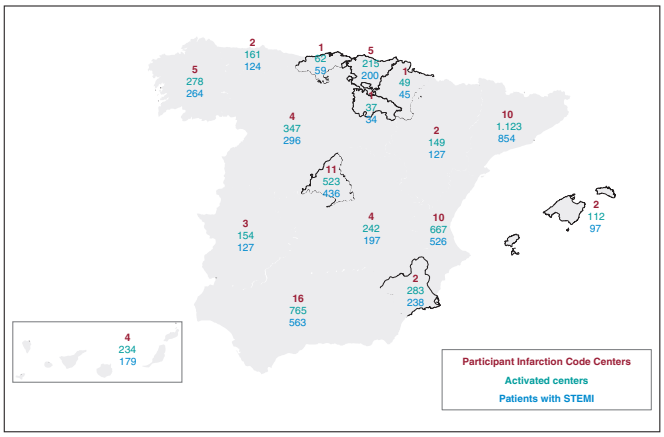

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Editorial

Class effect in TAVI: the time has come to know if they are all the same

Efecto de clase en el TAVI: ha llegado la hora de saber si son todos iguales

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The time has come. Over the past few years, we have been living a constant increase in the number of patients with aortic stenosis who are treated with transcatheter aortic valve implantation (TAVI). Although the latest indications of the clinical practice guidelines from the European Society of Cardiology[1] are somehow more restrictive than those of the American College of Cardiology[2] regarding age cut-offs and surgical risk we've seen a growing demand for TAVI in low-risk patients and, progressively, in younger patients in almost all anatomical settings.

Up until now, randomized clinical trials had mostly focused on comparing the TAVI technique to conventional aortic valve replacement surgery.[3,4] And although these studies with different models of transcatheter aortic valves laid the foundation for the indications published by the guidelines, very few of them make head-to-head comparisons among the different TAVI models currently available. As a matter of fact, most are observational, non-randomized or non-inferiority clinical trials. On the other hand, the variability of the different models currently available has been growing with technological advances to perform easier, safer, and more durable transcatheter heart valves. However, can we assume that there will be some sort of class effect in all TAVI models currently available?

In an article recently published in *REC: Interventional Cardiology*, Elnaggar et al.[5] compared 2 models of top transcatheter heart valves currently available (the Evolut PRO, Medtronic, United States, and the SAPIEN 3, Edwards Lifesciences, United States) using an easy randomized design. Although the study has significant limitations (a rather clinical compared to methodological protocol), it seems reasonable to start discussing whether the different TAVI models available have similar results in non-selected and randomized populations. As it occurred with coronary stents, presumably in no time, we'll be seeing more comparative trials like this studying not TAVI vs surgery, but TAVI vs TAVI in different clinical and anatomical settings. In the study conducted by Elnaggar et al.[5] no significant differences regarding in-hospital mortality between both models were seen, but a difference regarding paravalvular leak favorable to the SAPIEN 3 vs the Evolut PRO device in a population not previously screened through coronary computed tomography angiography. As described in the methodology and further discussion, the method used in the study to assess annular size and anatomy was unusual. The protocol included an intraoperative transesophageal echocardiography plus in-situ balloon inflation to measure the annulus and select the size of the valve based on the coverage index. This may have impacted implantation results following size selection and coronary artery calcium assessment as predictors of paravalvular leak, and not based on today's gold standard (computed tomography). Regarding the need for pacemaker implantation after TAVI, the authors say that this difference was not significant (7.1% vs 5.8% favorable to the SAPIEN 3) although a difference was seen in the rate of baseline right branch bundle block (16.9% in the SAPIEN 3 group vs 0% in the Evolut PRO group). Therefore, we should mention that the baseline population was more favorable regarding the predictors of pacemaker implantation in the Evolut PRO compared to the SAPIEN 3. The latter, however, showed a lower—although not statistically significant—absolute rate of pacemaker implantation. Finally, the composite endpoint defined by the authors as device success was favorable to the SAPIEN 3 (98%) vs the Evolut PRO (86%) and included lack of mortality, paravalvular leak grade ≥ II at discharge, the need for a second valve, conversion to surgical aortic valve replacement or valve embolization. The study focused on procedural results with a follow-up limited to the length of stay (median of 7 days).

In any case, and beyond any methodological constraints, comparative trials show the strengths and weaknesses of different transcatheter aortic valve models even with experienced operators, which probably debunks the theory that a single model in expert hands fits every patient. If we want excellent results in patients and longer life expectancies, we'll probably need to profit from what each model has to offer depending on the patient's anatomy. Also, in high-volume centers that treat young or low-risk patients, the use of different TAVI models should be mandatory for better valve selection regarding the patients' clinical and anatomical characteristics. As a matter of fact, there is compelling evidence that the hemodynamics of supra-annular models is better compared to that of annular coaptation models, especially, in small annuli[6,7] or that, with a significant load of calcium, latest generation balloon-expandable models have better results regarding paravalvular leak,[8] etc. Still, several questions remain unanswered that can all be summarized in the headline of this editorial: is there a class effect in all TAVI models currently available?

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In view of the reports that compare the results of different models,[9,10] similar immediate results are likely during primoimplantation with all of them since the technique is highly reproducible. However, like we said before, the population where indications are trying to be expanded requires excellent results and small differences that seem irrelevant in absolute terms but are very important in this context of excellence if we want TAVI to become the gold standard to treat aortic stenosis regardless of age and surgical risk. Considering the durability data available to this date (median of nearly 8 years)[11] when offering this therapy to young patients with longer life expectancies compared to this expected durability, the term «lifetime plan» comes into play. Now the index TAVI needs much more than excellent results regarding severe cardiovascular complications, paravalvular leak, need for pacemaker implantation or rate of stroke. Now, valve selection needs to be planned and carefully individualized to better suit the patient's anatomy anticipating a possible second TAVI in the future (TAVI-in-TAVI). Come to this point, very few will still advocate for class effect. The different designs and adaptations made to the patient's anatomy will be key in a crucial aspect regarding planning a second procedure years after the index one: access to coronary arteries following the risk of sinus sequestration or occlusion due to outer skirts and height of the first and second valves. This is where intra- or supra-annular designs, the valve total height, strut amplitude, the possibility of commissural alignment, laceration techniques, prosthesis-patient mismatch, etc. come into play. In conclusion, a significant combination of factors that still need to be studied before answering some of these questions. Undoubtedly, virtual, and three-dimensional simulation technologies play a key role in research and clinical application with decision-making algorithms to choose the best alternative for our patients. Therefore, former studies have already discussed these aspects while trying to elucidate how different models behave in this complex TAVI-in-TAVI setting.[12] Also, comparisons have been made with surgical explantation of TAVI with structural failure.[13,14] Currently, the rate of these events is not high, but the most plausible thing is that as the patients' mean age drops, the rate of valve degeneration will increase parallel to the need for dealing with this problem.

All things considered it seems highly likely that there will be no class effect in TAVI considering how different the designs currently available behave beyond implantation. There is, however, great reproducibility of the transfemoral transcatheter technique with excellent short- and mid-term results. Some questions remain, though, on the long-term outcomes that will surely be answered as scientific evidence as it has been the case since this technique was born 20 years ago.

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CONFLICTS OF INTEREST

C.A. Urbano Carrillo is a proctor for Edwards Lifesciences and participates in consulting groups for Medtronic España.

REFERENCES

1. Vahanian A, Beyersdorf F, Praz F, et al.; ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;43:561-632.
2. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143:e35-e71.
3. Mack MJ, Leon MB, Thourani VH, et al.; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med*. 2019;380:1695-1705.
4. Popma JJ, Deeb GM, Yakubov SJ, et al.; Evolut Low Risk Trial Investigators. Low risk trial, transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med*. 2019;380:1706-1715.
5. Elnaggar HM, Schoels W, Mahmoud MS, et al. Transcatheter aortic valve implantation using Evolut PRO versus SAPIEN 3 valves: a randomized comparative trial. *REC Interv Cardiol*. 2022. https://doi.org/10.24875/RECICE.M22000351.
6. Schmidt S, Fortmeier V, Ludwig S, et al. Hemodynamics of self-expanding versus balloon-expandable transcatheter heart valves in relation to native aortic annulus anatomy. *Clin Res Cardiol*. 2022;111:1336-1347.
7. Abdelghani M, Mankerious N, Allali A, et al. Bioprosthetic Valve Performance After Transcatheter Aortic Valve Replacement With Self-Expanding Versus Balloon-Expandable Valves in Large Versus Small Aortic Valve Annuli: Insights From the CHOICE Trial and the CHOICE-Extend Registry. *JACC Cardiovasc Interv*. 2018;11:2507-2518.
8. Abdel-Wahab M, Mehilli J, Frerker C, et al. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA Cardiol*. 2014;311:1503-1514.
9. Webb J, Wood D, Sathananthan J, Landes U. Balloon-expandable or self-expandable transcatheter heart valves. Which are best? *Eur Heart J*. 2020;41:1900-1902.
10. Pagnesi M, Kim WK, Conradi L, et al. Transcatheter Aortic Valve Replacement With Next-Generation Self-Expanding Devices: A Multicenter, Retrospective, Propensity-Matched Comparison of Evolut PRO Versus Acurate neo Transcatheter Heart Valves. *JACC Cardiovasc Interv*. 2019;12:433-443.
11. Blackman DJ, Saraf S, MacCarthy PA, et al. Long-Term Durability of Transcatheter Aortic Valve Prostheses. *J Am Coll Cardiol*. 2019;73:537-545.
12. Meier D, Akodad M, Landes U, et al. Coronary access following redo TAVR. Impact of THV design, implant technique, and cell misalignment. *J Am Coll Cardiol Interv*. 2022;15:1519-1531.
13. Bapat VN, Zaid S, Fukuhara S, et al.; EXPLANT-TAVR Investigators. Surgical Explantation After TAVR Failure: Mid-Term Outcomes From the EXPLANT-TAVR International Registry. *JACC Cardiovasc Interv*. 2021;14:1978-1991.
14. Fukuhara S, Nguyen CTN, Yang B, et al. Surgical Explantation of Transcatheter Aortic Bioprostheses: Balloon vs Self-Expandable Devices. *Ann Thorac Surg*. 2022;113:138-145.

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Editorial

3D quantitative coronary angiography based vessel FFR: clinical evidence and future perspectives

RFF vascular basada en angiografía coronaria cuantitativa 3D: evidencia clínica y perspectivas de futuro

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Endorsed by the current clinical practice guidelines, the indication to perform percutaneous coronary intervention (PCI) of intermediate coronary stenosis should be guided by either fractional flow reserve (FFR) or instantaneous wave-free ratio (iFR) if evidence of ischemia is lacking.[1] Despite these clear recommendations, the uptake of physiology in clinical practice remains low supporting the development of new non-invasive tools that no longer mandate the need for dedicated coronary guidewires or microcatheters along with the need to administer hyperemic agents in case of FFR.[1]

Advances in computational power and three-dimensional quantitative coronary angiography has facilitated the development of angiography-based-FFR indices, thus allowing easy, online physiological lesion assessments. Besides anatomical and angiographic exclusion criteria like severe tortuosity, aorto-ostial lesions or overlapping vessels, pivotal studies demonstrated that with angiography-based-FFR indices the need for invasive coronary artery instrumentation and hyperemic agents can, in most cases, be avoided.[2]

Currently, 4 angiography-based-FFR indices have emerged and are currently commercially available.[1] Despite workflow differences and embedded simplified computational fluid dynamics models, these indices demonstrated to have a good diagnostic performance with pressure guidewire based FFR as a reference.[1]

Among these, vessel fractional flow reserve (vFFR, CAAS Workstation 8.5 Pie Medical Imaging, Netherlands) uses a computational fluid dynamic approach based on simplified Navier–Stokes equations and 2 angiographic views separated, at least, 30 degrees to generate a 3D reconstruction of the coronary artery. Using aortic pressure as inlet boundary condition, the algorithm applies automated and harmonized optimal end-diastolic frame selection in the 2 views by electrocardiogram triggering, thus allowing physiological lesion assessment without the need for full cardiac tree assessment or manual frame counting.[3]

This review provides an overview of the currently available clinical evidence on the use of vFFR (table 1 and figure 1).

Vessel fractional flow reserve was first validated in 2 retrospective, single-center studies where the technology demonstrated an excellent diagnostic performance in intermediate coronary artery lesions compared to FFR, which was consistent among different anatomical and patient subsets including tandem lesions, and patients presenting with non-ST-segment elevation acute coronary syndrome.[3,4] These findings were later confirmed in the multicenter, prospective FAST II study, in which vFFR computed offline by local site personnel and a blinded core lab showed excellent diagnostic accuracy in identifying lesions with invasive guidewire-based FFR ≤ 0.80 (area under the curve [AUC], 0.93; $P < .001$). Positive and negative predictive values, sensitivity and specificity of vFFR were 90%, 90%, 81% and 95%, respectively.[5] The system allows accurate automated vessel contour detection with manual correction required in merely 9.3% of vessel contours.[5] Regarding reproducibility, vFFR showed a low inter-observer variability when computed offline by blinded academic operators (r = 0.95; $P < .001$) or local personnel vs a blinded core lab (r = 0.87; $P < .001$). Additionally, a low coefficient of variation (3.92%) was observed when vFFR was analyzed at 2 different timeframes by an independent core lab.[6]

Following these promising data, we explored the potential value of vFFR in a variety of clinical and procedural settings (table 1 and figure 1).

First, the evaluation of left main coronary artery (LMCA) lesions remains challenging and often warrants a multimodality approach, including physiological assessment and intravascular imaging. Since patients with LMCA disease are often under-represented in the studies, a dedicated analysis comparing vFFR to intravascular ultrasound in patients with non-ostial LMCA disease was performed. vFFR was shown to correlate well to the LMCA minimum lumen area (MLA) as assessed by intravascular ultrasound (r = 0.79; $P = .001$) and to have excellent diagnostic accuracy identifying LMCA lesions with MLA < 6.0 mm^2 (AUC = 0.95; $P = .001$).[7]

Second, the use of physiology in the ACS setting has been topic of disussion as the benefit of physiology-guided-PCI has been mainly demonstrated in patients with stable disease.[1] The latter is an important limitation since most patients present with ACS, which in up to 31% of cases occurs in the context of plaque rupture/erosion or calcium nodules located in intermediate coronary artery lesions. Conversely, a thrombotic component was identified in 602/695 of the culprit lesions (87%), which may affect the validity of both the pressure guidewire and the angiography-based-FFR assessments (TACTIS Registry, TCT 2022). In that perspective, the FAST OCT study (NCT04683133) will assess the agreement between vFFR and optical coherence tomography detected causes of luminal obstruction in intermediate lesions of patients presenting with ACS.

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Table 1. Major studies trials investigating the diagnostic performance of vessel fractional flow reserve (vFFR)

Study/Author	Year	Study design	Number of vessel (patient)	Primary endpoint
Pre-PCI setting				
FAST study	2019	Retrospective	100 (100)	AUC = 0.93 (95%CI, 0.88-0.97)
FAST EXTEND	2020	Retrospective	294 (294)	AUC = 0.94 (95%CI, 0.92-0.97)
FAST II	2021	Prospective	334 (334)	AUC = 0.93 (95%CI, 0.90-0.96)
FAST Heart Team	2022	Retrospective	1248 (416)	Mismatch between vFFR and revascularization = 29.8%
FAST III	Ongoing	Prospective		
Imaging				
Tomaniak et al. (Left main coronary artery disease)	2022	Retrospective	63 (63)	AUC = 0.95 (95%CI, 0.89-1.0)
FAST OCT	Ongoing	Prospective		
Post-PCI setting				
FAST POST	2021	Retrospective	100 (100)	AUC = 0.98 (95%CI, 0.96-1.0)
FAST OUTCOME	2022	Retrospective	832 (748)	vFFR tertiles = TVF 24.6%, 21.5% vs 17.1%
STEMI and multivessel disease				
FAST STEMI II	Ongoing	Prospective		

95%CI, 95% confidence interval; AUC, area under the curve; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TVF, target vessel failure.

Whether the use of vFFR can be extended to patients with ST-segment elevation acute coronary syndrome and multivessel disease will be explored in the ongoing FAST STEMI program.

Next to the potential for online use, the concept of angiography-based-FFR caries significant potential in an offline setting where this technology could be used for clinical decision-making in patients with multivessel disease or those referred for heart team discussion. In a recent retrospective analysis, 3-vessel vFFR screening demonstrated a discordance between lesion significance and revascularization in 30% of the cases.[8]

Third, post-PCI physiological assessment has gained attention since several studies demonstrated that low post-PCI FFR values are detectable in up to 58% of vessels.[9] Although the relevance of low post-PCI FFR was demonstrated by a significantly increased risk for future adverse cardiovascular events, the uptake of post-PCI FFR in the routine clinical practice is still limited.[9] Hypothetically, the concept of having a wire-free method to detect suboptimal stent deployment, residual disease, and additional procedural optimization is promising. In the retrospective, single-center FAST POST study, vFFR demonstrated a good correlation with conventional invasive post-PCI FFR (r = 0.88), and a higher accuracy in the identification of patients with FFR values < 0.90 (AUC = 0.98) compared to three-dimensional quantitative coronary angiography (AUC = 0.62).[10] In the light of these results, the hypothesis that post-PCI vFFR may predict future adverse cardiac events was proven in the FAST OUTCOME study.[11]

Fourth, the ability to predict functional outcomes of PCI may entail another step forward in the identification of patients who could benefit the most from PCI and thereby avoid the risk of a futile invasive procedure. Recent developments in vFFR software have allowed to simulate the effects of a 'virtual' PCI and estimate post-PCI FFR (residual vFFR). Using pre-PCI virtual pullbacks, residual vFFR showed a good correlation with invasive post-PCI FFR and post-PCI vFFR values (r = 0.84, and r = 0.77, respectively), and good discriminative ability to identify post-PCI FFR < 0.90 (AUC = 0.93).[12] Of note, the current algorithm assumes an almost perfect PCI result, and thus, cannot account for heavy calcifications or stent underexpansion suggesting a potential need for future hybrid technologies combining multimodality invasive and non-invasive imaging modalities and physiology tools.

Finally, following the positive data from the FAVOR III outcome trial that proved the superiority of quantitative flow ratio (QFR, Pulse Medical Imaging Technology, China) vs angiography-guided-PCI in a Chinese population, the results of, at least, 5 currently ongoing angiography based FFR outcome trials (FAVOR III Europe Japan trial [NCT03729739], PIONEER IV [NCT04923191], FAST III [NCT04931771], LIPSIA STRATEGY [NCT03497637], FLASH FFR II [NCT04575207]) are eagerly awaited and may enhance guideline adoption.[2] Specific to vFFR, the ongoing multicenter, randomized FAST III trial will assess whether a vFFR-based diagnostic strategy yields non-inferior clinical outcomes compared to an FFR-based strategy.

Up until the results of these studies will be released, angiography-based-FFR indices, including vFFR, remains an appealing alternative to conventional physiological indices in a broad selection of anatomical and clinical scenarios with the potential to increase the use of physiology and improve patient outcome.

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AUTHOR'S CONTRIBUTIONS

A. Scoccia contributed to the drafting of this manuscript, and made a critical review of its intellectual content. J. Daemen also contributed to the drafting of this manuscript, made a critical review of its intellectual content, and gave his final approval to the version that would eventually be published.

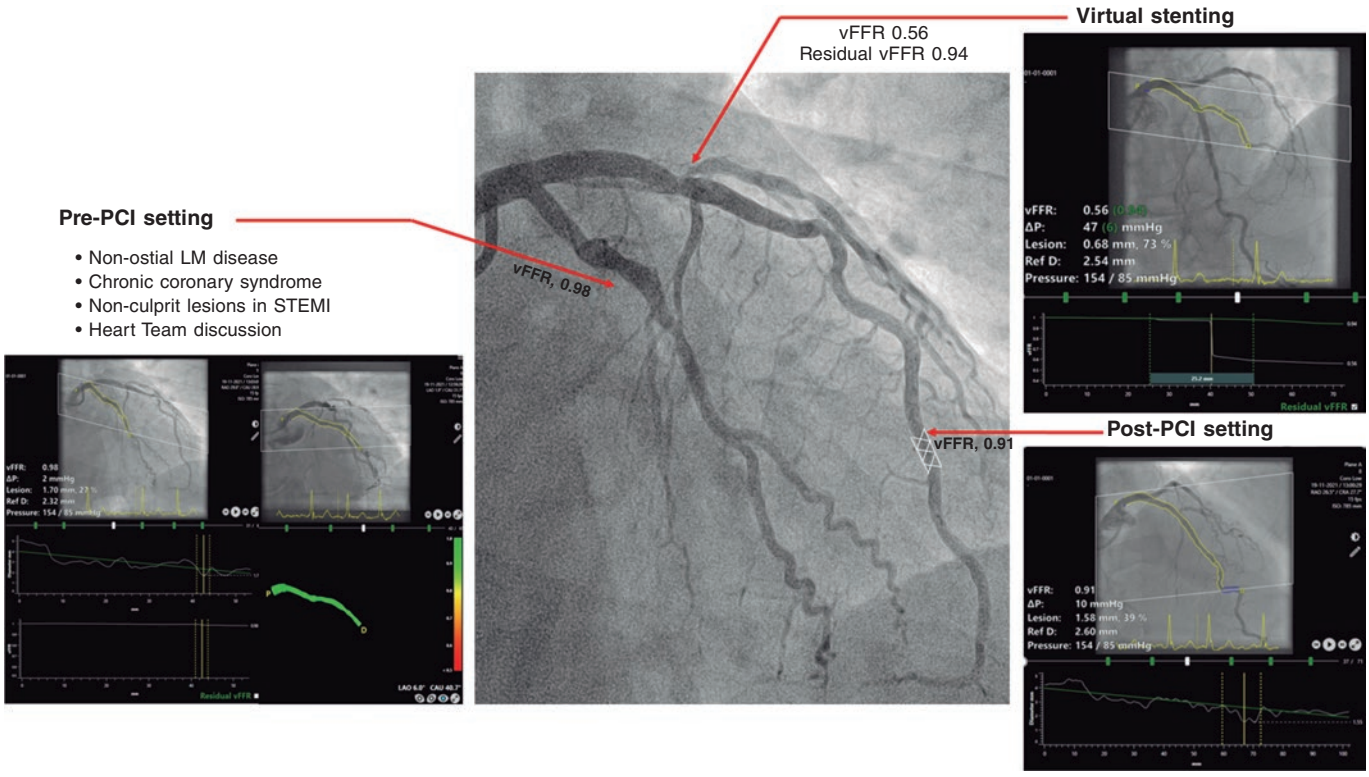

Figure 1. Clinical application of vessel fractional flow reserve (vFFR). LM, left main; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

CONFLICTS OF INTEREST

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REFERENCES

1. Kogame N, Ono M, Kawashima H, et al. The Impact of Coronary Physiology on Contemporary Clinical Decision Making. *JACC Cardiovasc Interv.* 2020;13:1617-1638.
2. 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.
3. 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.* 2020;16:591-599.
4. 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.
5. 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.
6. Scoccia A, Neleman T, Kardys I, et al. Reproducibility of 3D vessel Fractional Flow Reserve (vFFR): A core laboratory variability analysis of FAST II study. *Cardiovasc Revasc Med.* 2022;44:101-102.
7. Tomaniak M, Masdjedi K, van Zandvoort LJ, et al. Correlation between 3D-QCA based FFR and quantitative lumen assessment by IVUS for left main coronary artery stenoses. *Catheter Cardiovasc Interv.* 2021;97:E495-E501.
8. Tomaniak M, Masdjedi K, Neleman T, et al. Three-dimensional QCA-based vessel fractional flow reserve (vFFR) in Heart Team decision-making: a multicentre, retrospective, cohort study. *BMJ Open.* 2022;12:e054202.
9. Hwang D, Koo BK, Zhang J, et al. Prognostic Implications of Fractional Flow Reserve After Coronary Stenting: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2022;5(9):e2232842.
10. Masdjedi K, van Zandvoort LJ, Balbi MM, et al. Validation of novel 3-dimensional quantitative coronary angiography based software to calculate fractional flow reserve post stenting. *Catheter Cardiovasc Interv.* 2021; 98:671-677.
11. Neleman T, Scoccia A, Masdjedi K, et al. The prognostic value of angiography-based vessel fractional flow reserve after percutaneous coronary intervention: The FAST Outcome study. *Int J Cardiol.* 2022;359:14-19.
12. Tomaniak M, Neleman T, Ziedses des Plantes A, et al. Diagnostic Accuracy of Coronary Angiography-Based Vessel Fractional Flow Reserve (vFFR) Virtual Stenting. *J Clin Med.* 2022;11:1397.

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Original article

Transcatheter aortic valve implantation using Evolut PRO versus SAPIEN 3 valves: a randomized comparative trial

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ABSTRACT

Introduction and objectives: Advances made in transcatheter aortic valve implantation (TAVI) valvular technology have resulted in better outcomes and fewer complications compared with older generations. We studied the rate and determinants of paravalvular leak (PVL) using Evolut PRO vs SAPIEN 3 valves as well as other perioperative and in-hospital outcomes.
Methods: A total of 110 consecutive patients with severe aortic stenosis scheduled for transfemoral TAVI were randomly selected to receive the SAPIEN 3 (N = 59) or the Evolut PRO valve (N = 51). Annular dimensions were determined by transesophageal echocardiography guided balloon sizing. The following postoperative and in-hospital endpoints were assessed: PVL, conduction defects, valve embolization, need for a second valve, annular rupture, stroke, vascular complications, acute kidney injury, and in-hospital mortality. We also studied the possible anatomical determinants of PVL.
Results: There were no relevant baseline differences between the 2 groups regarding clinical and echocardiographic characteristics. In-hospital complications were comparable between both valves apart from a significantly higher rate of immediate postoperative PVL and at discharge (≥ grade II) between the Evolut PRO and the SAPIEN 3 valves (19.6% vs 6.8%) and (5.9% vs 1.7%), respectively. Of the anatomical variables described, the left ventricular outflow tract/ascending aorta angle, aortic angulation, and calcification had a significant impact on PVL in the Evolut PRO valves. The left ventricular outflow tract/ascending aorta angle revealed a negative correlation with implantation depth in the Evolut PRO valves but not in the SAPIEN 3 ones.
Conclusions: Both valves demonstrated favorable comparable outcomes except for a significantly higher rate of PVL in patients implanted with Evolut PRO valves.

Keywords: Aortic stenosis. Transcatheter aortic valve implantation. TAVI. SAPIEN 3. Evolut PRO.

Implante percutáneo de válvula aórtica con Evolut PRO comparada con SAPIEN 3: estudio comparativo aleatorizado

RESUMEN

Introducción y objetivos: Los avances en la tecnología de implante percutáneo de válvula aórtica (TAVI) han dado lugar a mejores resultados y menos complicaciones en comparación con las generaciones anteriores. Se estudió la incidencia y los determinantes de las fugas paravalvulares (FPV) con las válvulas Evolut PRO y SAPIEN 3, así como otros resultados periprocedimiento y hospitalarios.
Métodos: Se seleccionó aleatoriamente a 110 pacientes consecutivos con estenosis aórtica grave programados para TAVI transfemoral para recibir una válvula SAPIEN 3 (n = 59) o una Evolut PRO (n = 51). Las dimensiones anulares se determinaron mediante el dimensionamiento del balón guiado por ecocardiografía transesofágica. Tras el procedimiento y durante la hospitalización, se evaluaron los siguientes objetivos: FPV, defectos de conducción, embolización de la válvula, necesidad de una segunda válvula, rotura anular, accidente vascular cerebral, complicaciones vasculares, daño renal agudo y mortalidad intrahospitalaria. También se estudiaron los posibles determinantes anatómicos de la FPV.
Resultados: No hubo diferencias basales relevantes entre los 2 grupos en cuanto a las características clínicas y ecocardiográficas. Las complicaciones intrahospitalarias fueron comparables entre ambos tipos de válvulas, excepto una incidencia significativamente mayor de FPV (de grado II o superior) inmediata tras el procedimiento y al alta con las válvulas Evolut PRO en comparación con las SAPIEN 3 (19,6 frente a 6,8% y 5,9 frente a 1,7%, respectivamente). De las variables anatómicas, el ángulo entre el tracto de salida del ventrículo izquierdo y la aorta ascendente, la angulación aórtica y la calcificación tuvieron un impacto significativo en la FPV en las válvulas Evolut PRO. El ángulo entre el tracto de salida del ventrículo izquierdo y la aorta ascendente tuvo una correlación negativa con la profundidad de implantación en las válvulas Evolut PRO, pero no en las válvulas SAPIEN 3.

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Conclusiones: Ambas válvulas demostraron resultados favorables comparables, excepto por una incidencia significativamente mayor de FPV en los pacientes con válvulas Evolut PRO.

Palabras clave: Estenosis aórtica. Implante percutáneo de válvula aórtica. TAVI. SAPIEN 3. Evolut PRO.

Abbreviations

AS: aortic stenosis. **PVL:** paravalvular leak. **TAVI:** transcatheter aortic valve implantation. **VARC:** Valve Academic Research Consortium.

INTRODUCTION

Over the past decade, the self-expandable CoreValve (Medtronic Ltd, United States) and the balloon-expandable SAPIEN valve (Edwards Lifesciences Ltd, United States) were the valves most commonly used for transcatheter aortic valve implantation (TAVI).[1]

There are few studies comparing Evolut PRO (Medtronic Ldt, United States) vs SAPIEN 3 (Edwards Lifesciences Ltd, United States), like the SMART trial for small aortic annuli[2] and the ALSTER-TAVI all-comers registry.[3] However, comparative randomized clinical trials are lacking. Therefore, we designed the present randomized study to provide a head-to-head comparison between these 2 valves regarding procedural data and in-hospital outcomes especially paravalvular leak (PVL). Although the transcatheter heart valves used in this trial are not the latest generation valves of the CoreValve and SAPIEN families (currently, the Evolut-Pro plus and the SAPIEN Ultra), this is the first randomized clinical trial to compare a self-expanding valve with an outer skirt to a balloon expandable valve (with an outer skirt too).

METHODS

Study population

A total of 110 consecutive patients with severe symptomatic aortic stenosis eligible for TAVI were randomly assigned to receive the Evolut PRO valve (51 patients) or the SAPIEN 3 valve (59 patients) at Duisburg Heart Center, Duisburg, Germany, from December 2019 through May 2020. All patients undergoing TAVI for severe aortic stenosis with the SAPIEN 3 and the Evolut PRO via femoral access were included. Patients who underwent TAVI with other valve types like transapically implanted aortic valves, bicuspid aortic valves, and valve-in-surgical-bioprosthesis implantation were excluded. All procedures were performed after obtaining the patients' written informed consent and in compliance with the national research committee ethical standards.

Procedural aspects

TAVIs were performed under local anesthesia and conscious sedation. Femoral cutdown was used in all the patients. Annular dimensions were obtained by transesophageal echocardiography-guided balloon sizing during the procedure. With this technique we were able to measure annuli with transesophageal echocardiography and then choose a balloon equal to annular size. Balloon inflation during rapid pacing and aortic angiography were performed with 3 different possibilities in mind *a)* the balloon completely fills the annulus with no para-balloon leak or waisting indicative that annular size equals the balloon size; *b)* para-balloon leak is indicative that the annulus is 1 mm to 2 mm larger than balloon size; *c)* balloon waisting is indicative that the annulus is 1 mm to 2 mm smaller than balloon size.[4] Valve type (SAPIEN 3 or Evolut PRO) was randomly selected (using simple randomization method; Monday cases for Evolut and Thursday cases for SAPIEN). Valve size was based on the annular dimensions as suggested by the manufacturers. Based on annular diameter and the diameter of the valve finally selected, a so-called cover index was calculated.[5]

Endpoints

Our primary endpoints were PVL, in-hospital mortality, and the rate of permanent pacemaker implantation (PPI). The study secondary endpoints were valve embolization, need for a second valve, aortic rupture or dissection, stroke or transient ischemic attack, major vascular complications, and acute kidney injury. Endpoints were defined according to the Valve Academic Research Consortium-2 (VARC-2) definitions.[6]

PVL assessment

Immediate PVL was semi-quantitatively assessed using Seller's criteria 7: 0/4 (absent); 1/4 (mild); 2/4 (moderate); 3/4 (moderate-to-severe); and 4/4 (severe).[7] Transvalvular pressure gradients were obtained invasively using the pullback method. Aortic regurgitation index (AR index) was calculated.[8]

In case of significant PVL ≥ grade II, if needed, balloon postdilatation using the VACS III or NUCLEUS balloon (NuMED, United States) or else implantation of second valve was used. TTE was performed at discharge to quantify PVL according to the main VARC-2 criteria.[9]

Assessment of anatomical factors possibly associated with PVL

The following measurements were supported by Philips software (Philips Medical, The Netherlands): the left ventricular outflow tract/ascending aorta (LVOT/AAo) angle was defined as the angle between the axis of the first 4 cm of the ascending aorta (contact surface with the upper part of the prosthesis), and the LVOT axis (the valve landing zone) indicated by a line perpendicular to the plane of the aortic valve annulus).[10]

Aortic angulation (AA) angle was defined as the angle between the horizontal plane and the plane of aortic annulus.[11] We categorized it into < 48° and ≥ 48°.[12]

Both angles were measured in the optimal fluoroscopic deployment position with all 3 coronary cusps in the same plane (figure 1). Valve implantation depth was assessed in the deployment position on the fluoroscopy from the native aortic annular margin on the side of both the non-coronary cusp (NCC) and left coronary cusp to the proximal edge of the deployed valve on the corresponding side[13] (figure 2).

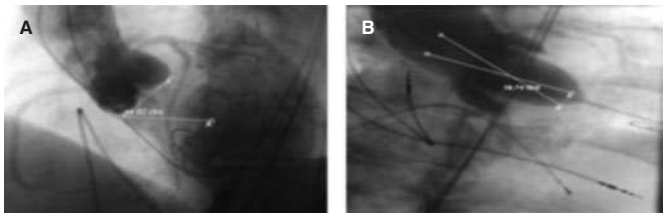

Figure 1. Measurement of different angles. AA, aortic angulation (49.62º). **B:** LVOT/AAo angle (18.74º). AAo, ascending aorta; LVOT, left ventricular outflow tract.

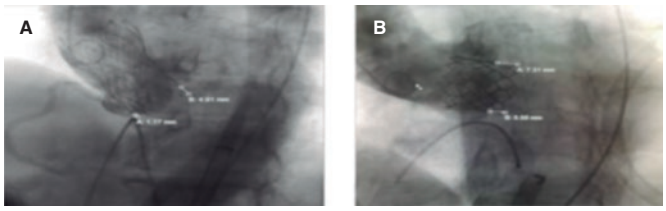

Figure 2. Measurement of implantation depth in the Evolut PRO value. **A:** [A = 1.17 mm associated with the NCC, and B = 4.91 mm associated with the LCC], and SAPIEN 3. **B:** [A = 5.65 mm associated with the NCC, and B = 7.31 mm associated with the LCC]. Note high implantation associated with the NCC due to increased LVOT/AAo angle in the Evolut PRO (A) but not in the SAPIEN 3 valve (B). AAo, ascending aorta; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non-coronary cusp.

Aortic root calcification was fluoroscopically assessed as inexistent, mild (small, isolated calcification spots), moderate (multiple large calcification spots) or severe (extensive calcification).[13] Presence or absence of LVOT and mitral annular calcification were also noted.

Statistical analysis

Data was collected and analyzed using the SPSS (Statistical Software Package for the Social Sciences, version 20, IBM, and Armonk, United States). Continuous data was expressed as mean ± SD or median (range). Nominal data was expressed as frequency (percentage). For the comparison of nominal and continuous data, the chi-square test and the Student's *t* test were used, respectively. Pearson correlation was used to assess the correlation between implantation depth with LVOT and AA angles based on the type of valve. The level of confidence was kept at 95% and hence, *P* values < .05 were considered statistically significant. Univariable logistic regression analysis was performed for predictors of significant PVL. ROC analysis was performed for the optimum cut-off value of the LVOT/AAo angle for the outcome of significant PVL.

Regarding sample size, assuming a 1:1 ratio in treatment assignments and an estimated rate of a composite primary endpoint (PVL, in-hospital mortality and rate of pacemaker implantation) of 8% in each study group, we estimated that a total of 52 patients were required in each group for the study to reach an 80% statistical power % at a 1-sided alpha level of 0.05

RESULTS

Baseline characteristics

A total of 110 consecutive patients with severe symptomatic aortic stenosis eligible for TAVI were randomly assigned to receive the Evolut PRO (51 patients) or the SAPIEN 3 valve (59 patients). There was no crossover between both study arms. Baseline clinical characteristics were comparable between both types of valves apart from a significantly higher body mass index among SAPIEN 3 patients and a significantly high baseline right bundle branch block in the SAPIEN group (table 1).

Table 1. Patient characteristics associated with the type of valve implanted

	Type of valve		*P*
	Evolut PRO (N = 51)	SAPIEN 3 (N = 59)	
Age (years)	82.6 ± 6.4	81.2 ± 5.8	.22
Sex			.39
Male	54.9	59.3	
Female	45.1	40.7	
Body mass index (kg/m²)	26.4± 4.7	28.7 ± 4.7	.01[a]
Body surface area (m²)	1.9 ± 0.4	1.9 ± 0.2	.08
Peripheral artery disease	11.8	6.8	.28
Hypertension	76.5	83.1	.26
Diabetes mellitus	29.4	37.3	.25
Ischemic heart disease	62.0	45.8	.06
Previous revascularization (PCI/CABG)	41.2	37.3	.53
Previous history of stroke	5.9	5.1	.58
Previous pacemaker	9.8	6.8	.40
Chronic chest disease	9.8	23.7	.31
NYHA class			.09
II	13.7	15.3	
III	86.3	78.0	
IV	0.0	6.8	
STS score	3.8 ± 2.6	3.5 ± 2.2	.51
STS class (%)			.65
Low (< 4%)	58.8	66.1	
Intermediate (4% to 8%)	35.3	27.1	
High (> 8%)	5.9	6.8	
ECG findings			.95
Sinus	43.1	45.8	
Paced	7.8	6.8	
Atrial fibrillation	49.0	47.5	
Total preoperative conduction defects	19.6	22.0	.47
Baseline RBBB	0.0	16.9	.001[b]

Unless otherwise indicated, data are expressed as no. (%). Preoperative conduction defects included atrioventricular block, intraventricular conduction delay, left anterior hemiblock, left bundle branch block, and RBBB. CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; OSAS, obstructive sleep apnea syndrome; PCI, percutaneous coronary intervention; RBBB, right bundle branch block; STS, Society of Thoracic Surgery risk score.

[a] Significant *P* values.

[b] Highly significant *P* values.

Table 2. Echocardiographic and fluoroscopic data among the different study groups

	Type of valve		*P*
	Evolut PRO (N = 51)	SAPIEN 3 (N = 59)	
Mean PG (mmHg)	42.3 ± 7.7	42.8 ± 9.9	.78
Maximum PG (mmHg)	68.5 ± 10.5	67.3 ± 12.0	.56
Aortic valve area (mm)	0.9 ± 0.7	0.9 ± 0.2	.46
Ejection fraction (%)			
Class of ejection fraction	48.4 ± 11.7	50.9 ± 11.7	.25
Preserved (> 50%)	62.7	67.8	.76
Mildly impaired (40% to 50%)	17.6	15.3	
Moderately impaired (30% to 40%)	9.8	11.9	
Severely impaired (< 30%)	9.8	5.1	
Flow gradient (%)			
HFHG	74.5	71.2	.91
LFLG/Impaired EF	19.6	22.0	
LFLG/Preserved EF	5.9	6.8	
Aortic measurements (by TEE)			
Aortic valve area (mm)	0.7 ± 0.1	0.7 ± 0.2	.22
Annulus (mm)	23.8 ± 2.1	24.5 ± 1.9	.07
LVOT (mm)	21.1 ± 2.1	21.6 ± 2.4	.26
Sinus of Valsalva (mm)	30.7 ± 3.6	31.2 ± 3.8	.45
Sinotubular junction (mm)	25.9 ± 3.1	26.4 ± 3.5	.37
Ascending aorta (mm)	33.3 ± 5.9	33.7 ± 4.6	.68
Distance of STJ/LVOT (mm)	20.1 ± 10.5	19.4 ±3.2	.62
Aortic root calcification (%)			
Annular calcification			.49
Mild	66.7	71.2	
Moderate	27.5	27.1	
Severe	5.9	1.7	
Sinotubular calcification	5.9	8.5	.44
LVOT calcification	19.6	11.9	.19
Mitral annular calcification	15.7	18.6	.44
LVOT/AAo angle (°)	13.7 ± 5.1	13.9 ± 5.2	.84
AAo angle (°)	46.5 ± 9.4	47.5 ± 12.1	.62

AAo, ascending aorta; Ao, aorta; EF, ejection fraction; HFHG, high flow-high gradient; LFLG, low flow-low gradient; LVOT, left ventricular outflow tract; PG, pressure gradient; STJ, sinotubular junction; TEE, transesophageal echocardiography.

Table 3. Procedural data associated with each type of valve

	Type of valve		*P*
	Evolut PRO (N = 51)	SAPIEN 3 (N = 59)	
Route (%)			.51
Right femoral	60.8	59.3	
Left femoral	39.2	40.7	
Annulus by TEE (mm)	23.8 ± 2.1	24.5 ± 1.9	.07
Balloon size (mm)	22.5 ± 1.9	22.6 ± 1.9	.63
Balloon sizing (mm)	23.4 ± 1.7	23.6 ± 1.9	.44
Valve size (%)			
23	0.0	30.5	
26	43.1	45.8	
29	56.9	23.7	
Sheath size (Fr)	16.0	14.5 ± 0.9	< .001
Sheath outer diameter (mm)	7.3 ± 0.1	6.2 ± 0.3	< .001
Femoral artery diameter (mm)	7.9 ±1.1	8.2 ± 0.9	.20
Sheath femoral artery ratio	0.9 ± 0.1	0.8 ± 0.1	< .001
Cover index (%)			
TEE	16.4 ± 5.6	5.2 ± 4.2	< .001
Balloon	18.3± 3.3	8.9 ± 3.3	< .001
Valve mean pressure gradient	9.8	12.2	.01
AR index (%)	28.4 ± 7.8	30.7 ± 7.4	.11
Implantation depth (mm)			
LCC	5.8 ± 2.3	4.2 ± 1.7	< .001
NCC	6.3 ± 2.5	5.27 ± 1.7	.01
Amount of contrast (mL)	145.5 ± 48.8	128.6 ± 33.2	.03
Radiation (mGy)	4944.4 ± 2294.8	4557.8 ± 3133.9	.46

AR, aortic regurgitation; LCC, left coronary cusp; NCC, non-coronary cusp; TEE, transesophageal echocardiography.

Echocardiographic and fluoroscopic findings

The baseline echocardiographic and fluoroscopic findings of both groups were comparable (table 2).

Procedural data in relation to the type of valve used

There were few differences in procedural data related to valve design and sheath size as shown on table 3.

Outcomes in association with the type of valve used

There was a significant difference in PVL (both immediate and at hospital discharge) and consequently more balloon postdilatation in

Table 4. In-hospital outcomes in patients treated with the Evolut PRO vs the SAPIEN 3 valve

	Type of valve		*P*
	Evolut PRO (N = 51)	SAPIEN 3 (N = 59)	
Immediate PVL			.01
No/trace	19 (37.3)	46 (78)	
Grade I	22 (43.1)	9 (15.2)	
≥ grade II	10 (19.6)	4 (6.8)	
Balloon postdilatation	8 (15.7)	3 (5.1)	.35
PVL at discharge			.01
No/trace	26 (50.9)	49 (83.1)	
Grade I	22 (43.1)	9 (15.3)	
Grade II	2 (3.9)	1 (1.7)	
Grade III	1 (2)	0	
Grade IV	0	0	
Overall new-onset conduction defects	9 (17.6)	10 (16.9)	.56
New-onset LBBB	4 (7.8)	4 (6.7)	.40
Postoperative pacemaker implantation	4 (7.8)	3 (5.1)	.25
Vascular complications			.66
Major vascular complications	2 (3.9)	2 (3.4)	
Minor vascular complications	4 (7.9)	3 (5.1)	
Bleeding complications	0	0	
*Acute kidney injury**	3 (5.9)	2 (3.4)	.28
Stroke	1 (2)	0	.46
Valve embolization	1 (2)	0	.46
Need for second valve	2 (3.9)	0	.30
In-hospital mortality rate	2 (3.9)	0	.30

Data are expressed as no. (%). PVL, paravalvular leak.
* Acute kidney injury including all stages of the disease.

the Evolute compared to the SAPIEN 3 group. The use of significantly larger amounts of contrast with the Evolut PRO valves may explain the increased number of acute kidney injury described in this group compared to the SAPIEN valve group. Results were favorable to the SAPIEN 3 valve regarding the endpoints of stroke or in-hospital mortality. However, no statistically significant differences were reported. The rates of device success (absence of a significant PVL (≥ grade II) at hospital discharge, need for second valve implantation, valve embolization, the performance of the prosthetic heart valve, and mortality) were 86% and 98% with the Evolut PRO and SAPIEN 3 valves, respectively; *P* = .01 (table 4).

Impact of anatomical factors on PVL

Calcification and the LVOT/AAo angle had a greater impact on PVL in the Evolut PRO compared to the SAPIEN 3 valve. The LVOT/AAo angle was categorized based on the receiver operating characteristic (ROC)-derived cut-off value for the endpoint of significant PVL ≥ grade II: cut-off value = 11°, 80% sensitivity, and 35.8% specificity, area under the curve (0.57; 95% confidence interval, 0.474-0.666; *P* = .37.) On the other hand, the AA angle did not seem to be very relevant to PVL within the groups (table 5).

Table 6 shows the univariate analysis of predictors of ≥ grade II PVL immediately after the procedure. As demonstrated, moderate and severe valvular calcification, LVOT calcification, and the LVOT/AAo angle contribute to PVL significantly.

Impact of LVOT/AAo and AA angles on implantation depth

There was a significant negative correlation between the implantation depth of the Evolut PRO valve at the NCC and LVOT/AAo angles (r = -0.38; *P* = .01). There was no such correlation with the SAPIEN 3 valve (table 7).

DISCUSSION

In this study 2 important findings were made. First, implantation of the Evolut PRO valve was associated with a higher risk of significant PVL compared to the SAPIEN 3 valve. Secondly, the rate of PPI was equal in both groups. Otherwise, both types of valves yielded similar outcomes.

Reducing PVL is an important challenge regarding TAVI as it is associated with worse outcomes especially with the current use of these devices in lower-risk patients.[14]

A randomized comparison between the CoreValve and SAPIEN XT valves in the CHOICE trial revealed a lower rate of moderate-to-severe PVL in the SAPIEN XT group.[15] In the SOLVE-TAVI trial, the non-inferiority of 2 devices (SAPIEN 3 and Evolut R) was reported in terms of their primary efficacy composite endpoint (death, stroke, paravalvular regurgitation, and new pacemaker implantation).[16] Currently, the SAPIEN 3 Ultra and Evolut PRO+ have been developed with early favorable outcomes.[17]

In our study, relevant PVL (≥ grade II) was more common in patients who received the Evolut PRO compared to the SAPIEN 3 valve (9.6% vs 6.8%, respectively). Enríquez-Rodríguez et al. reported a lower rate (2.5%) of moderate to severe PVL with the SAPIEN 3 valves possibly due to the presence of an external sealing cuff.[18]

Obviously, anatomical factors are important for the occurrence of PVL. We observed that larger LVOT/AAo angles were associated with a higher rate of PVL, particularly with the Evolut PRO valve. Sherif et al. demonstrated that the risk of PVL increases with larger LVOT/AAo angles.[10] We also observed that the LVOT/AAo angle affects implantation depth in association with the NCC with the Evolut PRO, but not with the SAPIEN 3 valves. It is quite conceivable that implantation depth impacts the rate of PVL.

Sherif et al. were the first ones to report on the association between increased AA angles and postoperative PVL with self-expanding valves.[10] A subsequent retrospective study conducted by Abramowitz et al. described a higher rate of complications (eg, postoperative PVL in patients with horizontal aortas (defined by an AA ≥ 48° as seen on the cardiac CT scan) who received self-expanding valves.[11] We observed that AA angles impacted PVL in patients who received Evolut PRO valves even if these angles were < 48° with no significant differences in the rate of PVL for AA angles < 48° or ≥ 48°.

Table 5. Association between anatomical factors and PVL in patients treated with the Evolut PRO vs the SAPIEN 3 valves

	Evolut PRO valve (N = 51)		SAPIEN 3 Valve (N = 59)		*P*[a]	*P*[b]	*P*[c]
	< Mild PVL	≥ Mild PVL	< Mild PVL	≥ Mild PVL			
Number	37.3	62.7	77.9	22.0			.01
Annular calcification					.03	.2	
Mild	31.4	35.3	59.3	11.9			.001
Moderate	5.9	21.6	16.9	10.2			.024
Severe	0.0	5.9	1.7	0.0			.046
LVOT calcification	1.7	17.6	3.4	8.5	.04	.001	.323
Mitral annular calcification	0.0	15.7	15.3	3.4	.001	.2	.035
LVOT/AAo angle[a]					.01	.001	
< 11°	17.6	15.7	25.4	1.7			.002
≥ 11°	19.6	47.1	52.5	20.3			.03
AAo angle (%)					.78	.34	
< 48°	23.5	37.2	45.8	15.2			.003
> 48°	13.7	25.5	32.2	6.8			.001

LVOT, left ventricular outflow tract; AAo, ascending aorta.
An LVOT/AAo angle of 11° is the cut-off vale for the rate of PVL as detected by the ROC curve.
Data are expressed as percentage (%).
[a] *P* value within the Evolut PRO group.
[b] *P* value within the SAPIEN 3 group.
[c] *P* value from a chi-square score between both groups.

Table 6. Univariate analysis of predictors of significant immediate postoperative PVL (grade ≥ 2)

Variable	Univariate	
	OR (95%CI)	*P*
Severe calcification	35.000 (3.138-390.431)	.004
LVOT calcification	10.921 (3.208-37.174)	< .001
LVOT/AAo angle	1.047 (0.940-1.165)	.003
AA	1.016 (0.967-1.067)	.524
Valve type (Evolut PRO)	2.750 (0.872-8.669)	.084
TEE cover index	1.099 (1.018-1.188)	.016
Cover index by balloon sizing	1.108 (1.001-1.226)	.049
LCC implantation depth	1.199 (0.953-1.510)	.122
RCC implantation depth	1.167 (0.914-1.489)	.215

P value was significant if < .05. 95%IC, 95% confidence interval; AA, aortic angulation; AAo, ascending aorta; AR, aortic regurgitation; LCC, left coronary cusp; LVOT, left ventricular outflow tract; PVL, paravalvular leak; RCC, right coronary cusp; TEE, transesophageal echocardiography.

Table 7. Correlation of implantation depth (in both valves) with the LVOT/AAo and AA angles

	Type of valve			
	Evolut PRO		SAPIEN 3	
	LCC	NCC	LCC	NCC
LVOT/AAo angle (°)	-0.23 (0.09)	-0.38 (0.01)	0.09 (0.46)	0.16 (0.21)
AAo angle (°)	0.13 (0.33)	0.06 (0.65)	0.02 (0.87)	0.06 (0.61)

r indicates strength of correlation and *P* value indicates significance of correlation. *P* value was significant if < .05. AAo, ascending aorta; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non-coronary cusp.

In this study we also observed 6 patients with AA angles ≤ 30° (3 patients with Evolut PRO and 3 patients with SAPIEN 3). All of them were free of PVL immediately after valve deployment. One could speculate that AA angles ≤ 30° are the best for Evolut PRO valve implantation, but the small size of the sample prevents us from drawing any definitive conclusions.

In our study, the rates of device success determined by the absence of a significant PVL (≥ grade II) at hospital discharge, need for a second valve, valve embolization, the performance of the prosthetic heart valve, and the mortality rate according to VARC definition[9] were 86% and 98% with the Evolut PRO and SAPIEN 3 valve, respectively. Similarly, Li et. al found a high device success rate for both the SAPIEN 3 and the Evolut R valve (94% and 96%, respectively).[19]

We found similar rates of postoperative conduction defects and PPI for both Evolut PRO and SAPIEN 3 valve types (7.8% and 5.1%, respectively). Popma et al.[20] and Vlastra et al.[21] reported lower rates of PPI with new generation balloon expandable valves compared to new-generation self-expanding valves. The comparable rates of conduction defects and PPI with either valve in our study was probably due to the lower implantation depth of Evolut PRO valves.

Li et al. reported higher rates of postdilatation of up to 30% with the Evolut R compared to the SAPIEN 3 valve.[19] This was not seen in our study (15.7% and 5.1%, respectively; $P = .35$). This was probably so thanks to the proper positioning of the Evolut PRO valve and routine predilatation in all our cases.

In this study, in-hospital mortality was similar in both valve groups. Li et al. also reported that mortality was not associated with the type of valve implanted.[19] The CHOICE trial also showed a comparable mortality rate with the use of older-generation valves (CoreValve and SAPIEN XT).[15]

The rates of stroke were similar for both the Evolut PRO and the SAPIEN 3 valve and lower compared to those seen with older generation devices.[15,19,22,23] The operators' experience and improved delivery systems are likely to account for the reduced risk of thromboembolic complications.

Regardless of the type of valve used, acute kidney injury seemed to be slightly more common in our study (5.9% and 3.5% for the Evolut PRO and the SAPIEN 3, respectively) than previously reported. Husser et al.[24] noted a rate of 2.7% in SAPIEN 3 valves while Kodali et al.[25] reported rates of 1.7%. However, large multicenter studies usually have stricter inclusion criteria so the baseline kidney function of the patients included was better.[19]

Despite increased sheath/femoral artery ratios with the Evolut PRO valve, the rate of bleeding or vascular complications was similar compared to the SAPIEN 3 valve. Similar results were reported by Li et al.[19] and Panchal et al.[26]

Limitations

This was a single-center study with a small sample size and limited statistical power. As routine computed tomography scan was not part of our study, specific information on the anatomy of the aortic root was not available and no adjustment was performed based on the annular dimensions or degree/distribution of aortic annular calcification. Also, angiography-based measurements of the LVOT/AAo and AA angles may be inaccurate. However, this may have helped exclude selection bias as some operators are reluctant to use self-expanding valves in view of heavy calcifications or severe angulation.

Follow-up was limited to the length of stay (average 1 week). However, this seems reasonable since we focused on procedural aspects. Furthermore, in comparable studies, in-hospital outcome and 30-day follow-up results were quite similar.

CONCLUSIONS

This randomized study demonstrated comparable procedural and in-hospital outcomes for the Evolut PRO and SAPIEN 3 valves except for a significantly higher rate of PVL associated with the Evolut PRO valves. The PVL reported was associated with the LVOT/AAo angle in Evolut PRO group, which also impacted negatively the implantation depth of this type of valve.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

Idea and design: H. M. Elnaggar, M. S. Mahmoud, W. Schoels, and Y. T. Kishk. Administrative support: W. Schoels, M. Kullmer, and M. Dia. Provision of study materials or patients: M. S. Mahmoud, M. Algowhary, and H. M. Elnaggar. Data collection and assembly: M. S. Mahmoud, M. Kullmer, and M. Dia. Data analysis and interpretation: M. S. Mahmoud, Y. T. Kishk, M. Algowhary, and H. M. Elnaggar. Manuscript drafting and final approval: all authors.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THE TOPIC?

- Self-expanding (Evolut platform) and balloon-expandable (SAPIEN series) valves are the most commonly used TAVI devices.
- Outcomes between both types of valves are similar with a relative increase of PVL and conduction defects in the Evolut type.
- Also, there are some anatomical challenges when deploying self-expanding valves such as severe aortic angulation (horizontal aorta).
- There is no prospective randomized clinical trials comparing Evolut PRO (self-expanding valve with external skirt) to SAPIEN 3 valves.

WHAT DOES THIS STUDY ADD?

- This is considered the first prospective randomized clinical trial that compared the Evolut PRO valve (self-expanding valve with external skirt) to the SAPIEN 3 valve.
- This study demonstrated comparable favorable outcomes between both types of valves apart from a significantly higher PVL in the Evolut PRO group.
- Also, in our study, LVOT/AAo and AA angulation had an impact on PVL in the Evolut PRO group compared to the SAPIEN 3 group. However, AA angulation had no impact on PVL within the groups.
- The LVOT/AAo angle was negatively associated with implantation depth in the case of the Evolut PRO valve with no effect on SAPIEN 3 valves whatsoever, which may have impacted the development of PVL in the Evolut PRO group.

REFERENCES

1. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. *J Am Coll Cardiol*. 2013;61:1585-1595.
2. Herrmann HC, Abdel-Wahab M, Attizzani GF, et al, Rationale and design of the SMall Annuli Randomized to Evolut or SAPIEN Trial (SMART Trial). *Am Heart J*. 2022;243:92-102.
3. Paitazoglou C, Meincke F, Thorsten Hanke M, et al. The ALSTER-TAVI All-Comers Registry: Procedural and 1-Year Clinical Outcomes of Balloon-Expandable vs Self-Expanding Contemporary TAVI Valves. *J Invasive Cardiol*. 2021;33:E356-E364.
4. Mahmoud MS, Kishk YT, Algowhary M, et al. Balloon Sizing for Transcatheter Aortic Valve Implantation Using 3 rd Generation Valves, Does It Still Work? *Int Med J*. 2021;28:604-609.

5. Détaint D, Lepage L, Himbert D, et al. Determinants of significant paravalvular regurgitation after transcatheter aortic valve implantation: impact of device and annulus discongruence. *JACC Cardiovasc Interv*. 2009; 2:821-827.
6. Wang J, Yu W, Jin Q, et al. Risk factors for post-TAVI bleeding according to the VARC-2 bleeding definition and effect of the bleeding on short-term mortality: a meta-analysis. *Can J Cardiol*. 2017;33:525-534.
7. Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: Technic, indications and interpretations in 700 cases. *Am J Cardiol*. 1964;14:437-447.
8. Sinning JM, Hammerstingl C, Vasa-Nicotera M, et al. Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation. *J Am Col Cardiol*. 2012;59:1134-1141.
9. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Thorac Cardiovasc Surg*. 2013;145:6-23.
10. Sherif MA, Abdel-Wahab M, Stöcker B, et al. Anatomic and procedural predictors of paravalvular aortic regurgitation after implantation of the Medtronic CoreValve bioprosthesis. *J Am Col Cardiol*. 2010;56:1623-1629.
11. Abramowitz Y, Maeno Y, Chakravarty T, et al., Aortic angulation attenuates procedural success following self-expandable but not balloon-expandable TAVR. *JACC Cardiovasc Imaging*. 2016;9:964-972.
12. Di Stefano D, Colombo A, Mangieri A, et al. Impact of horizontal aorta on procedural and clinical outcomes in second-generation transcatheter aortic valve implantation. *EuroIntervention*. 2019;15:e749-e756.
13. Mostafa AE, Richardt G, and Abdel-Wahab M. Clinical utility of a predictive model for paravalvular aortic regurgitation after transcatheter aortic valve implantation with a self-expandable prosthesis. *Egypt Heart J*. 2017;69:253-259.
14. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2017;376:1321-1331.
15. Abdel-Wahab M, Mehilli J, Frerker C, et al. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA Cardiol*. 2014;311:1503-1514.
16. Webb J, Wood D, Sathananthan J, Landes U. Balloon-expandable or self-expandable transcatheter heart valves. Which are best? *Eur Heart J*. 2020;41: 1900-1902.
17. Jiang T, Hasan SM, Faluk M, Patel J. Evolution of Transcatheter Aortic Valve Replacement| Review of Literature. *Curr Probl Cardiol*. 2021;46:100600.
18. Enríquez-Rodríguez E, Amat-Santos IJ Jiménez-Quevedo P, et al. Comparison of the hemodynamic performance of the balloon-expandable SAPIEN 3 versus self-expandable Evolut R transcatheter valve: a case-matched study. *Rev Esp Cardiol*. 2018;71:735-742.
19. Li Y-M, Tsauo J-Y, Liao Y-B, Zhao Z-G, Chen M. Comparison of Third Generation Balloon-Expandable Edwards Sapien 3 Versus Self-Expandable Evolut R in Transcatheter Aortic Valve Implantation: A Meta-Analysis. *Ann Palliat Med*. 2020;9:700-708.
20. Popma JJ, Reardon MJ, Khabbaz K, et al. Early clinical outcomes after transcatheter aortic valve replacement using a novel self-expanding bioprosthesis in patients with severe aortic stenosis who are suboptimal for surgery: results of the Evolut R US study. *JACC Cardiovasc Interv*. 2017; 10:268-275.
21. Vlastra W, Chandrasekhar J, Muñoz-Garcia AJ, et al. Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transfemoral transcatheter aortic valve implantation: from the CENTER-collaboration. *Eur Heart J*. 2019;40:456-465.
22. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med*. 2011;364:2187-2198.
23. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med*. 2014;370: 1790-1798.
24. Husser O, W.-K. Kim, et al. Multicenter comparison of novel self-expanding versus balloon-expandable transcatheter heart valves. *JACC Cardiovasc Interv*. 2017;10:2078-2087.
25. Kodali S, Thourani VH, White J, et al. Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. *Eur Heart J*. 2016;37:2252-2262.
26. Panchal HB, Barry N, Bhatheja S, Albalbissi K, Mukherjee D, Paul T. Mortality and major adverse cardiovascular events after transcatheter aortic valve replacement using Edwards valve versus CoreValve: A meta-analysis. *Cardiovasc Revasc Med*. 2016;17:24-33.

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Original article

Prospective assessment of clinical outcomes of transcatheter aortic valve implantation in a cohort of patients based on their risk profile

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ABSTRACT

Introduction and objectives: Transcatheter aortic valve implantation (TAVI) is an increasingly used procedure to treat severe aortic stenosis (AS) that should be monitored in the real-world routine clinical practice. We assessed TAVI outcomes (SAPIEN 3) in terms of the patient's health-related quality of life (HRQoL), clinical endpoints, and resource utilization considering a valid risk score.
Methods: This was an observational prospective study including all consecutive patients with severe AS treated with TAVI (Edwards SAPIEN 3, transfemoral access) conducted during the calendar year of 2018. A systematic assessment of the patients' HRQoL (EQ-5D-5L, the 36-item Short Form Health Survey, and the Kansas City Cardiomyopathy Questionnaire), clinical endpoints, and resource utilization (length of stay at the hospital/intensive care unit setting) was implemented. Assessment was scheduled before the procedure (baseline), at discharge, and 1, 6, and 12 months after implantation. Multivariate regression models were applied to test outcomes while controlling the patients' risk (eg, Society of Thoracic Surgeons risk score).
Results: A total of 76 patients (50% female) with a mean age of 82.05 ± 4.76 years, and 55% with intermediate-high risk were included. The rates of successful impantation and cardiac death were 97.37% and 2.63%, respectively, at 1 year. Significant reductions in mean and maximum gradients were achieved and maintained at follow-up. The mean length of stay at the hospital (5.2 6 ± 4.05) and intensive care unit setting (0.22 ± 0.64) was short. Significant improvements (all adjusted $P < .05$) were detected in the Kansas City Cardiomyopathy Questionnaire overall summary scores, EQ-5D-5L, and the 36-item Short Form (physical component summary).
Conclusions: This research highlights how positive clinical outcomes translated into significant improvements in relation to the patients' HRQoL. Use of resources —generally low— was based on the Society of Thoracic Surgeons risk score. (SARU Study; code: 2017-01, Murcia, Spain).

Keywords: Aortic valve stenosis. Quality of life. Health resources. Length of stay. Clinical endpoint. Burden of illness.

Evaluación de los resultados en salud del implante valvular aórtico transcatéter en una cohorte de pacientes según su perfil de riesgo

RESUMEN

Introducción y objetivos: El uso del implante percutáneo de válvula aórtica (TAVI, *transcatheter aortic valve implantation*) está aumentando en el tratamiento de la estenosis aórtica grave. Por ello, el uso de TAVI en la vida real debe monitorizarse. Evaluamos los resultados del TAVI en términos de calidad de vida relacionada con la salud (CVRS), resultados clínicos y uso de recursos teniendo en cuenta un marcador de riesgo válido.
Métodos: Estudio observacional prospectivo incluyendo todos los pacientes consecutivos con estenosis aórtica grave tratados con TAVI (Edwards SAPIEN 3, acceso transfemoral) en 2018. Se evaluaron de forma sistemática la CVRS (EQ-5D-5L, *Short Form-36 Health Survey, Kansas City Cardiomyopathy Questionnaire*), los resultados clínicos y el uso de recursos (estancia en planta/unidad de cuidados intensivos). La evaluación se hizo antes de la intervención (basal), al alta y después de 1,6 y 12 meses del implante. Se aplicaron modelos de regresión multivariante para evaluar los resultados mientras se controlaba el riesgo del paciente (por ejemplo, escala de riesgo de la *Society of Thoracic Surgeons*).

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***Resultados*:** Se incluyó a 76 pacientes (el 50% mujeres), con una edad media de 82,05 ± 4,76, y el 55% con riesgo intermedio-alto. Hubo un 97,37% de éxito del implante y la tasa de muerte de causa cardiovascular fue del 2,63% al año. Se consiguieron reducciones significativas en los gradientes medios y máximos, y se mantuvieron durante las visitas de seguimiento. Las estancias medias en planta (5,26 ± 4,05 días) y en la unidad de cuidados intensivos (0,22 ± 0,64 días) fueron bajas. Se detectaron mejoras significativas (todo ajustado $p < 0,05$) en el *Kansas City Cardiomyopathy Questionnaire* (puntuaciones generales), el EQ-5D-5L y el *Short Form-36* (componente físico).
***Conclusiones*:** Esta investigación destaca resultados clínicos positivos que se traducen en mejoras significativas en términos de calidad de vida de los pacientes. El uso de recursos, que fue en general bajo, también fue dependiente de la escala de riesgo de la *Society of Thoracic Surgeons.* (Estudio SARU, código: 2017-01, Murcia, España).

Palabras clave: Estenosis valvular aórtica. Calidad de vida. Recursos sanitarios. Estancia. Resultado clínico. Carga de la enfermedad.

Abbreviations

AS: Aortic stenosis. **HRQoL:** Health-related quality of life. **HRU:** Healthcare resource utilization. **KCCQ:** Kansas City Cardiomyopathy Questionnaire. **STS:** Society of Thoracic Surgeons. **TAVI:** transcatheter aortic valve implantation.

INTRODUCTION

Aortic stenosis (AS) is the most common cause of valvular heart disease[1] with an estimated prevalence of 3%-5% in people ≥ 65 years to 7.4% in people > 85 years.[2,3] Severe AS is the leading cause of valvular surgery among adults. AS typically has a variable but long latent period (asymptomatic) followed by a rapid progression stage after symptom onset (eg, dyspnea, angina or syncope), and has a poor prognosis if aortic valve replacement is not performed in a timely manner.[4,5]

Although open heart surgery has been the gold standard treatment for many years, aortic valve procedures have progressively become less invasive. Transcatheter aortic valve implantation (TAVI) has become the treatment of choice for inoperable patients with symptomatic, severe AS,[6] and a valid alternative for high- and intermediate-surgical risk patients with improved clinical results regarding survival and functional capacity.[7,8] Similarly, with new evidence from recent clinical trials, the indication for TAVI was extended to low-risk patients.[9,10]

According to current clinical guidelines,[11] the multidisciplinary decision regarding procedures to solve AS requires an individualized and appropriate assessment of the candidates to optimize the benefits achieved in these patients (eg, regarding survival and symptom amelioration). To this end, significant factors impact the patients' surgical risk (eg, surgeon-specific risk-adjusted composite according to the Society of Thoracic Surgeons [STS] score), the patient's quality-adjusted life expectancy, baseline characteristics like frailty (eg, ≥ 2 score in the Katz scale), modifiable risk factors, and comorbidities (eg, chronic obstructive pulmonary disease, pulmonary hypertension, liver disease, previous stroke, anemia, and other systemic conditions). In Europe, recent guidelines recommend TAVI for patients > 75 years. Also, that all patients with AS between 70 and 75 years should be referred for TAVI assessment regardless of their surgical risk.[12]

Due to the wider indication for TAVI and the ageing demographic factor seen in Western countries,[3] TAVI is increasingly used in the routine clinical practice across Europe. This underscores the importance of monitoring TAVI outcomes, particularly among elderly patients to better characterize performance in the real-world practice.

Therefore, our objective was to prospectively assess TAVI (SAPIEN 3, Edwards Lifesciences, United States) outcomes regarding the patient's health-related quality of life (HRQoL), and the clinical outcomes considering their surgical risk. Also, as secondary endpoint, a description of healthcare resource utilization adjusted for surgical risk (STS score) was intended.

METHODS

Study design

This was a prospective, observational study of all consecutive patients with severe, symptomatic AS treated with elective TAVI via transfemoral access with SAPIEN 3 at the regional Hospital Universitario Virgen de la Arrixaca, a tertiary hospital and a regional referral center for cardiothoracic surgery and interventional cardiology located in Murcia, Spain. Patients received TAVI regardless of the study as part of the routine clinical practice. The recruitment stage was during the calendar year of 2018. In this study we present the observed results from the systematic djustent conducted 1 year after TAVI.

According to the ESC/EACTS guidelines,[6] implantation decision was made by the heart team and all procedures followed the recommendations established by the manufacturer's SAPIEN 3 valve instructions for use. All patients were followed for, at least, 12 months after TAVI and systematically assessed according to the hospital clinical protocol. Written patient information was provided to each participant, and the patient's consent on data collection was signed before being included in the study that was conducted in full compliance with the recommendations guiding biomedical research in human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland back in 1964. The study protocol was approved by the assigned ethics Committee (Murcia, SARU Study; code: 2017-01. Effective date, 02/06/2017).

Clinical assessment was conducted at baseline (preoperative), post-intervention (perioperative), and 30 days, 6 months, and 1 year after the procedure. The main objective clinical variables included echocardiographic measurements (eg, paravalvular and total aortic regurgitation, left ventricular ejection fraction, mean and maximum aortic valve gradient, effective orifice area), and major clinical events automatically available in the medical records (eg, all-cause and cardiovascular mortality, stroke, bleeding complications, myocardial infarction, new-onset atrial fibrillation, major vascular complications, permanent pacemaker implantation, rehospitalization and

acute kidney injury). In addition, the patients' New York Heart Association (NYHA) functional class IV was systematically registered. The patients' risk profile was characterized based on the STS risk score which was validated for the in-hospital and 30-day mortality rates following surgical aortic valve replacement.[13] Additionally, postoperative complications were defined based on a modified version of the Valve Academic Research Consortium criteria,[14] and this score was routinely applied based on the clinical protocols of our referral hospital.

Finally, length of stay (LOS)–at the hospital and the intensive care unit (ICU) settings–associated with the TAVI procedure was automatically registered for each patient based on hospital medical records and described as a secondary endpoint in this research.

Measurement of patient's health-related quality of life

A comprehensive assessment was implemented by combining a patient-reported disease-specific tool that has a higher ability to capture changes in the patient's health status during the observation period, and 2 generic tools to establish comparisons with findings from other procedures or diseases and with the Spanish normal population. Patients' health-related quality of life was evaluated at baseline and during per protocol medical visits for health management (6 months and 1 year after TAVI).

Disease-specific tools

The Kansas City Cardiomyopathy Questionnaire (KCCQ)[15] is a 23-item self-administered disease-specific questionnaire originally developed for patients with heart failure to monitor their reported symptoms and evaluate how and to what extent their heart failure impacts their quality of life (QoL) within a 2-week recall period. The KCCQ includes 6 distinct domains (physical function, symptoms, symptom stability, social limitation, self-efficacy, and quality of life) added to 2 summary scores: the clinical summary score (CSS) and the overall summary score (OSS). Summary scores can be transformed into 0–100 scales with higher scores being indicative of better levels of wellbeing to facilitate score interpretation. This tool has been recently revised and qualified for its use in heart failure by the United States Food and Drug Administration[16] with minimal clinically important differences defined as 5-point changes in summary scales.[17] Also, the KCCQ has a sound psychometrical performance when measuring functional status and HRQoL in patients with severe, symptomatic AS.[18]

Generic tools to measure health-related quality of life

The EQ-5D-5[19]—a patient-reported measure—includes a descriptive system and the EQ visual analogue scale (EQ-5D-5L VAS). The former includes 5 different domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses to the EQ-5D-5L descriptive system were assigned preference-based (utility) weights from the Spanish population. The EQ-5D-5L VAS reflects the patient's self-rated health on a vertical visual analogue scale (from 0, 'the worst health you can imagine' up to 100, 'the best health you can imagine').[20,21]

The Medical Outcomes Study Short Form-36 (SF-36)[22] is one of the most widely used and evaluated generic HRQoL questionnaires. It includes 8 dimensions and 2 summary scores (physical component summary [PCS] and mental component summary [MCS]). In this study we used a standardization of summary scores based on age and gender using the Spanish population normative data.[23]

Statistical approach

First, an exploratory analysis was performed to characterise the analytic cohort presented in this manuscript. Descriptive statistics were used for continuous variables (eg, mean, standard error of measurement) and frequency tables or proportions for discrete variables. McNemar's test for dependent samples was used to compare NYHA health states at follow-up. Regarding the objective of this study, multivariate models (linear general models with repeated measures at different time points —baseline, 6M, and 12M— as intra-subject factors) were computed to better assess the potential benefits of both regarding clinical endpoints and the patients' HRQoL at follow-up (baseline, 6M, and 12M) while considering the patients' comorbidities and risk profile at baseline. To this end, the STS predicted risk of mortality score was included because it is a weighted index of the patients' risk robustly estimated using a Bayesian hierarchical model for both mortality and major complication events. This model considers 24 meaningful preoperative variables like age, sex, body surface area, atrial fibrillation, chronic heart failure, NYHA functional classification, chronic obstructive pulmonary disease, diabetes mellitus, need for insulin use, arterial hypertension, previous cardiac surgeries, concomitant mitral stenosis, unstable angina, previous percutaneous coronary intervention, and other variables. Based on the estimated STS score, patients were classified into 3 risk groups: high (≥ 8%), intermediate (≥ 4%), and low mortality risk (< 4%).[13] Importantly, this score was also considered in the secondary endpoint associated with the description of the LOS (at both the hospital and ICU settings) related to TAVI procedures.

Regarding the size of the sample required to conduct the adjusted analyses described above, the estimated minimal sample size was set at 60 TAVI patients to compare within and between subject differences at 3 different time points of evaluation, effect size (f) was 0.25, statistical power (1-β), 0.9, and risk of type-I error (1-α), 0.95 assuming a weak correlation among repeated measures (0.3).

The software statistical package SPSS 27.0 for Windows (IBM Corp., United States) and the R software (The R Project for Statistical Computing, Institute for Statistics and Mathematics, Austria) were used for analysis.

RESULTS

A total of 76 consecutive patients, 50% female, with a mean age of 82.05 ± 4.76 years underwent elective TAVI during the study period comprising the analytical cohort. STS (surgical risk) score was 5.4 ± 3.41 while 42.5%, 43.8%, and 13.7% of the cases were classified as low-, intermediate-, and high-risk patients, respectively. A complete description of comorbidities is shown on table 1. Previous coronary artery bypass graft was reported in 1 patient. A total of 6 cases (7.9%) were valve-in-valve procedures, and in 71 cases (93.4%) vascular access was via right femoral artery. Only 1 patient required general anaesthesia before TAVI (table 1 of the supplementary data). The patients' functional status (NYHA classification) at baseline was remarkably impaired in most cases with 61.84%, and 19.74% of the patients having NYHA functional class III and IV, respectively.

Clinical outcomes

Successful implantation was achieved in 74 cases (97.37%), and 2 patients (2.63%) died within the first 30 days after the procedure (both cardiovascular causes). In this period, the observed rates of major complications or rehospitalizations were low (table 2), and

Table 1. Preoperative characteristics of TAVI patients (*N* = 76)

Previous disease	n	%
Dyslipidemia	51	67.11
Arterial hypertension	66	86.84
Previous stroke		
With effects	1	1.32
Without effects	4	5.26
TIA	4	5.26
Liver disease	0	0.00
Diabetes mellitus		
Diet	1	1.32
Oral agents	22	28.95
Insulin	17	22.37
No treatment	1	1.32
CKD	26	34.21
Smoker		
Active smoker	2	2.63
Non-smoker	48	63.16
Former smoker	25	32.89
Oncological disease	8	10.53
COPD	9	11.84

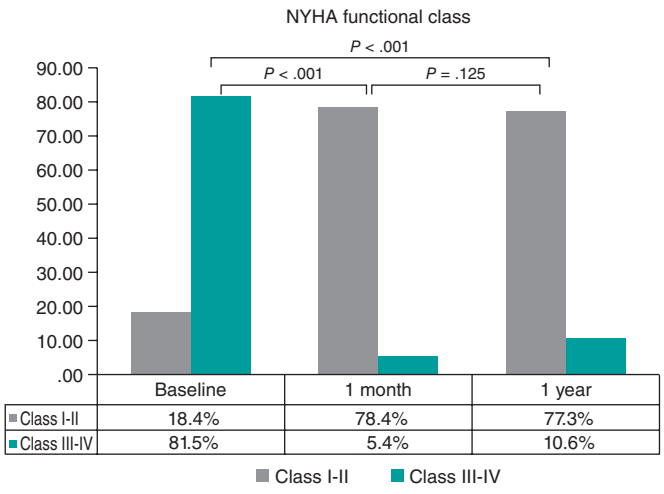
COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; DM, diabetes mellitus; TIA, transient ischemic attack.

Table 2. Clinical outcomes seen at 30 days and 1 year (*N* = 76)

Variable	n	%
Successful implantation	74	97.37
Death (30d)	2	2.63
Cardiovascular death (30d)	2	2.63
AMI (30d)	0	0.00
Stroke (30d)	3	3.95
Major bleeding (30d)	4	5.26
All-cause rehospitalization (30d)	4	5.26
Permanent pacemaker implantation (30d)	5	6.60
CV rehospitalization (30d)	2	2.63
All deaths (1y*)	9	11.84
All cardiovascular deaths (1y)	2	2.63

* All deaths reported a 1 year: Multiple myeloma: n = 1; sepsis (respiratory tract infection): n = 1; sepsis (renal disease): n = 1; pulmonary disease: n = 1; hepatocellular carcinoma: n = 1; stroke: n = 1; cardiac tamponade: n = 1 (cardiovascular death within 30d); thyroid cancer: n = 1; sudden cardiac death: n = 1 (cardiovascular death within 30d).
AMI, acute myocardial infarction; CV, cardiovascular.

permanent pacemaker implantation was required for 5 patients. One year after TAVI, no additional cardiovascular deaths were reported. However, 7 patients died of other causes (table 2). We should mention that the sample mortality rate was similar to that of a comparable general population (figure 1 of the supplementary data). According to echocardiographic measurements, significant benefits in mean and maximum gradients, and aortic regurgitation were achieved and maintained at follow-up (figure 2 of the supplementary data). Notably, among survivors, 78.4% of patients had a NYHA functional class I-II at 1 month, a benefit that was maintained at 1 year with 77.3% of patients in these functional levels.



No. of missing cases: baseline n = 0; 1 month n = 12; 1 year n = 8.
McNemar tests for dependent samples.

Figure 1. New York Heart Association (NYHA) functional class at follow-up.

HRQoL assessment

The patients' HRQoL across the observational period according to STS risk score at baseline is shown on figure 1. In both summary scores of the KCCQ (OSS and CSS), statistically and clinically significant improvements after TAVI were seen. In OSS cases, the mean differences reported between baseline and 6 months ranged between 18.94 points (low risk) and 29.97 points (intermediate risk) indicative of a meaningful benefit (all $P < .001$). Similarly, the mean differences regarding the CSS ranged between 13.03 points and 27.3 points (low and intermediate, respectively). In addition, in both scales the observed benefit was maintained at follow-up with no differences being reported at 6 months and 1 year ($P > .8$ in both summary scales). Remarkably, these improvements were repeated across the 3 risk groups (figure 2).

Regarding generic questionnaires, a positive impact was also seen in EQ-5D-5L VAS scores and the SF-36 Physical Component Summary, postoperatively, in all patients ($P < .006$ and $P < .004$, respectively). However, the size of detected differences was smaller considering the respective scales. No statistically significant differences were seen in the mental component summary ($P = .395$). In addition, values in all groups were comparable to normative population based on age and sex since baseline (mean—95% confidence interval [95%CI]—at baseline: 47.44, 44.70, and 50.18; 6 months: 49.77, 47.36, and 52.17; and 1 year: 48.64, 46.04, and 50.83-; $P = .52$). Finally, EQ-5D-5L index values were fairly similar across all time points with a slight increase observed at 6 months ($P = .054$ compared to baseline) and a mild drop at 1 year, not reaching statistical significance compared to baseline values (mean—95%CI—at baseline: 0.77, 0.71, and 0.83; 6 months: 0.80, 0.75, and 0.85; and1 year: 0.74, 0.68, and 0.80; $P = .499$).

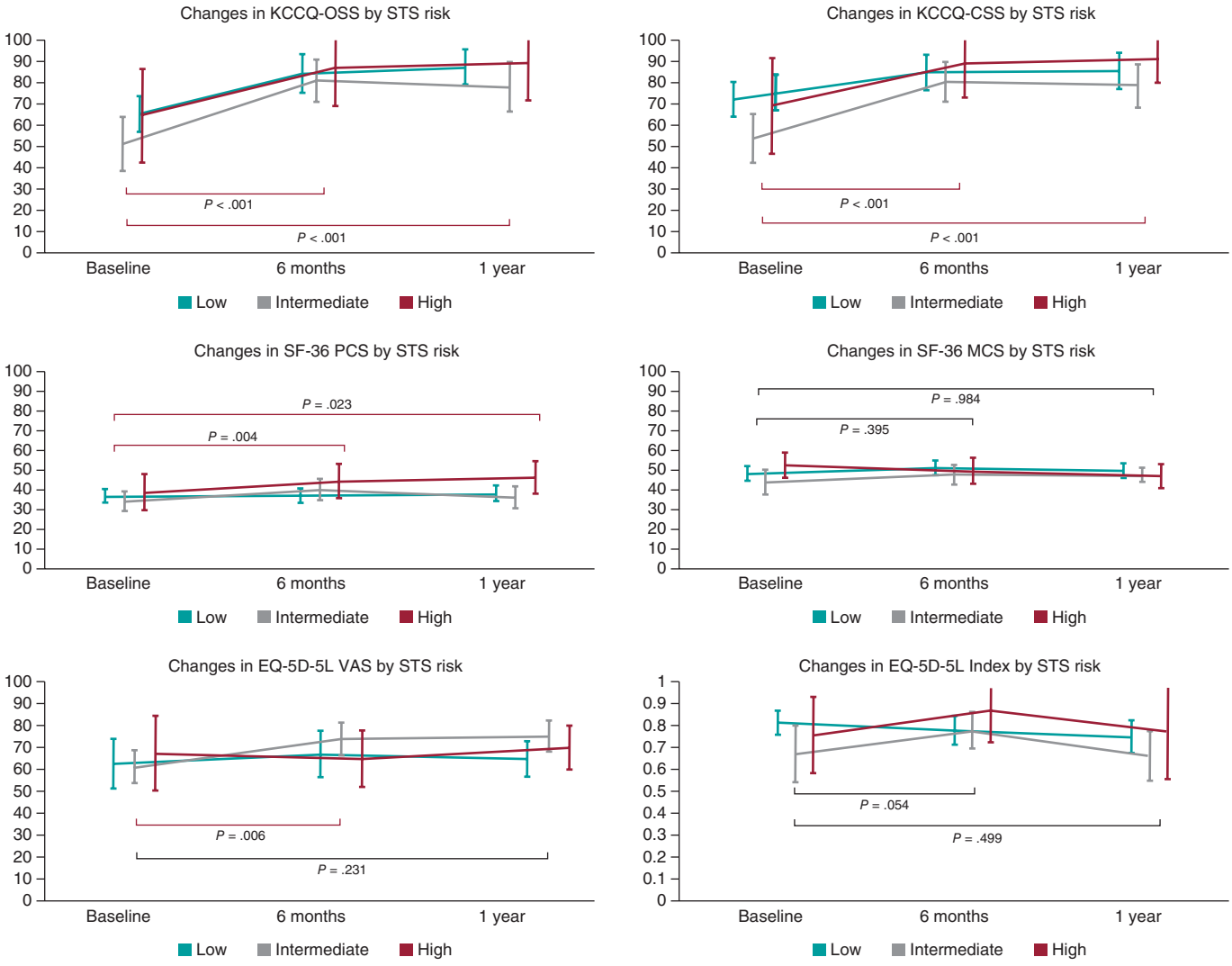


Figure 2. Changes in patient's health-related quality of life at follow-up (n = 55, out of 67 survivors at 1 year; 82.1% of the sample). No differences in mean/median baseline values were seen in any of the health-related quality of life (HRQoL) measures taken between the patients who completed all the measurements and those with missing values at study period. EQ-5D-5 VAS, EQ visual analogue scale; KCCQ, Kansas City Cardiomyopathy Questionnaire; KCCQ CSS, KCCQ clinical summary score; KCCQ OSS, KCCQ overall summary score; SF-36 MCS, Medical Outcomes Study Short Form-36 Mental Component Summary; SF-36 PCS, SF-36 Physical Component Summary.

Secondary endpoint: description of the procedure-related length of stay

Mean LOS at the hospital setting was limited with a mean stay of 5.26 days (± 4.05), and only 10 patients (13.2%) required intensive care, 5 of whom (6.6% of the overall sample) remained at the ICU setting ≤ 1 day, 3 (3.9%) for 2 days, and 2 (2.6%) for 3 days. In figure 3, the ICU and hospital stays are shown based on the patients' baseline risk (very low in all subgroups).

DISCUSSION

Ideally, severe, and symptomatic AS should be treated with a valve implanted via minimally invasive procedures while securing minimal perioperative and long-term risks, optimizing hemodynamic response, avoiding patients' dependency on lifelong anticoagulation therapy, and maximizing their ability to do activities of daily living, and wellbeing. Insights from clinical trials indicate that the management of AS is moving in this direction.[7,9] However it is still important to evaluate each innovation in real practice. This study provides new evidence on the performance of TAVI in elderly patients—mean age > 80 years—under real-world practice through a systematic prospective assessment of clinical outcomes, LOS, and patients' reported outcomes 1 year after the procedure.

In our study, a noticeable positive clinical effect of TAVI was seen in all STS subgroups. Mean and maximum aortic gradients along with valve regurgitation improved significantly after the procedure, and major complications were kept at very reasonable rates. These outcomes were very similar to those recently published on SAPIEN 3.[24] Also, regarding the NYHA scale, the percentage of patients with satisfactory functional status increased immediately after the procedure and was maintained at 1 year among survivors.

Importantly, these clinical benefits translated into meaningful improvements in the patients' HRQoL. Particularly, the OSS of the KCCQ showed a mean change from baseline from 18.9 points in low-risk patients up to near 30 points in intermediate risk 6 months after treatment). Also, this benefit was preserved at 1 year with

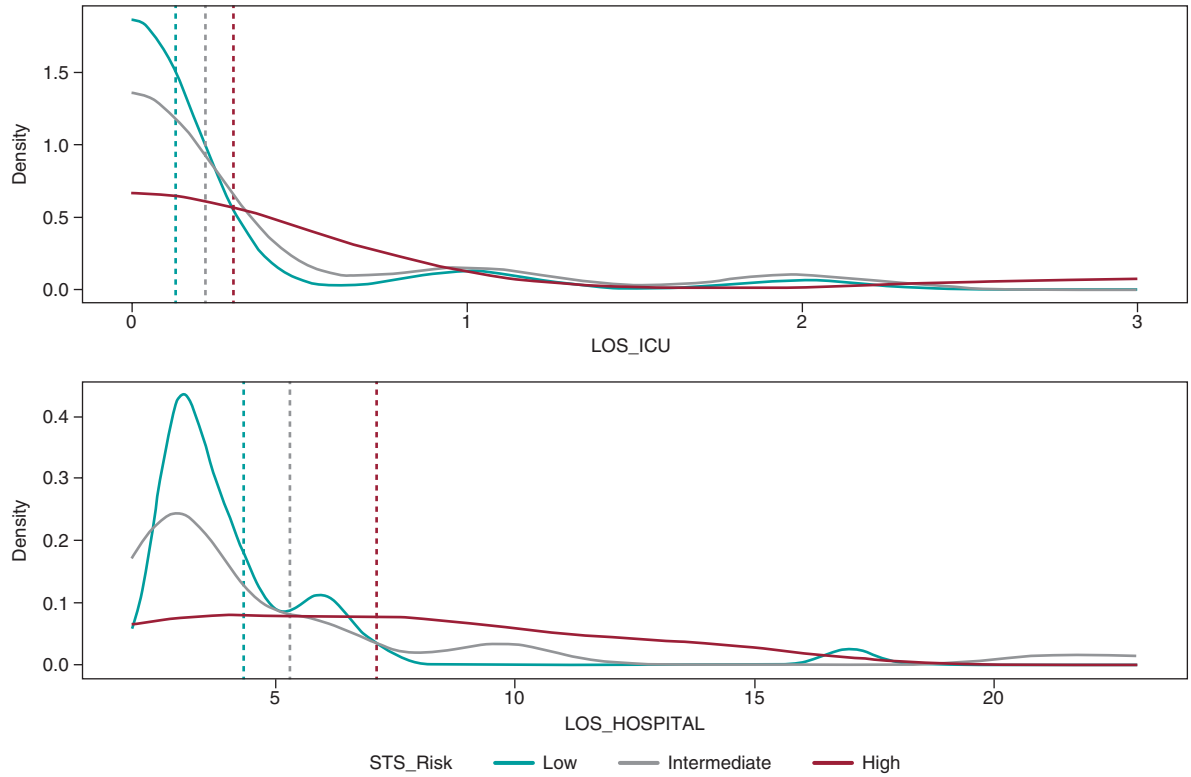


Figure 3. Length of stay (the hospital and the ICU settings) according to STS PROM score; n = 76 for LOS at the hospital setting, and n = 73 for LOS at the ICU setting. ICU, intensive care unit; LOS, length of stay; STS, Society of Thoracic Surgeons.

ranges between 21.9 points in low risk to 26.7 points in intermediate risk. These increments reported in the KCCQ were clearly over the minimal clinically important differences described in the medical literature for this tool.[17] Actually, these results are especially important considering than a 10 points drop in KCCQ OSS scores turned out to be a prognostic factor for patients with AS associated with 34% more chances of dying at 12 months.[18] Therefore, the HRQoL of older patients who survived 1 year improved significantly. Our results are similar to those from a former research that studied clinical outcomes from TAVI in clinical trials and registries including the SAPIEN 3. For instance, Baron et al.[24]—according to data from the SAPIEN 3 intermediate-risk registry—found changes at 1 year from TAVI in OS of 23.1 points (21.8-24.9; $P > .001$) among intermediate-risk patients. Their cohort had similar baseline characteristics and underwent TAVI with the same device (they did, however, include transfemoral and transapical access). In our study, we saw that this enhanced self-perceived health is also maintained in elderly patients classified as low- and high-risk patients.

Regarding generic tools, a positive trend was also detected in the EQ-5D-5L VAS and the PCS of the SF-36 (a summary component more focused on the overall functional performance of patients) with significant differences at 6 months and 1 year. We should mention that no differences were found at follow-up regarding the mental component summary. Also, the patients' mental health was slightly lower compared to that reported in their reference population since baseline. Similarly, regarding the estimated utilities from the EQ-5D-5L, a global positive trend was seen at 6 months from baseline and a slight drop after 1 year. Nevertheless, all changes detected with this tool were minimal. This finding was surprising considering the great benefit demonstrated with both the OSS and the CSS of the KCCQ. However, as the EQ-5D-5L captures health-related quality of life more globally together with the mean age of the patients included, the slight decline seen could reflect general deterioration of health accumulated over the 1-year observational period (mean age of the sample > 80 years).

Furthermore, consistent with recent experiences in centers of excellence regarding TAVI in Italy, the Netherlands, and the UK, where authors tested novel standardized clinical care pathways to optimize the process with early discharge while reducing complications and LOS,[25] we saw a very limited hospital stay with only 13% of patients requiring ICU admission (6.5% of the patients needed 3 days at the ICU). In our center, following an individualized protocol for candidates eligible for TAVI, we saw very high-quality outcomes in elderly patients while minimizing the procedure-related LOS.

Limitations

Inherently to the nature of this observational study, our findings are subject to a few limitations. First, our findings come from the experience of a single center in a tertiary referral hospital very familiar with the procedure so the extrapolation of these results might be affected by the experience of the heart team. Importantly, sample size, especially in the high-risk group, was limited and subject to high dispersion of values and missing data at follow-up. Therefore, further research with a larger number of patients stratified by risk should confirm our findings. Despite this limitation, we should mention that our results observed in the intermediate-risk group are similar to those reported with larger samples allowing for extensive propensity score cohort adjustment.[24]

Also, in this analysis, we decided to use the STS score as a measure of patient-risk characterization because, even when we acknowledge that this was originally developed for surgical aortic valve replacement, it is a valid prognostic measure of mortality and occurrence of major complications in TAVI making up a comprehensive

assessment of the patients' health status.[13,26] However, as it has been described in recent research,[27,28] it would also be helpful to include a measure of frailty to complete thedjusttments. Unfortunately, this information was not routinely collected through a standard form as part of the standard clinical management when this study was conducted. Nevertheless, we should mention that in our center, the heart team involved in the decision-making process regarding the individualized management of the patients' clinical condition, always considers frailty as a key parameter to better adjust the provision of care. Also, precisely due to this preoperative assessment most patients classified as low risk by the STS score (42.5%) were treated with TAVI instead of open surgery. Hence, frailty is a core aspect of this process, always among other important factors like patient preference, history of chest radiation, previous coronary artery bypass graft or porcelain aorta, and others. Although through the comprehensive analysis of clinical and patient-reported outcomes a consistent and positive tendency in outcomes has been shown, we should mention that our results come from a cohort of patients treated in 2018. Consequently, it would be interesting to conduct a new study in multiple centers to obtain data to compare the evolution of the current clinical practice outcomes to those from 2018. Therefore, further research is warranted to continue this monitorization of outcomes in larger samples of patients.

CONCLUSIONS

In conclusion, this research provides clinical and patient-reported evidence on the performance of TAVI in elderly patients with clinical benefits maintained 1 year after the intervention. Furthermore, the short hospital stay observed provides exploratory insights into the benefits of standardized protocols created to manage low- to high-risk patients safely and efficiently.

FUNDING

Edwards Lifesciences provided funds for the analysis of this study that was conducted and interpreted independently by clinicians and methodological experts.

AUTHORS' CONTRIBUTIONS

E. Pinar, J. García de Lara, J. Hurtado, B. Martí-Sánchez, G. Leithold, and J. Cuervo were involved in the study idea and design, and in the analysis of the study data. All authors were involved in the interpretation of the results and in the critical revision of the paper regarding its intellectual content and agree on the final version of the manuscript to be published.

CONFLICTS OF INTEREST

J. Cuervo, who works for Axentiva Solutions, disclosed that Axentiva Solutions has received financial support in the form of consultancy payments from Edwards Lifesciences towards the design and analysis of the study, and for medical writing support. B. Martí-Sánchez, and P. González work for Edwards Lifesciences. E. Pinar, J. García de Lara, J. Hurtado, M. Robles, G. Leithold, and K. Rand 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.M23000363.

WHAT IS KNOWN ABOUT THE TOPIC?

- Severe AS is the leading cause of valvular surgery among adults.
- TAVI has become the treatment of choice for inoperable patients with symptomatic, severe AS, and a valid alternative for patients at high- and intermediate-surgical risk with improved clinical results regarding survival and functional capacity.
- There are factors that influence TAVI results like surgical risk, patient's life expectancy, baseline characteristics, modifiable risk factors, and comorbidities.

WHAT DOES THIS STUDY ADD?

- Through a comprehensive assessment including clinical, functional, and quality of life variables, this study shows a positive performance of TAVI in elderly patients at follow up.
- Improvement in mean and maximum aortic gradients, and valve regurgitation.
- Higher percentage of patients with a satisfactory functional status according to the NYHA scale after the intervention.
- Clinical benefits also translated into HRQoL improvements, and effect that was seen among all risk groups.
- Overall, in this consecutive sample of patients, the TAVI-related LOS (hospital) was short.

REFERENCES

1. Iung B, Delgado V, Rosenhek R, et al. Contemporary Presentation and Management of Valvular Heart Disease: The EURObservational Research Programme Valvular Heart Disease II Survey. *Circulation*. 2019;140:1156-1169.
2. 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.
3. Durko AP, Osnabrugge RL, Van Mieghem NM, et al. Annual number of candidates for transcatheter aortic valve implantation per country: current estimates and future projections. *Eur Heart J*. 2018;39:2635-2642.
4. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of Aortic-Valve Sclerosis with Cardiovascular Mortality and Morbidity in the Elderly. *N Engl J Med*. 1999;341:142-147.
5. Otto CM, Burwash IG, Legget ME, et al. Prospective study of asymptomatic valvular aortic stenosis: Clinical, echocardiographic, and exercise predictors of outcome. *Circulation*. 1997;95:2262-2270.
6. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Hear J*. 2017;38:2739-2791.
7. Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet*. 2016;387:2218-2225.
8. Herrmann HC, Thourani VH, Kodali SK, et al. One-Year Clinical Outcomes With SAPIEN 3 Transcatheter Aortic Valve Replacement in High-Risk and Inoperable Patients With Severe Aortic Stenosis. *Circulation*. 2016;134:130-140.
9. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med*. 2019;380:1695-1705.
10. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. *N Engl J Med*. 2019;380:1706-1715.

11. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice. *Circulation*. 2021;143:e35-e71.
12. Kuck K-H, Bleiziffer S, Eggebrecht H, et al. Konsensuspapier der Deutschen Gesellschaft für Kardiologie (DGK) und der Deutschen Gesellschaft für Thorax-, Herz- und Gefäßchirurgie (DGTHG) zur kathetergestützten Aortenklappenimplantation (TAVI) 2020. *Der Kardiol.* 2020;14:182-204.
13. Kumar A, Sato K, Narayanswami J, et al. Current Society of Thoracic Surgeons Model Reclassifies Mortality Risk in Patients Undergoing Transcatheter Aortic Valve Replacement. *Circ Cardiovasc Interv*. 2018;11:e006664.
14. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: The valve academic research consortium-2 consensus document. *J Am Coll Cardiol*. 2012;60:1438-1454.
15. Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol.* 2000;35:1245-1255.
16. US Food and Drug Administration -Center for Devices and Radiological Health. Medical Device Development Tool (MDDT) Qualification Decision Summary For Kansas City Cardiomyopathy Questionnaire (KCCQ). 2021. Available at https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt. Accessed 20 Nov 2022.
17. Butler J, Khan MS, Mori C, et al. Minimal clinically important difference in quality of life scores for patients with heart failure and reduced ejection fraction. *Eur J Heart Fail*. 2020;22:999-1005.
18. Arnold S V, Spertus JA, Lei Y, et al. Use of the Kansas City Cardiomyopathy Questionnaire for monitoring health status in patients with aortic stenosis. *Circ Heart Fail*. 2013;6:61-67.
19. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20:1727-1736.
20. Hernandez G, Garin O, Pardo Y, et al. Validity of the EQ-5D-5L and reference norms for the Spanish population. Qual Life Res. 2018;27:2337-2348.
21. Ramos-Goñi JM, Pinto-Prades JL, Oppe M, Cabasés JM, Serrano-Aguilar P, Rivero-Arias O. Valuation and Modeling of EQ-5D-5L Health States Using a Hybrid Approach. *Med Care*. 2017;55:e51-e58.
22. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30:473-483.
23. Vilagut G, Ferrer M, Rajmil L, et al. The Spanish version of the Short Form 36 Health Survey: a decade of experience and new developments. Gac Sanit. 2005;19:135-150.
24. Baron SJ, Thourani VH, Kodali S, et al. Effect of SAPIEN 3 Transcatheter Valve Implantation on Health Status in Patients With Severe Aortic Stenosis at Intermediate Surgical Risk: Results From the PARTNER S3i Trial. *JACC Cardiovasc Interv*. 2018;11:1188-1198.
25. Barbanti M, van Mourik MS, Spence MS, et al. Optimising patient discharge management after transfemoral transcatheter aortic valve implantation: the multicentre European FAST-TAVI trial. EuroIntervention. 2019;15:147-154.
26. Hemmann K, Sirotina M, De Rosa S, et al. The STS score is the strongest predictor of long-term survival following transcatheter aortic valve implantation, whereas access route (transapical versus transfemoral) has no predictive value beyond the periprocedural phase. *Interact Cardiovasc Thorac Surg.* 2013;17:359-364.
27. Green P, Arnold S V, Cohen DJ, et al. Relation of frailty to outcomes after transcatheter aortic valve replacement (from the PARTNER trial). *Am J Cardiol*. 2015;116:264-269.
28. Goudzwaard JA, de Ronde-Tillmans MJAG, El Faquir N, et al. The Erasmus Frailty Score is associated with delirium and 1-year mortality after Transcatheter Aortic Valve Implantation in older patients. The TAVI Care & Cure program. *Int J Cardiol*. 2019;276:48-52.

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Original article

Clinical outcomes of patients undergoing percutaneous coronary intervention treated with colchicine

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ABSTRACT

Introduction and objectives: The role of inflammation in the pathogenesis of coronary artery disease, and that resulting from percutaneous coronary intervention (PCI) is increasingly recognized, yet the effect of colchicine in attenuating peri-PCI inflammation remains unknown. This meta-analysis investigated the efficacy of colchicine in patients undergoing PCI for secondary prevention of coronary artery disease.
Methods: The Web of Science, PubMed, Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials and ClinicalTrials.gov databases were searched. Data on studies assessing the efficacy profile of colchicine in patients undergoing PCI were pooled using a random-effects model.
Results: In 13 studies of 7414 patients, no differences were observed between patients treated with colchicine compared to those without for all-cause mortality (OR, 1.1; 95%CI, 0.72-1.56; I^2 = 0%), cardiovascular mortality (OR, 0.98; 95%CI, 0.42-2.28; I^2 = 14.2%), myocardial infarction (OR, 0.84; 95%CI, 0.65-1.08; I^2 = 1.4%) or coronary revascularization (OR, 0.64; 95%CI, 0.28-1.42; I^2 = 49.3%). However, patients treated with colchicine had a lower risk of stroke (OR, 0.33; 95%CI, 0.15-0.72; I^2 = 0%).
Conclusions: Adding colchicine to standard medical therapy in patients undergoing PCI did not decrease all-cause mortality, cardiovascular mortality or urgent revascularization. However, it showed a trend towards a lower risk of myocardial infarction and a significantly lower risk of stroke.

Keywords: Coronary artery disease. Percutaneous coronary intervention. Inflammation. Colchicine.

Resultados clínicos en pacientes sometidos a angioplastia coronaria percutánea tratados con colchicina

RESUMEN

Introducción y objetivos: La importancia de la inflamación en la patogénesis de la enfermedad coronaria, así como tras la angioplastia percutánea, es un fenómeno reconocido. Sin embargo, el efecto de la colchicina para atenuar la inflamación tras la intervención coronaria percutánea se desconoce. Este metanálisis investigó la eficacia de la colchicina en pacientes que se sometieron a intervención coronaria percutánea con el objetivo de prevención secundaria
Métodos: Se revisaron las bases de datos Web of Science, PubMed, OVID MEDLINE, Embase, Cochrane Central Register of Controlled Trials y ClinicalTrials.gov, y se analizaron los datos de los estudios que investigaban la eficacia de la colchicina en pacientes que se sometieron a angioplastia coronaria percutánea, usando un modelo de efectos aleatorios.
Resultados: En 13 estudios, que incluyeron un total de 7.414 pacientes, no se observó ninguna diferencia entre los tratados con colchicina y los no tratados con colchicina en cuanto a mortalidad por cualquier causa (OR = 1,1; IC95%, 0,72-1,56; I^2 = 0%), mortalidad por causa cardiovascular (OR = 0,98; IC95%, 0,42-2,28; I^2 = 14,2%), infarto de miocardio (OR = 0,84; IC95%, 0,65-1,08; I^2 = 1,4%) y revascularización coronaria (OR = 0,64; IC95%, 0,28-1,42; I^2 = 49,3%). Sin embargo, los pacientes tratados con colchicina mostraron un menor riesgo de accidente vascular cerebral (OR = 0,33; IC95%, 0,15-0,72; I^2 = 0%).

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Conclusiones: Agregar colchicina a la terapia medica estándar en pacientes sometidos a angioplastia coronaria percutánea no modificó la mortalidad por cualquier causa, la mortalidad por causa cardiovascular ni la revascularización coronaria, pero si mostró una tendencia a un menor riesgo de infarto de miocardio y un menor riesgo significativo de accidente vascular cerebral.

Palabras clave: Enfermedad coronaria. Angioplastia percutánea. Inflamación. Colchicina.

Abbreviations

ACS: acute coronary syndrome. **MI:** myocardial infarction. **NSTEMI:** non-ST-elevation acute myocardial infarction. **PCI:** percutaneous coronary intervention. **RCT:** randomized controlled trial.

INTRODUCTION

Despite increasingly effective primary and secondary preventive treatments, coronary artery-related events continue to be the leading cause of morbidity and mortality worldwide.[1,2] Lifestyle changes (eg, weight loss, low-salt diet, smoking cessation), medical therapy (eg, anti-hypertensive, lipid-lowering, glucose-lowering, and antithrombotic regimens) in addition to coronary revascularization via percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) constitute the multifaceted approach of this disease. Yet despite the advances made in this multimodality approach, cardiovascular morbidity and mortality remain high.

More recently, the central role played by inflammation in the pathogenesis of coronary artery disease from atherosclerotic plaque formation to acute coronary syndrome (ACS), and PCI itself have gained important recognition. Colchicine, an anti-inflammatory agent indicated for multiple inflammatory conditions including pericarditis, gout, and familial Mediterranean fever, has gained attention as a potential attenuator of atherosclerotic inflammation. Acting via the inhibition of tubulin polymerization and eventually blunting immune cell activation and inflammatory response,[3,4] recent evidence suggests a benefit of colchicine in the management of the cardiovascular events of patients with clinical signs of coronary artery disease.[5] However, its impact among patients in the peri-PCI period remain controversial.

Recent trials have begun exploring the effects of colchicine in the PCI setting, albeit with mixed results. In the Colchicine-PCI trial of patients with non-ST-segment elevation acute coronary syndrome, the administration of colchicine immediately before and after PCI resulted in lower interleukin-6 and high-sensitivity C-reactive protein (hsCRP) levels at 24 hours, but did not show fewer PCI-related myocardial injuries.[6] This trial was followed by COPE-PCI that found that when administered 6-to-24 hours before the PCI, colchicine did in fact reduce PCI-related myocardial injuries in a population of patients with stable angina and non-ST-elevation acute myocardial infarction (NSTEMI).[7] Nevertheless, the more recent COVERT-MI trial[8] found no difference in infarct size or left ventricular remodeling on the cardiac magnetic resonance imaging in patients treated with colchicine compared to those untreated with this agent.

These individual studies may not provide properly powered analyses, particularly in low-rate events such as strokes, on the impact of colchicine regarding secondary prevention in patients in the peri-PCI period, thus prompting the need for a systematic appraisal and meta-analysis of the quality of evidence and treatment effects on major adverse cardiovascular events.

METHODS

Protocol

The search process of this meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and is registered with PROSPERO (CRD42021247704). The meta-analysis did not require specific institutional review board approval since it utilized results published in former studies. All relevant information can be found in the trials included. The corresponding author had full access to all the data and final responsibility on the decision to submit the manuscript for publication. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Search strategy

We performed a comprehensive literature search of all published studies—retrospective, observational, and randomized controlled trials—available on Web of Science, Embase, PubMed, Ovid MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov (inception through August 23, 2021, without language restrictions. Case reports, letters to the editor, reviews, and book chapters were not included in this meta-analysis. The keywords used in the search were 'colchicine,' 'coronary artery disease,' 'coronary heart disease,' 'angina,' 'myocardial infarction,' 'acute myocardial infarction,' 'myocardial ischemia,' 'acute coronary syndrome,' 'ischemic heart disease,' 'percutaneous coronary intervention,' 'percutaneous transluminal angioplasty,' 'percutaneous coronary revascularization,' and 'myocardial revascularization' including their subheadings, MeSH terms, and all synonyms. References for each of the studies se lected were also screened (the detailed search strategy can be found on the supplementary data). The search process was reported according to the Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Selection criteria

Studies were eligible if they included any the following criteria: *a)* compared the efficacy of colchicine treatment, at any dose and for any duration, to standard medical treatment with or without placebo; *b)* included populations of patients treated with PCI regardless of the indication; and *c)* reported, at least, 1 of the following cardiovascular outcomes: all-cause mortality, cardiovascular mortality, myocardial infarction (MI), stroke or urgent coronary revascularization. Study selection was conducted by 2 independent reviewers (C.E. Soria Jiménez, and J. Chang) first by

screening titles and abstracts and then by reviewing full texts and their corresponding references. In case of disagreement over eligibility, a third reviewer (H.M. García-García) assessed discrepancy, and decisions were reached by consensus.

Data collection and study endpoints

Data on study characteristics, patient characteristics, and endpoint event rates were independently drawn and organized into a structured dataset by 2 reviewers (C.E. Soria Jiménez, and F. Hayat), and then compared. All discrepancies resulted in the re-evaluation of primary data and involvement of a third reviewer (H.M. García García). Disagreements were resolved by consensus.

Endpoints

The prespecified primary endpoint was all-cause mortality. Secondary clinical endpoints were cardiovascular mortality, MI, stroke, and any revascularization. Each endpoint was assessed according to the definitions reported in the original study protocols (summarized on table 1 of the supplementary data).

Risk of bias

The risk of bias in each study was assessed using the revised Cochrane Risk of Bias tool (RoB 2.0) for randomized controlled trials (RCTs), and the Risk of Bias in Non-randomized Studies of Interventions assessment Tool from the Cochrane handbook (ROBINS-I) for observational studies. Two investigators (C.E. Soria Jiménez, and J. Sanz Sánchez) independently assessed 5 domains of bias in RCTs: (1) randomization process, (2) deviations from intended procedures, (3) missing outcome data, (4) outcome measurement, and (5) selection of results reported. The same investigators independently assessed 7 domains of bias in observational studies: (1) confounding, (2) selection of participants, (3) classification of procedures, (4) deviations from intended interventions, (5) missing outcome data, (6) outcome measurement, and (7) selection of results reported (table 2 and 3 of the supplementary data).

Statistical analysis

Odds ratios (OR) and 95% confidence intervals (95%CI) were estimated using the DerSimonian and Laird random-effects model with the estimate of heterogeneity taken from the Mantel-Haenszel method. The presence of heterogeneity among the studies was evaluated using the Cochran Q test referred to chi-square distribution ($P \leq .10$ was considered statistically significant) plus the I^2 test to assess inconsistencies. Values of 0% indicated no observed heterogeneity, and values ≤ 25%, ≤ 50%, and > 50% indicated low, moderate, and high heterogeneity, respectively. The presence of publication bias was investigated using Harbord test and visual estimation with funnel plots. We conducted a leave-one-out sensitivity analysis for all outcomes by iteratively removing 1 study at a time to confirm that our findings were not driven by any single study. To account for the different follow-up durations across the studies, another sensitivity analysis was conducted using a Poisson regression model with random intervention effects to calculate the means of inverse-variance weighting of trial-specific log stratified incidence rate ratios. Results were shown as incidence rate ratios, which are exponential coefficients of the regression model.

A meta-regression analysis was conducted using the empirical Bayesian method to estimate the between-study variance tau-squared to assess the effect of colchicine dosage, follow-up duration, percentage of patients with ACS, and percentage of those with diabetes mellitus on treatment effects on the primary endpoint.

Two-tailed P values < .05 were considered statistically significant. Statistical analyses were conducted using the Stata software version 13.1 (StataCorp LP, College Station, United States).

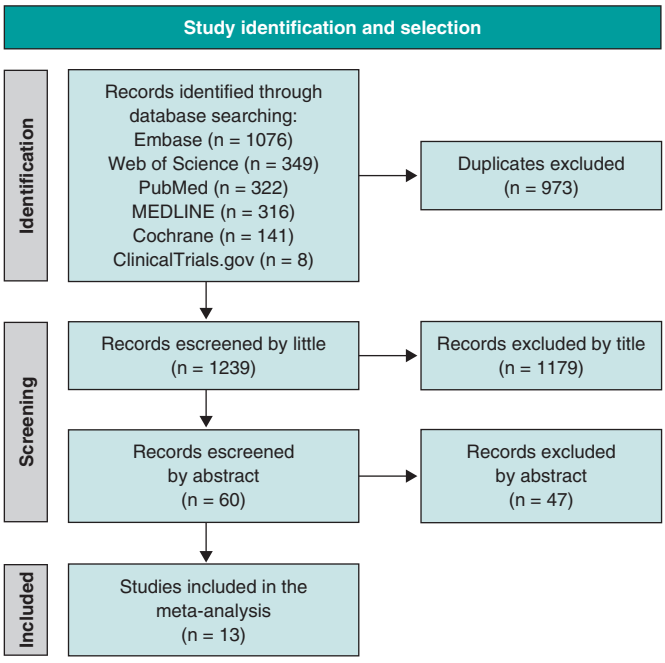

Figure 1. Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of database search results and study selection.

RESULTS

Search results

Figure 1 shows the PRISMA study search and selection process. Out of a total of 1239 unique reports, 12 RCTs[5-16] and 1 observational study[17] were identified and included in this analysis. The corresponding author of the COOL trial[15] was contacted regarding data from a number of patients treated with PCI; 58 out of a total of 80 patients evaluated (72.5%) underwent PCI. The study ultimately met the inclusion criteria and was included in our analysis. The main features of the studies included are shown on table 1. Data on the outcomes, mortality, MI, stroke, and urgent revascularization were reported in 12, 9, 5, and 6 trials, respectively. A total of 3741 and 3673 patients treated with and without colchicine were included (for a total of 7414 patients). Time elapsed from the PCI to the start of colchicine went from immediately before PCI to 13.5 days later as shown on table 1.

Baseline characteristics

Main baseline characteristics of the patients included are shown on table 2. Most patients were men with a mean age of 60 years, had ACS, and underwent revascularization with drug-eluting stents.

Publication bias and asymmetry

Funnel-plot distributions of pre-specified outcomes indicate absence of publication bias for all the outcomes (figures 1 to 5 of the supplementary data).

Table 1. Characteristics of trials selected

Trial/Author	Year	Study design	Multicenter	Patients (n)	Population	Colchicine dose and duration	Time elapsed from PCI to start of colchicine	Follow-up
COVERT-MI[8]	2021	RCT	Yes	192	Adults with a first-time STEMI referred for primary or bailout PCI	2 mg oral loading dose followed by daily oral 0.5 mg twice daily for 5 days	Loading dose immediately before PCI; if not possible, immediately after PCI	3 months
COPE-PCI[7]	2021	RCT	No	75	Adults with stable angina or NSTEMI undergoing angiography and PCI	1 mg followed by 0.5 mg 1 h later, 6 hrs to 24 hrs pre-PCI	6 hrs to 24 hrs before coronary angiogram	1 day
Colchicine-PCI[6]	2020	RCT	No	400	Adults with suspected ischemic heart disease or ACS referred for angiography with possible PCI	1.2 mg 1 h to 2 h pre-angiography, 0.6 mg 1 h later or immediately after the procedure if rushed for emergency angiography	1 h to 2 h before coronary angiography	1 month
COPS[9]	2020	RCT	Yes	795	Adults presenting with ACS and evidence of CAD treated with angiography and managed with PCI or medical therapy	0.5 mg twice daily for 1 month, then 0.5 mg daily for 11 months	Immediately after PCI and randomization	13.2 months
LoDoCo-MI[10]	2019	RCT	No	237	Adults who sustained a type 1 MI within the past 7 days	0.5 mg daily for 30 days	1.5 days following the index MI	1 month
Talasaz[11]	2019	RCT	No	196	Adults presenting with STEMI undergoing PCI	NA	NA	1 month
COLCOT I[5]	2019	RCT	Yes	4745	Adults with MI within the past 30 days who had completed some percutaneous revascularization	0.5 mg once daily for, at least, 2 years	13.5 days	42 months
Vaidya[17]	2018	Observational	No	80	Adults who presented with ACS < 1 month prior and underwent invasive coronary angiography and revascularization if indicated	0.5 mg once daily for 1 year	NA (< 1 month from ACS per inclusion criteria)	12.6 months
COLIN[12]	2017	RCT (Open-label)	No	44	Adults admitted for STEMI with occlusion of 1 of the main coronary arteries treated with PCI	1 mg once daily for 1 month	On the first day of the AMI	1 month
Deftereos 2015[13]	2015	RCT (Pilot)	Yes	151	Adults presenting with STEMI of ≤ 12-hour evolution from pain onset treated with PCI	2 mg loading dose, 0.5 mg twice daily for 5 days	Immediately after completion of diagnostic coronary angiography	5 days
Deftereos 2013[14]	2013	RCT	No	222	Adults with diabetes, aged 40-80 treated with PCI with bare metal stent	0.5 mg twice daily for 6 months	Within 24 hrs of index PCI	6 months
COOL[15]	2012	RCT	No	80	Adults with ACS or acute ischemic stroke	1 mg once daily for 30 days	Immediately after randomization	1 month
O'Keefe[16]	1992	RCT	No	197	Adults who underwent elective angioplasty (single or multivessel, new or restenosed lesions) for silent, stable or unstable angina; CABG	0.6 mg twice daily for 6 months	Somewhere between 12 hrs before and 24 hrs after balloon angioplasty	6 months

ACS, acute coronary intervention; CABG, coronary artery bypass graft; CAD, coronary artery disease; MI, myocardial infarction; NA, not available; NSTEMI, non-ST-elevation acute myocardial infarction; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; STEMI, ST-segment elevation myocardial infarction.

Table 2. Baseline characteristics of patients from each trial

Trial/Author	Mean Age	Men (%)	ACS (%)	DES (%)	HTN (%)	DM2 (%)	HLD (%)	Previous MI (%)	Previous PCI (%)	Previous CABG (%)	Underwent PCI (%)
COVERT-MI[8]	60	80.3	100	95.7	30.8	13.1	33.1	0	0	0	93
COPE-PCI[7]	64.7	71.5	58.7	97.0	54.5	22.9	63.5	17.5	16.0	NA	100
Colchicine-PCI[6]	66.3	93.5	49.5	NA	91.7	57.8	88.8	25.8	37.6	NA	100
COPS[9]	59.9	79.5	100.0	NA	50.5	19.0	46.0	15.0	13.0	4.5	88
LoDoCo-MI[10]	61.0	77.0	100.0	NA	47.5	22.0	NA	15.0	11.5	NA	90
Talasaz[11]	NA	NA	100.0	NA	NA	NA	NA	NA	NA	NA	100
COLCOT I[5]	60.6	80.9	100.0	NA	51.1	20.2	NA	16.2	16.9	3.2	93
Vaidya[17]	57.4	77.5	100.0	NA	53.8	31.3	85.0	51.3	63.8	NA	77.5
COLIN[12]	59.9	79.4	100.0	NA	43.4	13.7	36.5	NA	4.6	2.4	100
Deftereos 2015[13]	58.0	69.0	100.0	NA	39.5	21.5	52.0	0.0	NA	NA	100
Deftereos 2013[14]	63.6	65.5	31.0	0	48.5	100.0	NA	NA	NA	NA	100
COOL[15]	57.2	88.8	91.3	NA	42.5	16.3	47.5	17.5	0	NA	73
O'Keefe[16]	60.5	86.0	39.5	0	NA	12.0	NA	NA	NA	25.5	100

ACS, acute coronary syndrome; CABG, coronary artery bypass graft; DES, drug-eluting stent; DM2, diabetes mellitus type 2; HLD, hyperlipidemia; HTN, hypertension; MI, myocardial infarction; NA, not available; PCI, percutaneous intervention.

Risk of bias assessment

Table 2 and table 3 of the supplementary data summarize the results of the risk of bias assessment. A total of 11 trials were ranked as trials with a low overall risk of bias, 1 presented some concerns while another one was ranked as a trial with a high overall risk of bias.

Outcomes

No differences were seen between patients treated with colchicine and those treated without it or placebo regarding all-cause mortality (OR, 1.06; 95%CI, 0.72-1.55; I^2 = 0%), cardiovascular mortality (OR, 0.98; 95%CI, 0.42-2.28; I^2 = 14.2%) or coronary revascularization (OR, 0.64; 95%CI, 0.29-1.42; I^2 = 49.3%). However, patients treated with colchicine had a lower risk of stroke (OR, 0.38; 95%CI, 0.18-0.81; I^2 = 0%), and a trend towards a lower risk of MI (OR, 0.84; 95%CI, 0.66-1.07; I^2 = 0%) (figure 2).

Sensitivity analyses

In the leave-one-out sensitivity analysis, results were consistent with the primary analysis (tables 4 to 8 of the supplementary data). Similarly, in a sensitivity analysis on the use of estimated incidence rate ratios to account for different lengths of follow-up, findings remained unchanged (table 9 of the supplementary data).

When the risk ratios with random-effects models were estimated, findings remained consistent with the main analysis for all endpoints (table 10 of the supplementary data). Random effect meta-regression analyses found no significant impact of colchicine dosage (P = .33), follow-up duration (P = .88), percentage of patients with ACS (P = .37) or percentage of patients with diabetes mellitus (P = .96) on treatment effect regarding the primary endpoint (table 11 of the supplementary data).

DISCUSSION

This meta-analysis included 7414 patients across 12 RCTs and 1 observational study. It showed some clinical benefits on cardiovascular events with the addition of colchicine to standard medical therapy in patients undergoing PCI. Specifically, we found that the addition of colchicine compared to no colchicine or placebo reduced the risk of stroke showing a trend towards a lower risk of MI both with no observed heterogeneity. Additionally, we observed no differences in all-cause mortality, cardiovascular mortality or coronary revascularization. Significantly, colchicine dosage, follow-up duration, percentage of patients with ACS or diabetes mellitus showed no impact on treatment effect (see PRISMA checklist on table 12 of the supplementary data).

Our outcomes regarding all-cause and cardiovascular mortality are consistent with a prior meta-analysis of 5 RCTs conducted by Fu et al.,[18] that also found no significant reduction of mortality, MI, serious adverse events, and restenosis. One explanation for the lack of mortality benefit of both trials may be that although mortality rate was generally low and differences were largely not statistically significant in many of these trials, follow-up duration was generally short (≤ 30 days) in most studies, and it is possible that higher event rates may be seen with longer follow-up data. We should mention that the meta-analysis conducted by Fu et al.[18] included 1 RCT of patients treated with CABG, not PCI. It is possible that the inflammatory profiles of this cohort of patients differ from those treated with PCI (eg, multivessel coronary artery disease, longer postoperative recovery, and higher risk of postoperative complications). As a matter of fact, this mixed population may have led to the lack of reduction seen in the overall rate of MI, serious adverse events, and restenosis. Similarly, a prior meta-analysis conducted by Fiolet et al.[19] demonstrated that the addition of colchicine to standard medical therapy in patients with acute and chronic coronary syndromes reduced the risk of the primary endpoint significantly (a composite of MI, stroke, and cardiovascular mortality), and the individual endpoint of MI, stroke, and coronary revascularization with no differences

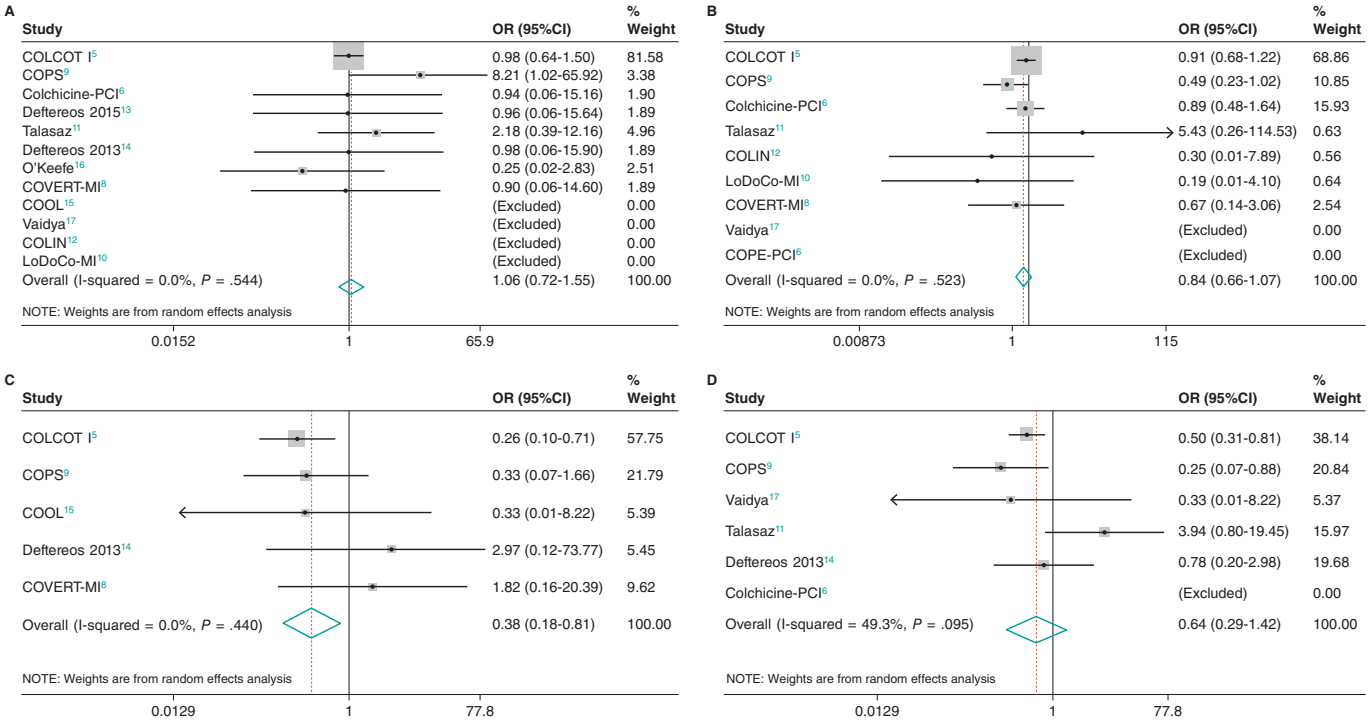

Figure 2. Forrest plot analyses for the main outcomes of death (A), myocardial infarction (B), stroke (C), and revascularization (D). 95%CI, confidence interval; OR, odds ratio.

whatsoever on all-cause or cardiovascular mortality. Our results demonstrating a lower risk of stroke and a trend towards a lower risk of MI are more consistent with this meta-analysis. A key difference among the different meta-analyses is the population of patients. Fiolet et al.[19] included the LoDoCo[20] and LoDoCo2[21] trials whose inclusion criteria were patients with chronic coronary disease and clinical stability for over 6 months. This amounted to > 50% of patients analyzed who were not in the peri-PCI period and likely had a different inflammatory profile at the time of colchicine administration. These 2 trials also had longer follow-ups (36 and 29 months, respectively) potentially allowing for more time to capture outcome differences like MI and urgent revascularization between the different treatment groups. In contrast, our meta-analysis only focused on patients in the peri-PCI as conducted by Fu et al.[18] and expanded the total number of studies analyzed to 12 RCTs and 1 observational study. As far as we know, our study is the largest meta-analysis ever conducted to this date to assess the effects of colchicine on the clinical outcomes of patients in the peri-PCI period.

Alkouli et al.[22] reported that the adjusted rate of ischemic stroke increased for patients treated with PCI due to ST-segment elevation myocardial infarction (STEMI) (0.6% to 0.96%), NSTEMI (0.5% to 0.6%), and unstable angina or stable ischemic heart disease (UA/SIHD, 0.3% to 0.72%). In turn, in-hospital mortality was higher (23.5% vs 11.0%, 9.5% vs 2.8%, and 11.5% vs 2.4% for STEMI, NSTEMI, and UA/SIHD cohorts, respectively), and post-PCI stroke was associated with a > 2-fold increase in LoS, a > 3-fold increase in non-home discharges, and a > 60% increase in cost. Given the increasing complexity of patients treated as well as the PCI techniques utilized over the past decade, effective preventive strategies and treatments are needed, and herein lies the opportunity for other anti-inflammatory drugs such as colchicine to further mitigate the morbidity and mortality of patients with post-PCI stroke. In the acute phase of MI, activated inflammasomes mount an intense inflammatory response.[23] There is also endothelial damage after PCI, which may result in atherosclerotic plaque destabilization with subsequent thromboembolism causing cerebrovascular events.[24] Colchicine may play a role preventing stroke by helping stabilize atherosclerotic plaques in patients undergoing PCI, though this effect may not be robust enough to overcome the direct endothelial injury present at the time of PCI.

Colchicine is a widely available drug with known anti-inflammatory properties. Its mechanism of action is yet to be fully elucidated but has been shown to work partly via the inhibition of NLRP3 (nucleotide-binding oligomerization domain-, leucine-rich repeat- and pyrin domain-containing protein 3) inflammasome, which ultimately downregulates interleukin-1B and interleukin-6, 2 known inflammatory mediators.[23-27] It also causes microtubule disruption and decreased neutrophil activation and extravasation. Since elevated levels of inflammatory biomarkers are an independent predictor of major adverse cardiovascular events[28-31] our results show that colchicine joining the current medical therapy is a potential addition to further attenuate inflammation regarding the secondary prevention of cardiovascular disease in patients undergoing PCI.

Some limitations of our study include the use of aggregate study-level data as opposed to patient-level data. While this limits subgroup analyses, the overall conclusions would remain the same. There was also a small percentage of patients in each of the studies analyzed who did not undergo PCI, which poses some limitations on the overall effects on a PCI population. However, in all studies, the vast majority of patients eventually underwent this procedure. Similarly, the LoDoCo2[21] trial enrolled patients who underwent PCI but was ultimately excluded from this analysis as patients required a period of clinical stability 6 months after PCI before starting colchicine therapy. A 6-month gap from PCI to colchicine initiation did not fit in with our period of interest (the peri-PCI period). The study conducted by O'keefe[16] was completed in an era of balloon angioplasty, and colchicine treatment in this setting may not be

comparable to patients who underwent PCI in the era of statins, modern stents, and antiplatelet agents. Additionally, most patients from our study underwent PCI due to the presentation of ACS, yet there were other clinical presentations including stable ischemic heart disease and unstable angina, and yet others that specifically excluded patients with acute MI. Given the different clinical status at presentation for PCI, it's likely that the inflammatory profile of these different populations of patients also varied resulting in different clinical outcomes. Nevertheless, despite variation in the inclusion and exclusion criteria, outcome definitions, and colchicine dose and duration, this did not introduce heterogeneity into our results.

CONCLUSIONS

In patients undergoing PCI, the addition of colchicine to optimal medical therapy resulted in a significant reduction of strokes, and a trend towards a lower risk of MI. However, this did not result in lower all-cause and cardiovascular mortality rates, and urgent revascularization.

FUNDING

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AUTHORS' CONTRIBUTIONS

M.B. Levine was involved in data curation and research. F. Hayat, and J. Chang were involved in data curation and research, as well as in drafting, editing, and reviewing the early draft of the manuscript. C.E. Soria Jiménez, J. Sanz Sánchez, and H. García-García were involved in project conceptualization, data curation, formal data analysis and investigation, methodology, project administration, resources, validation, visualization, as well as drafting, editing, and reviewing all manuscript drafts and its final version.

CONFLICTS OF INTEREST

H.M. García-García declared institutional grant support from Biotronik, Boston Scientific, Medtronic, Abbott, Neovasc, Shockwave, Phillips, and Corflow. The remaining authors declared no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- Inflammation plays a central role in the pathogenesis of coronary artery disease, and it's involved in percutaneous coronary interventions. Colchicine is a powerful anti-inflammatory drug. Its effect, however, attenuating peri-PCI inflammation remains unknown.

WHAT DOES THIS STUDY ADD?

- In this meta-analysis of 12 RCTs and 1 observational study, the addition of colchicine to patients undergoing PCI resulted in a lower risk of stroke. Other major adverse cardiovascular events did not show any significant differences.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000353.

REFERENCES

1. Fox KA, Poole-Wilson P, Clayton TC, et al. 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. *Lancet.* 2005;366:914-920.
2. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med.* 2007;356:1503-1516.
3. Deftereos S, Giannopoulos G, Papoutsidakis N, et al. Colchicine and the heart: pushing the envelope. *J Am Coll Cardiol.* 2013;62:1817-1825.
4. Nidorf SM, Eikelboom JW, Thompson PL. Colchicine for secondary prevention of cardiovascular disease. *Curr Atheroscler Rep.* 2014;16:391.
5. Tardif JC, Kouz S, Waters DD, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. *N Engl J Med.* 2019;381:2497-2505.
6. Shah B, Pillinger M, Zhong H, et al. Effects of Acute Colchicine Administration Prior to Percutaneous Coronary Intervention: COLCHICINE-PCI Randomized Trial. *Circ Cardiovasc Interv.* 2020;13:e008717.
7. Cole J, Htun N, Lew R, Freilich M, Quinn S, Layland J. Colchicine to Prevent Periprocedural Myocardial Injury in Percutaneous Coronary Intervention: The COPE-PCI Pilot Trial. *Circ Cardiovasc Interv.* 2021;14:e009992.
8. Mewton N, Roubille F, Bresson D, et al. Effect of Colchicine on Myocardial Injury in Acute Myocardial Infarction. *Circulation.* 2021;144:859-869.
9. Tong DC, Quinn S, Nasis A, et al. Colchicine in Patients With Acute Coronary Syndrome: The Australian COPS Randomized Clinical Trial. *Circulation.* 2020;142:1890-1900.
10. Hennessy T, Soh L, Bowman M, et al. The Low Dose Colchicine after Myocardial Infarction (LoDoCo-MI) study: A pilot randomized placebo controlled trial of colchicine following acute myocardial infarction. *Am Heart J.* 2019;215:62-69.
11. Talasaz AH, Jenab Y, Hosseini SH. P461. Colchicine before percutaneous coronary intervention in acute myocardial infarction. *Eur Heart J.* 2019(40):Suppl 1;ehz745.0994.
12. Akodad M, Lattuca B, Nagot N, et al. COLIN trial: Value of colchicine in the treatment of patients with acute myocardial infarction and inflammatory response. *Arch Cardiovasc Dis.* 2017;110:395-402.
13. Deftereos S, Giannopoulos G, Angelidis C, et al. Anti-Inflammatory Treatment With Colchicine in Acute Myocardial Infarction: A Pilot Study. *Circulation.* 2015;132:1395-1403.
14. Deftereos S, Giannopoulos G, Raisakis K, et al. Colchicine treatment for the prevention of bare-metal stent restenosis in diabetic patients. *J Am Coll Cardiol.* 2013;61:1679-1685.
15. Raju NC, Yi Q, Nidorf M, Fagel ND, Hiralal R, Eikelboom JW. Effect of colchicine compared with placebo on high sensitivity C-reactive protein in patients with acute coronary syndrome or acute stroke: a pilot randomized controlled trial. *J Thromb Thrombolysis.* 2012;33:88-94.
16. O'Keefe JH Jr, McCallister BD, Bateman TM, Kuhnlein DL, Ligon RW, Hartzler GO. Ineffectiveness of colchicine for the prevention of restenosis after coronary angioplasty. *J Am Coll Cardiol.* 1992;19:1597-1600.
17. Vaidya K, Arnott C, Martínez GJ, et al. Colchicine Therapy and Plaque Stabilization in Patients With Acute Coronary Syndrome: A CT Coronary Angiography Study. *JACC Cardiovasc Imaging.* 2018;11:305-316.
18. Fu C, Wang B. Colchicine administration for percutaneous coronary intervention: A meta-analysis of randomized controlled trials. *Am J Emerg Med.* 2021;46:121-125.
19. Fiolet A, Opstal T, Mosterd A, et al. Efficacy and Safety of Low-Dose Colchicine in Patients with Coronary Disease: A Systematic Review and Meta-Analysis of Randomized Trials. Eur Heart J. 2021;00:1-11.
20. Nidorf SM, Eikelboom JW, Budgeon CA, Thompson PL. Low-dose colchicine for secondary prevention of cardiovascular disease. *J Am Coll Cardiol.* 2013;61:404-410.
21. Nidorf SM, Fiolet ATL, Mosterd A, et al. Colchicine in Patients with Chronic Coronary Disease. *N Engl J Med.* 2020;383(19):1838-1847.
22. Alkhouli M, Alqahtani F, Tarabishy A, Sandhu G, Rihal CS. Incidence, Predictors, and Outcomes of Acute Ischemic Stroke Following Percutaneous Coronary Intervention. *JACC Cardiovasc Interv.* 2019;12:1497-1506.
23. Chen B, Frangogiannis NG. Immune cells in repair of the infarcted myocardium. *Microcirculation.* 2017;e12305.

24. de Winter RJ, Heyde GS, Koch KT, et al. The prognostic value of pre-procedural plasma C-reactive protein in patients undergoing elective coronary angioplasty. *Eur Heart J.* 2002;23:960-966.
25. Rajamäki K, Lappalainen J, Oörni K, et al. Cholesterol crystals activate the NLRP3 inflammasome in human macrophages: a novel link between cholesterol metabolism and inflammation. *PLoS One.* 2010;5:e11765.
26. Paschke S, Weidner AF, Paust T, Marti O, Beil M, Ben-Chetrit E. Technical advance: Inhibition of neutrophil chemotaxis by colchicine is modulated through viscoelastic properties of subcellular compartments. *J Leukoc Biol.* 2013;94:1091-1096.
27. Martinon F, Pétrilli V, Mayor A, Tardivel A, Tschopp J. Gout-associated uric acid crystals activate the NALP3 inflammasome. *Nature.* 2006;440:237-241.
28. Buffon A, Liuzzo G, Biasucci LM, et al. Preprocedural serum levels of C-reactive protein predict early complications and late restenosis after coronary angioplasty. *J Am Coll Cardiol.* 1999;34:1512-1521.
29. Kwaijtaal M, van Diest R, Bär FW, et al. Inflammatory markers predict late cardiac events in patients who are exhausted after percutaneous coronary intervention. *Atherosclerosis.* 2005;182:341-348.
30. Patti G, Di Sciascio G, D'Ambrosio A, Dicuonzo G, Abbate A, Dobrina A. Prognostic value of interleukin-1 receptor antagonist in patients undergoing percutaneous coronary intervention. *Am J Cardiol.* 2002;89:372-376.
31. Walter DH, Fichtlscherer S, Sellwig M, Auch-Schwelk W, Schächinger V, Zeiher AM. Preprocedural C-reactive protein levels and cardiovascular events after coronary stent implantation. *J Am Coll Cardiol.* 2001;37:839-846.

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Original article

Regional differences in STEMI care in Spain. Data from the ACI-SEC Infarction Code Registry

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ABSTRACT

Introduction and objectives: Geographical and organizational differences between different autonomous communities (AC) can generate differences in care for ST-segment elevation myocardial infarction (STEMI). A total of 17 heart attack code programs have been compared in terms of incidence rate, clinical characteristics, reperfusion therapy, delay to reperfusion, and 30-day mortality.
Methods: National prospective observational study (83 centers included in 17 infarction networks). The recruitment period was 3 months (April 1 to June 30, 2019) with clinical follow-up at 30 days.
Results: 4366 patients with STEMI were included. The incidence rate was variable between different AC ($P < .0001$), as was gender ($P = .003$) and the prevalence of cardiovascular risk factors ($P < .0001$). Reperfusion treatment was primary angioplasty (range 77.5%-97.8%), fibrinolysis (range 0%-12.9%) or no treatment (range 2.2%- 13.5%). The analysis of the delay to reperfusion showed significant differences ($P < .001$) for all the intervals analyzed. There were significant differences in 30-days mortality that disappeared after adjusting for clinical and healthcare network characteristics.
Conclusions: Large differences in STEMI care have been detected between the different AC, in terms of incidence rate, clinical characteristics, reperfusion treatment, delay until reperfusion, and 30-day mortality. The differences in mortality disappeared after adjusting for the characteristics of the patient and the care network.

Keywords: STEMI. Population characteristics. Angioplasty.

[◊] The investigators, centers, and organizations involved in the Infarction Code Working Group of the Interventional Cardiology Association of the Spanish Society of Cardiology are shown on the supplementary data.

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Diferencias regionales en la atención al IAMCEST en España. Datos del Registro de Código Infarto ACI-SEC

RESUMEN

Introducción y objetivos: Las diferencias geográficas y organizativas entre distintas comunidades autónomas (CCAA) pueden generar diferencias en la atención al infarto agudo de miocardio con elevación del segmento ST (IAMCEST). Se han comparado 17 programas de Código Infarto en términos de incidencia, características clínicas, tratamiento de reperfusión, retraso hasta la reperfusión y mortalidad a 30 días.
Métodos: Estudio observacional prospectivo nacional (83 centros en 17 redes de infarto). El periodo de selección fue de 3 meses (1 de abril a 30 de junio de 2019), con seguimiento clínico a 30 días.
Resultados: Se incluyeron 4.366 pacientes con IAMCEST. La tasa de incidencia fue variable entre las CCAA (p < 0,0001), igual que el sexo (p = 0,003) y la prevalencia de factores de riesgo cardiovascular (p < 0,0001). El tratamiento de reperfusión fue angioplastia primaria (rango 77,5-97,8%), fibrinolisis (rango 0- 12,9%) o ninguno (rango 2,2-13,5%). El análisis del retraso hasta la reperfusión mostró diferencias significativas (p < 0,001) para todos los intervalos analizados. Hubo diferencias significativas en la mortalidad cruda a 30 días que desaparecieron tras ajustar por las características clínicas y dependientes de la red asistencial (primer contacto, tiempo hasta la reperfusión y abordaje de críticos).
Conclusiones: Se han detectado diferencias en la atención al IAMCEST entre las distintas CCAA, en términos de incidencia, características clínicas, tratamiento de reperfusión, retraso hasta la reperfusión y mortalidad a 30 días. Las diferencias en mortalidad desaparecen tras ajustar por las características del paciente y de la red asistencial.

Palabras clave: IAMCEST. Características de la población. Angioplastia.

Abbreviations

ACI-SEC: Interventional Cardiology Association at the Spanish Society of Cardiology. **AC:** autonomous communities. **pPCI:** primary percutaneous coronary intervention. **STEMI:** ST-segment elevation myocardial infarction.

INTRODUCTION

Infarction Code networks are key to treat ST-segment elevation myocardial infarction (STEMI) in the shortest time possible while optimizing reperfusion therapy.[1] In Spain we have 17 different public regional STEMI networks, 1 in each autonomous community (AC) for a total of 83 pPCI-capable hospitals in programs on a 24/7/365 basis.[2] According to data from the Annual Activity Registry of the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC), back in 2019, a total of 22 529 interventional procedures were performed in patients with infarction.[3] Recently, an analysis of the ACI-SEC Infarction Code Registry revealed the characteristics of infarction care in Spain with 87.5%, 4.4%, and 8.1% of the patients with STEMI being treated with pPCI, fibrinolysis, and without reperfusion, respectively. The 30-day mortality rate of STEMI was 7.9% dropping down to 6.8% in patients treated with pPCI.[4]

The geographical differences and heterogeneity of the organizational infrastructure among the different Infarction Code programs available can lead to regional differences as a survey conducted among health professionals involved in these programs revealed recently.[5] These organizational differences can have an impact on the management of patients with STEMI. Their analysis and AC-based comparison facilitates finding matters where there is room for improvement to optimize treatment.

This analysis compared the incidence rate, clinical characteristics, type and time to reperfusion, the characteristics of pPCI, and the 30-day mortality rate of 17 different regional programs of the Infarction Code in Spain.

METHODS

Study design

The Registry design has already been introduced[4]. In conclusion, this was a national, observational, and prospective study of 83 centers from 17 different regional STEMI networks. The patients' recruitment period was 3 months—from April 1 through June 30, 2019—with a 30-day clinical follow-up.

Registry protocol was approved by the reference central ethics committee that did not deem the obtention of the informed consent necessary since data anonymity was guaranteed at any time.

Inclusion criteria

All consecutive patients who, during the study period, triggered the activation of different regional infarction care networks with a final diagnosis of STEMI and met the following criteria were included in the study: *a)* diagnosis of ST-segment elevation acute coronary syndrome with symptoms consistent with acute coronary syndrome, electrocardiogram showing ST-segment elevation or new-onset left bundle branch block or suspected posterior infarction of, at least, 24-hour evolution since symptom onset or *b)* recovered cardiac arrest with suspected coronary etiology or *c)* cardiogenic shock with suspected coronary etiology.

Definition and collection of variables

Clinical variables were registered in an online form and previously published.[4] The definitions of the different time intervals since

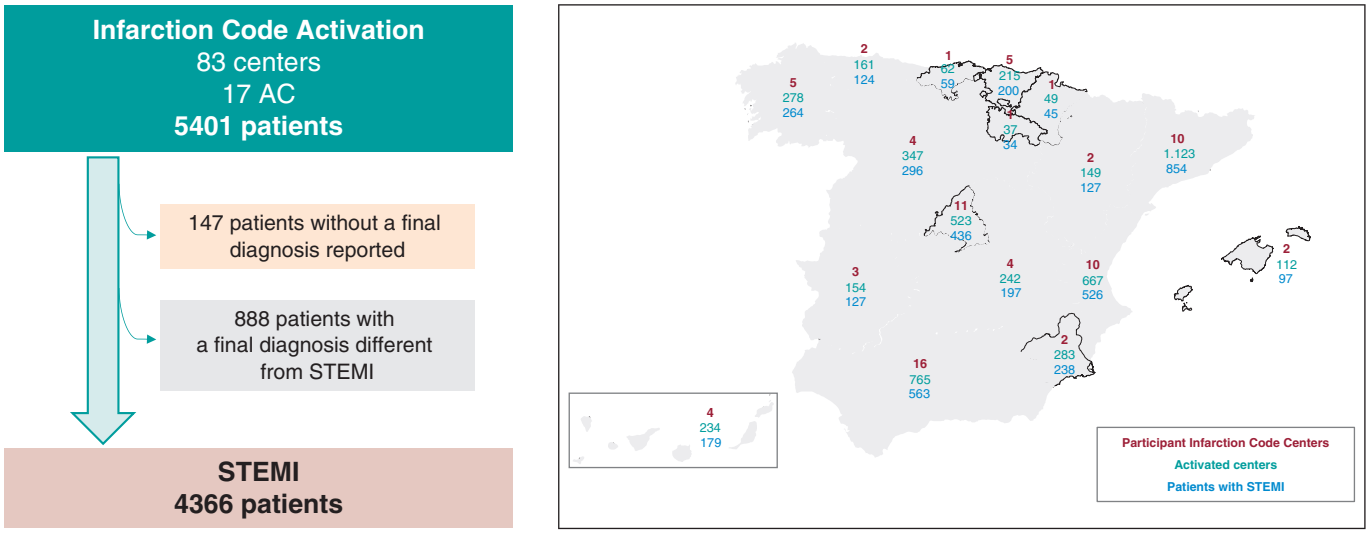


Figure 1. Flow of patients and distribution across the different autonomous communities (AC) based on participant centers, number of codes activated, and number of patients with ST-segment elevation myocardial infarction (STEMI) as final diagnosis.

symptom onset until reperfusion were given based on the recommendations established by the European clinical practice guidelines on the management of STEMI.[1] Subjective judgment from a local investigator was requested on the delay sustained by the patient since his first medical contact (existence of unjustified delay—yes/no—and reason why). To estimate the incidence rate (number of cases per million inhabitants) population data from the National Statistics Institute from 2019 were used.[6] Regarding the mortality adjusted analysis, the following characteristics of the care network were defined: the individual responsible for the first medical contact (emergency medical services, health center, non-pPCI-capable hospital, pPCI-capable hospital), time to reperfusion, and location where critical care was administered (intensive care unit or cardiac surgery intensive care unit).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. The categorical ones were expressed as frequencies and percentages. Inter-group comparisons of baseline variables were conducted using the chi-square test or the Student *t* test, when appropriate. Times to reperfusion were expressed as median and interquartile range and compared using the Mann-Whitney *U* test.

Poisson regression coefficient was used to estimate the 30-day mortality rate of each AC including patient-dependent factors (the confounding factors included were age, sex, hypertension, diabetes, dyslipidemia, smoking, previous ischemic heart disease, Killip classification, and anterior location of STEMI), and the healthcare network involved (location of the first medical contact, time between the onset of pain and reperfusion, and location where critically ill patients were treated).

The variable AC was introduced in the model in a second step, and a test of ratio of verisimilitude was performed to verify its statistical significance. When the AC variable was added, adjusted associations were obtained between AC and mortality. The Poisson regression coefficients became incidence rates using the marginal effect function. The estimated 30-day mortality rate for each AC was obtained from a mean distribution of confounding factors, which facilitated comparing mortality rate across the different AC. This method had been previously used in the acute myocardial infarction setting.[7-9] Since there could be a selection bias across the different AC in patients without reperfusion therapy, these were not included in the adjusted mortality analysis.

P values < .05 were considered statistically significant. The STATA statistical software package version 15 SE (Stata Corp, College Station, United States) was used.

RESULTS

Patients

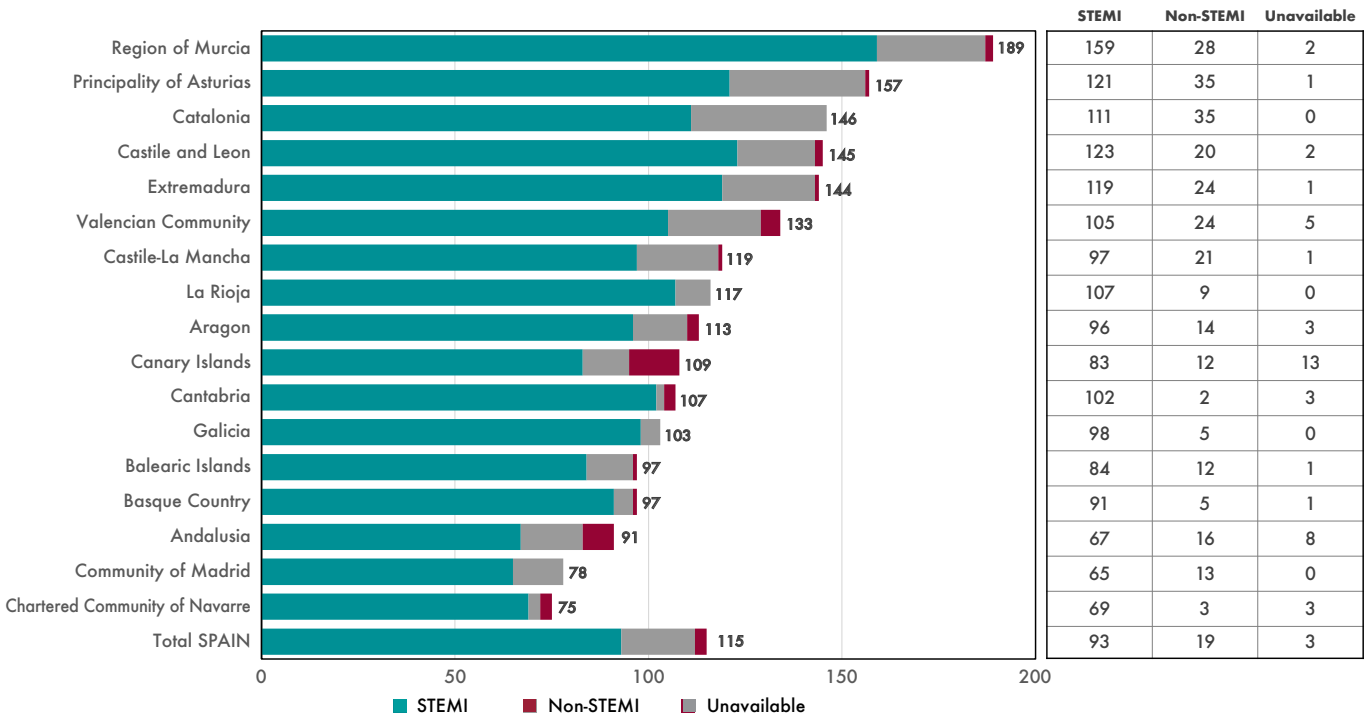
The registry included a total of 5401 patients, 4366 (81.2%) of whom had a final diagnosis of STEMI. The 888 patients (16.4%) with a diagnosis different from STEMI and the 147 (2.7%) without a final diagnosis were excluded from the analysis. Figure 1 shows the flow of patients and the AC-based distribution. Figure 2 shows the number of patients treated across the different AC plus the final diagnosis achieved adjusted by million inhabitants.[6] Table 1 shows the clinical characteristics of patients with STEMI across the different AC.

Reperfusion therapy used in patients with ST-segment elevation myocardial infarction

Out of the 4366 patients with STEMI, 3792 (86.9%) received pPCI, 189 (4.3%) fibrinolysis, and 353 (8.1%) no reperfusion therapy whatsoever. No reperfusion therapy was reported in 32 patients (0.7%). Figure 3 shows treatment distribution based on AC. Table 2 shows, across different AC and patients treated with cardiac catheterization, the angiographic findings and characteristics of interventional therapy had this procedure been performed.

Time intervals between symptom onset and reperfusion in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

Table 3 shows time intervals between symptom onset and reperfusion. Figure 4 shows the different time intervals analyzed for every AC with significant differences in all of them. Figure 5 summarizes



	STEMI	Non-STEMI	Unavailable
Region of Murcia	159	28	2
Principality of Asturias	121	35	1
Catalonia	111	35	0
Castile and Leon	123	20	2
Extremadura	119	24	1
Valencian Community	105	24	5
Castile-La Mancha	97	21	1
La Rioja	107	9	0
Aragon	96	14	3
Canary Islands	83	12	13
Cantabria	102	2	3
Galicia	98	5	0
Balearic Islands	84	12	1
Basque Country	91	5	1
Andalusia	67	16	8
Community of Madrid	65	13	0
Chartered Community of Navarre	69	3	3
Total SPAIN	93	19	3

Figure 2. Patients treated across the different autonomous communities (AC) adjusted for million inhabitants. AC were arranged from largest to smallest number of patients treated per million inhabitants. Regarding the population estimate per million inhabitants, population data from the National Statistics Institute were used.[6] STEMI, ST-segment elevation myocardial infarction.

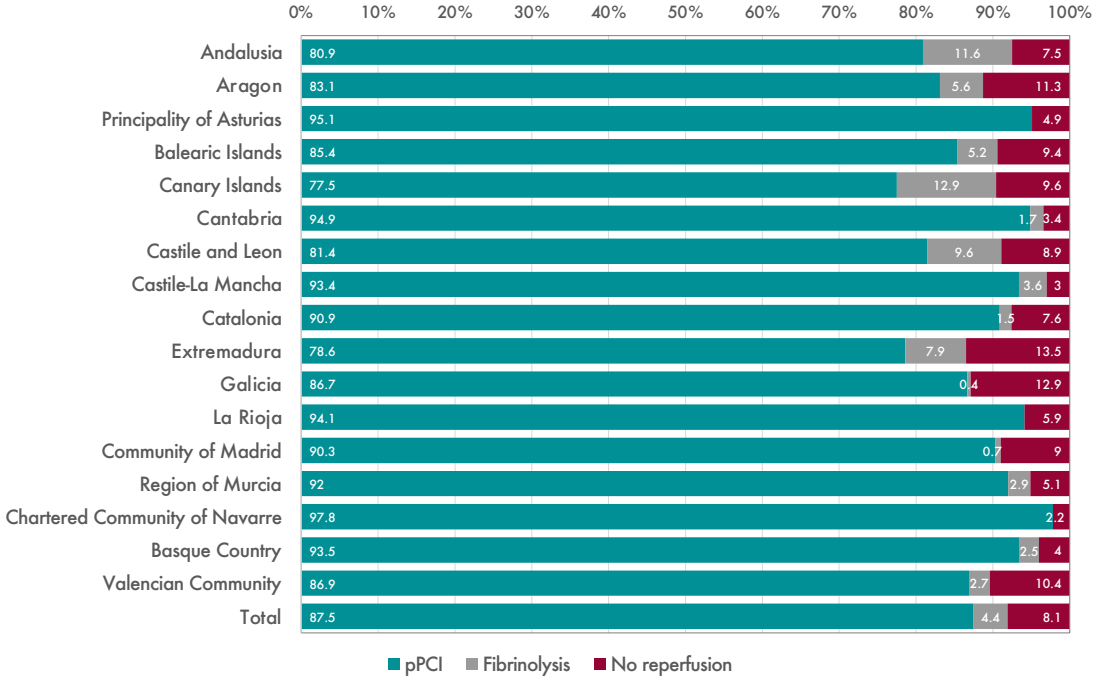


Figure 3. Distribution of reperfusion therapy in patients with ST-segment elevation myocardial infarction by autonomous communities. pPCI, primary percutaneous coronary intervention.

Table 1. Clinical characteristics of patients with ST-segment elevation myocardial infarction treated in the Infarction Code networks per autonomous community

	Age, years	Sex, women	AHT	Diabetes	Dyslipidemia	Active smoking	Previous IHD	Previous PCI	Previous stroke	Early Killip I	Early Killip IV	Anterior location
Andalusia	63 ± 13	110/563 (19.5)	297/560 (53.0)	159/558 (28.5)	252/559 (45.1)	264/557 (47.4)	60/561 (10.7)	59/559 (10.6)	31/556 (5.6)	423/541 (78.2)	31/541 (5.7)	223/521 (42.8)
Aragon	65 ± 14	30/127 (23.6)	62/127 (48.8)	28/125 (22.4)	56/127 (44.1)	59/124 (47.6)	13/124 (10.5)	17/126 (13.5)	7/122 (5.7)	99/124 (79.8)	13/124 (10.5)	56/120 (46.7)
Principality of Asturias	66 ± 13	40/124 (32.3)	61/124 (49.2)	34/122 (27.9)	54/124 (43.6)	41/123 (33.3)	20/123 (16.3)	19/123 (15.4)	7/123 (5.6)	96/123 (78.1)	11/123 (8.9)	57/122 (46.7)
Balearic Islands	63 ± 12	28/97 (28.9)	44/94 (46.8)	21/94 (22.3)	49/93 (52.7)	49/93 (52.7)	14/93 (15.1)	14/94 (14.9)	4/92 (4.4)	71/96 (74.0)	5/96 (5.2)	30/92 (32.6)
Canary Islands	60 ± 12	40/178 (22.5)	99/178 (55.6)	52/178 (29.2)	102/177 (57.6)	93/178 (52.3)	22/178 (12.4)	18/178 (10.1)	8/176 (4.6)	146/168 (86.9)	14/168 (8.3)	65/163 (39.9)
Cantabria	62 ± 13	15/59 (25.4)	31/59 (52.5)	21/58 (36.2)	27/58 (46.6)	31/57 (54.4)	10/58 (17.2)	10/59 (17.0)	3/57 (5.3)	46/56 (83.9)	2/56 (3.6)	25/58 (43.1)
Castile and Leon	64 ± 13	56/296 (18.9)	146/293 (49.8)	73/291 (25.1)	126/292 (43.2)	117/292 (40.1)	31/293 (10.6)	31/294 (10.5)	12/176 (4.1)	236/287 (82.2)	17/287 (5.9)	138/280 (49.3)
Castile-La Mancha	64 ± 13	26/197 (13.2)	108/194 (55.7)	58/192 (30.2)	99/196 (50.5)	92/193 (47.7)	19/192 (9.9)	18/194 (9.3)	9/194 (4.6)	157/196 (80.1)	12/196 (6.1)	89/194 (45.9)
Catalonia	63 ± 13	195/854 (22.8)	393/854 (46.0)	198/854 (23.2)	340/854 (39.8)	354/854 (41.4)	60/854 (7.0)	62/854 (7.3)	30/854 (3.5)	683/826 (82.7)	67/826 (8.1)	351/767 (45.8)
Extremadura	63 ± 13	18/127 (14.2)	74/127 (58.3)	26/126 (20.6)	52/126 (41.3)	48/127 (37.8)	17/126 (13.5)	14/126 (11.1)	4/127 (3.2)	91/122 (74.6)	11/122 (9.0)	56/121 (46.3)
Galicia	63 ± 13	63/264 (23.9)	130/262 (49.6)	48/259 (18.5)	138/261 (52.9)	100/215 (46.5)	18/261 (6.9)	25/262 (9.5)	12/263 (4.6)	195/251 (77.7)	31/251 (12.4)	103/233 (44.2)
La Rioja	59 ± 12	8/34 (23.5)	14/34 (41.2)	3/34 (8.8)	16/34 (46.1)	20/34 (58.8)	1/34 (3.0)	2/34 (5.9)	0/34 (0)	30/34 (88.2)	3/34 (8.8)	11/34 (32.4)
Community of Madrid	63 ± 13	105/436 (24.1)	212/432 (49.1)	88/430 (20.5)	208/431 (48.3)	177/428 (41.4)	41/429 (9.6)	43/429 (10.0)	11/429 (2.6)	347/424 (81.8)	35/424 (8.3)	174/419 (41.5)
Region of Murcia	64 ± 13	43/238 (18.1)	127/237 (53.6)	71/237 (30.0)	100/237 (42.4)	110/237 (46.4)	41/237 (17.3)	24/151 (15.9)	3/151 (2.0)	196/237 (82.7)	18/237 (7.6)	101/231 (43.7)
Chartered Community of Navarre	65 ± 14	14/45 (31.1)	18/44 (40.9)	9/45 (20.0)	29/45 (64.4)	16/45 (35.6)	3/45 (6.7)	4/44 (9.1)	3/45 (6.7)	31/43 (72.1)	4/43 (9.3)	16/44 (36.4)
Basque Country	64 ± 14	52/200 (26.0)	101/197 (51.3)	39/197 (19.8)	101/198 (51.0)	89/197 (45.2)	26/195 (13.3)	32/196 (16.3)	11/193 (5.7)	169/200 (84.5)	12/200 (6.0)	83/199 (41.7)
Valencian Community	63 ± 13	119/526 (22.6)	293/519 (56.5)	163/514 (31.7)	212/514 (41.3)	235/514 (45.7)	56/515 (10.9)	53/511 (10.4)	21/513 (4.1)	445/520 (85.6)	34/520 (6.5)	217/503 (43.1)
P	.054	.003	.038	< .0001	< .0001	.007	< .0001	.011	.61	.016	.25	.44
Total	63 ± 13	962/4365 (22.0)	2210/4335 (51.0)	1091/4314 (25.3)	1961/4326 (45.3)	1895/4268 (44.4)	452/4318 (10.5)	445/4234 (10.5)	176/4222 (4.2)	3462/4248 (81.5)	320/4248 (7.5)	1795/4101 (43.8)

AHT, arterial hypertension; IHD, ischemic heart disease; PCI, percutaneous coronary intervention.
Data are expressed as no. (%) or mean ± standard deviation.

the causes of unjustified delays between the first medical contact and reperfusion for every AC.

Mortality analysis in patients with ST-segment elevation myocardial infarction

Table 4 includes unadjusted mortality data at hospital admission and 30 days, and mortality for the adjusted model.

30-day mortality rate was different across different AC ($P < .001$). When the analysis was adjusted for patient-dependent factors and the healthcare network, mortality difference across the AC lost its statistical significance ($P = .19$).

DISCUSSION

This study is a comparative of how the different STEMI care programs work in Spain. Results show differences in the incidence rate, the patients' clinical profile, revascularization therapy, the characteristics of the interventional procedure performed, infarction care times, and the 30-day unadjusted mortality rate. Although mortality differences

Table 2. Angiographic findings and characteristics of interventional procedures in patients with ST-segment elevation myocardial infarction treated with cardiac catheterization per autonomous community

	Radial access	No. of diseased vessels	Early TIMI grade-0/1 flow	Final TIMI grade-3 flow	Need for hemodynamic support	Thrombus aspiration in IRA	BMS implantation in IRA	DES implantation in IRA	pPCI	Bailout PCI	Elective PCI after fibrinolysis	Coronary angiography without PCI
Andalusia	456/534 (85.4)	1.49 ± 0.69	416/535 (77.8)	502/536 (93.7)	15/563 (2.7)	76/563 (13.5)	48/563 (8.5)	456/563 (81.0)	471/557 (84.6)	36/557 (6.5)	27/557 (4.9)	23/557 (4.1)
Aragon	111/122 (91.0)	1.62 ± 0.78	90/120 (75.0)	114/122 (93.4)	5/127 (3.9)	41/127 (32.3)	0/127 (0)	103/127 (81.1)	108/124 (87.1)	6/124 (4.8)	1/124 (0.8)	9/124 (7.3)
Principality of Asturias	99/121 (81.8)	1.54 ± 0.77	106/121 (87.6)	111/121 (91.7)	5/124 (4.0)	39/124 (31.5)	10/124 (8.1)	98/124 (79.0)	118/123 (95.9)	0/123 (0)	0/123 (0)	5/123 (4.1)
Balearic Islands	79/92 (85.9)	1.46 ± 0.67	67/92 (72.8)	85/92 (92.4)	0/124 (0)	27/97 (27.8)	4/97 (4.1)	80/97 (82.5)	89/96 (92.7)	4/96 (4.2)	0/96 (0)	3/96 (3.1)
Canary Islands	138/169 (81.7)	1.54 ± 0.76	131/170 (77.1)	155/169 (91.7)	6/179 (3.6)	29/179 (16.2)	3/179 (1.7)	150/179 (83.8)	145/176 (82.4)	6/176 (3.4)	15/176 (8.5)	10/176 (5.7)
Cantabria	17/56 (30.4)	1.50 ± 0.68	51/57 (89.5)	55/56 (98.2)	1/59 (1.7)	31/59 (52.5)	0/59 (0)	51/59 (86.4)	57/59 (96.6)	0/59 (0)	1/59 (1.7)	1/59 (1.7)
Castile and Leon	263/281 (93.6)	1.55 ± 0.74	192/241 (79.7)	225/247 (91.1)	15/296 (5.1)	27/296 (9.1)	9/296 (3.0)	249/296 (84.1)	255/291 (96.6)	12/291 (4.1)	16/291 (5.5)	8/291 (2.8)
Castile-La Mancha	164/191 (85.9)	1.68 ± 0.73	164/192 (85.4)	186/190 (97.9)	9/197 (4.6)	75/197 (38.1)	10/197 (5.1)	172/197 (97.3)	185/196 (94.4)	2/196 (1.0)	4/196 (2.0)	5/196 (2.6)
Catalonia	727/781 (93.1)	1.48 ± 0.70	594/844 (70.4)	787/827 (95.2)	ND	259/854 (30.3)	117/854 (13.7)	653/854 (76.5)	807/849 (95.1)	8/849 (0.9)	3/849 (0.4)	31/849 (3.7)
Extremadura	119/121 (98.4)	1.65 ± 0.79	104/122 (85.3)	104/122 (85.3)	6/127 (4.7)	18/127 (14.2)	12/127 (11.0)	98/127 (77.2)	112/126 (88.9)	8/126 (6.4)	2/126 (1.6)	4/126 (3.2)
Galicia	228/242 (94.2)	1.53 ± 0.84	182/229 (79.5)	214/229 (93.5)	20/264 (7.6)	77/264 (29.2)	4/264 (1.5)	215/264 (81.4)	246/264 (93.2)	0/264 (0)	0/264 (0)	18/264 (6.8)
La Rioja	29/34 (85.3)	1.15 ± 0.36	30/34 (88.2)	31/34 (91.2)	0/24 (0)	10/34 (29.4)	3/34 (8.8)	27/34 (79.4)	33/34 (97.1)	0/34 (0)	0/34 (0)	1/34 (2.9)
Community of Madrid	395/421 (93.8)	1.48 ± 0.69	329/402 (81.8)	392/425 (92.2)	23/436 (5.3)	80/436 (18.4)	15/436 (3.4)	352/436 (80.5)	421/434 (97.0)	3/434 (0.7)	0/434 (0)	10/434 (2.3)
Region of Murcia	213/237 (89.9)	1.48 ± 0.64	175/234 (74.8)	223/236 (94.5)	4/238 (1.7)	56/238 (23.5)	5/238 (2.1)	209/238 (87.2)	226/238 (95.0)	7/238 (2.9)	0/238 (0)	5/238 (2.1)
Chartered Community of Navarre	31/36 (86.1)	2.00 ± 0.86	34/43 (79.1)	39/45 (86.7)	6/45 (13.3)	22/45 (48.9)	2/45 (4.4)	39/45 (86.7)	44/45 (97.8)	0/45 (0)	0/45 (0)	1/45 (2.2)
Basque Country	179/198 (90.4)	1.51 ± 0.67	153/198 (77.3)	191/199 (96.0)	7/200 (3.5)	100/200 (50.0)	3/200 (1.5)	174/200 (87.0)	194/199 (97.5)	4/199 (2.0)	1/199 (0.5)	0/199 (0)
Valencian Community	484/514 (94.2)	1.59 ± 0.76	390/496 (78.6)	461/497 (92.8)	8/256 (1.5)	145/526 (27.6)	34/526 (6.5)	423/526 (80.4)	482/518 (93.1)	10/518 (1.9)	4/518 (0.8)	22/518 (4.3)
P	< .0001	.84	< .0001	.002	< .0001	< .0001	< .0001	.004	< .0001			
Total	3732/4150 (89.9)	1.50 ± 0.71	3208/4130 (77.7)	3875/4147 (93.4)	110/4366 (2.5)	1112/4366 (25.5)	281/4366 (6.4)	3548/4366 (81.3)	3992/4329 (92.2)	106/4329 (2.5)	74/4329 (1.7)	157/4329 (3.6)

BMS, bare metal stent; CL, cath lab; DES, drug-eluting stent; ECG, electrocardiogram; EMS, emergency medical services; FMC, first medical contact; IRA, infarct-related artery; PCI, percutaneous coronary intervention; pPCI, primary percutaneous coronary intervention.
The type of procedure performed (pPCI, bailout angioplasty, elective PCI after fibrinolysis or coronary angiography without PCI) is on the total number of patients treated with coronary angiography, not on the total number of patients with ST-segment elevation myocardial infarction.
Data are expressed as no. (%).

reduce, they're still significantly different after adjusting for the patients' risk and clinical characteristics. Also, they disappear after adjusting for whoever is responsible for the first medical contact, time to reperfusion, and location where critical care is administered, all of them factors associated with the way each network is organized.

Both functioning and results of infarction care networks are highly influenced by different factors like geography, the number of capable centers, transfer times, the availability of the right resources, infrastructure, and the characteristics of each healthcare system.[2] In Spain, the plan of each AC has been designed independently. Also, the services rendered by the different AC is not homogeneous since resource allocation by the different administrations of the 17 Spanish AC is decentralized[2] in such a way that there are inequalities in the ways these networks are organized.[2,5,10,11] A recent consensus document on the requirements and sustainability of pPCI programs in

Table 3. Location of the first medical contact and time intervals between the first medical contact and reperfusion per autonomous community

	First EMS care	First care provided at the health center	First non-pPCI-capable center care	First pPCI-capable center care	Transfer without going to the CL right away*	Time of onset of pain to FMC	Time of FMC to ECG	Time of FMC to pPCI-capable center in transferred patients	Time from FMC to reperfusion	Time from onset of pain to reperfusion
Andalusia	206/537 (38.4)	138/537 (25.7)	93/537 (17.3)	100/537 (18.6)	188/427 (44.0)	60 [30-123]	5 [3-10]	80 [50-120]	113 [70-170]	195 [135-330]
Aragon	46/123 (37.4)	23/123 (18.7)	42/123 (34.1)	12/123 (9.8)	23/110 (20.9)	62.5 [18.5-170]	7 [4-12.5]	84.5 [45-145]	116.5 [70.5-177.5]	229 [126-345]
Principality of Asturias	32/123 (26.0)	18/123 (14.6)	36/123 (29.3)	37/123 (30.1)	4/86 (4.7)	80 [32-210]	10 [5-22]	85 [60-119]	108 [73-137]	215 [134.5-351]
Balearic Islands	33/95 (34.7)	26/95 (27.4)	27/95 (28.4)	9/95 (9.5)	3/85 (3.5)	70 [30-164]	6 [5-10]	100 [55-139]	124 [85-169]	197.5 [143.5-391]
Canary Islands	28/178 (15.7)	103/178 (57.9)	22/178 (12.4)	25/178 (14.0)	77/152 (50.7)	75 [37.5-150]	9 [5-15]	85 [55-133]	122 [95-172]	220 [159-385]
Cantabria	15/58 (25.9)	19/58 (32.8)	13/58 (22.4)	11/58 (19.0)	26/46 (56.5)	53 [25-145]	5 [4.5-10]	60 [35-93]	110 [81-188]	210 [134-303.5]
Castile and Leon	97/290 (33.5)	70/290 (27.2)	68/290 (23.5)	46/290 (15.9)	70/237 (29.5)	90 [35-221]	8 [4-15]	115 [70-165]	135 [85-197]	242.5 [163-432.5]
Castile-La Mancha	69/196 (35.2)	61/196 (31.1)	30/196 (17.3)	36/196 (18.4)	49/160 (30.6)	68 [30-160]	10 [5-15]	86.5 [58-114]	109 [80-155]	205 [150-322]
Catalonia	332/847 (39.2)	161/847 (19.0)	256/847 (30.2)	98/847 (11.6)	115/730 (15.8)	63 [30-160]	6 [3-14]	75 [55-105]	104 [80-138]	180 [127-288]
Extremadura	43/126 (34.1)	36/126 (28.6)	22/126 (17.5)	25/126 (19.8)	27/93 (29.0)	81.5 [44-135]	10 [5-12]	91.5 [60-143]	121 [90-178]	240 [160-360]
Galicia	84/264 (31.8)	111/264 (42.1)	28/264 (10.6)	41/264 (15.5)	ND	60 [26-179]	9 [5-19]	95 [70-140]	115 [88.5-163]	194 [134-353]
La Rioja	10/34 (29.4)	9/34 (26.5)	6/34 (17.7)	9/34 (26.5)	3/25 (12.0)	76.5 [35-110]	4.5 [1-10]	70 [46-86]	90.5 [67-114]	159.5 [118.5-212.5]
Community of Madrid	196/429 (45.7)	37/429 (8.6)	80/429 (18.7)	116/429 (27.0)	142/309 (45.6)	63 [35-140]	6 [3-12]	60 [42-85]	95 [75-130]	178.5 [135-257.5]
Region of Murcia	102/238 (42.9)	36/238 (15.1)	74/238 (31.1)	26/238 (10.9)	25/212 (11.8)	56.5 [24-131]	5 [5-10]	80 [60-120]	103 [79-160]	175 [130-305]
Chartered Community of Navarre	22/45 (48.9)	7/45 (15.6)	3/45 (6.7)	13/45 (28.9)	12/32 (37.5)	63.5 [29.5-124.5]	1 [0-5]	50 [35-91]	90 [69-140]	175 [128-262]
Basque Country	76/199 (38.2)	28/199 (14.1)	37/199 (18.6)	58/199 (29.2)	61/138 (44.2)	80 [32-184]	6.5 [3-11]	61 [49-77]	97 [75-135]	210 [134-345]
Valencian Community	128/521 (24.6)	146/521 (28.0)	128/521 (24.6)	119/521 (22.8)	98/398 (24.6)	82 [35-180]	5 [0-10]	94 [65-135]	120 [93-165]	220 [146-348]
P	< .0001	< .0001	< .0001	< .0001	< .001	.001	.0001	.0001	.0001	.0001
Total	1519/4303 (35.3)	1038/4303 (24.1)	965/4303 (22.4)	781/4303 (18.2)	923/3240 (28.5)	67 [30-165]	7 [4-15]	80 [55-120]	110 [80-154]	197 [135-330]

CL, cath lab; ECG, electrocardiogram; EMS, emergency medical services; FMC, first medical contact; pPCI, primary percutaneous coronary intervention.
* Patients treated early in a non-pPCI-capable center requiring immediate transfer to a pPCI-capable center.
Data are expressed as no. (%) or mean [interquartile range]. Times are expressed in minutes.

Spain proposed measures to homogenize and secure their sustainability.[2,12] Our study data reinforce the need for taking measures like the proposals made in the said consensus document.

Differences in the patients' clinical profile

Registry data demonstrated a difference in the number of codes activated per million inhabitants. Also, in the number of patients with STEMI per million inhabitants across the different AC. These differences are multifactorial and can be seen, historically, in the ACI-SEC annual activity registry reports.[3] Some AC have older populations and more cardiovascular risk factors, which could account for the higher rate of infarction reported.[6] However, the lack of a unified criterion on the indication for Infarction Code activation could also account for these differences seen.[5]

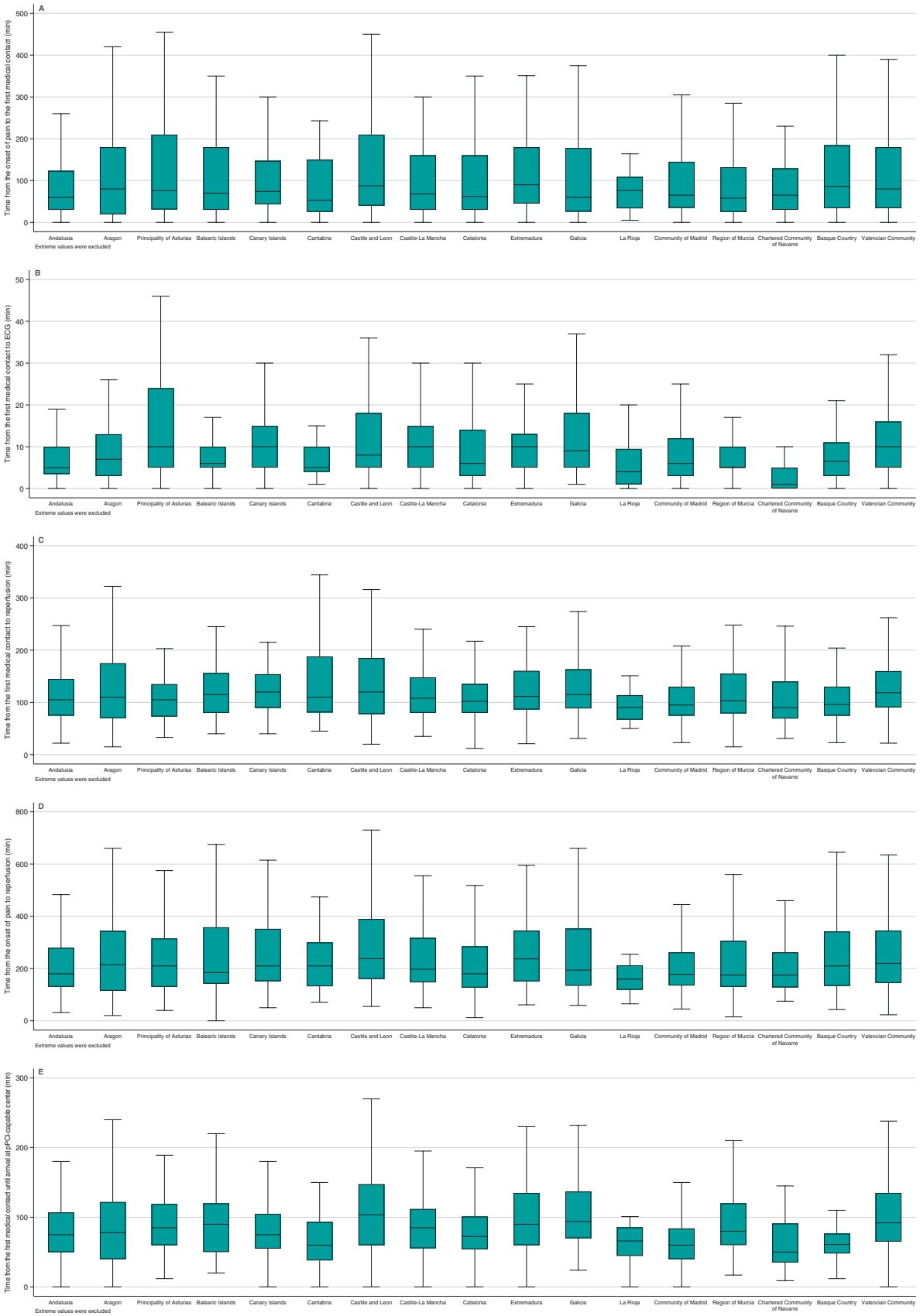


Figure 4. Time intervals between symptom onset and reperfusion in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention (pPCI) for every autonomous community. **A:** time in min from the onset of pain to the first medical contact. **B:** time in min from the first medical contact to the electrocardiogram (ECG). **C:** time in min from the first medical contact to reperfusion. **D:** time in min from the onset of pain to reperfusion. **E:** time in min from the first medical contact to the arrival at the pPCI-capable center in patients requiring transfer from a non-pPCI-capable center.

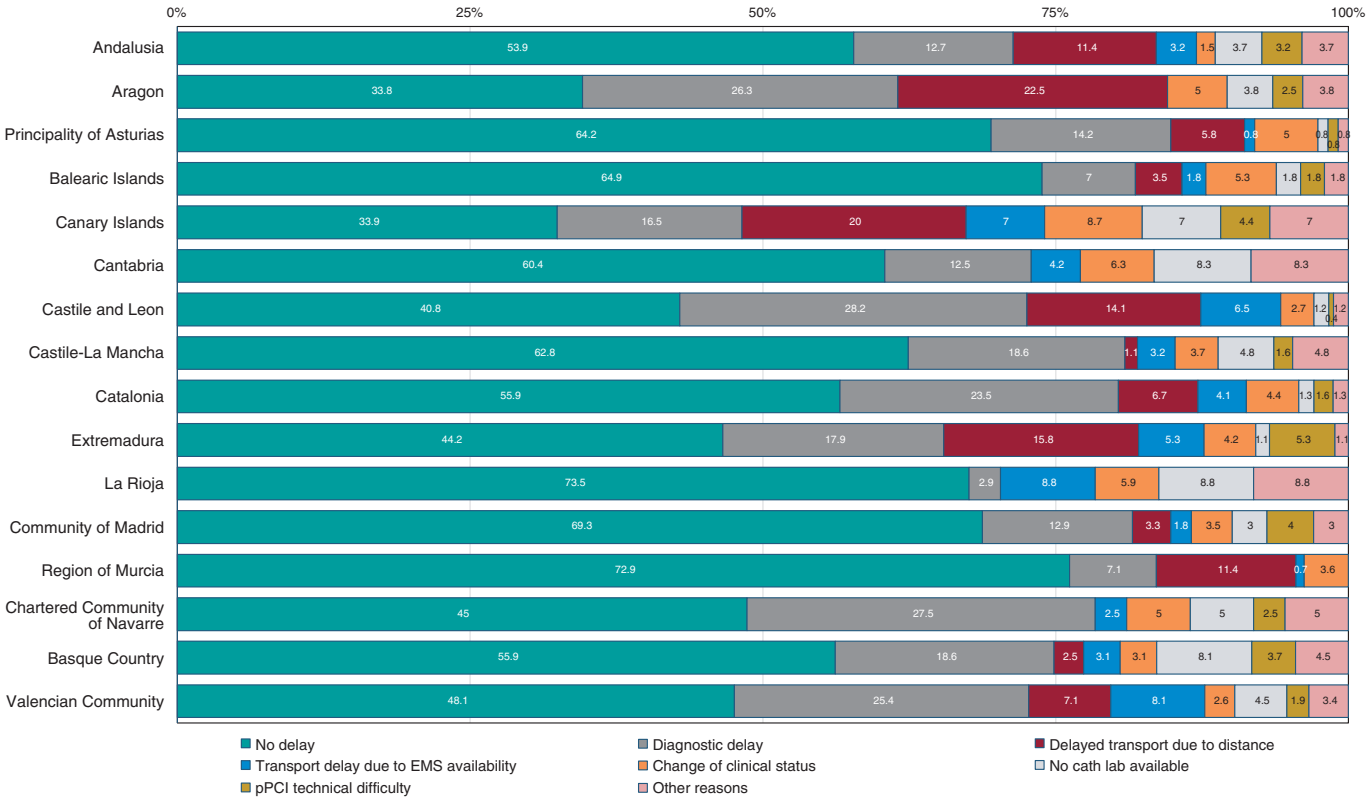


Figure 5. Causes of unjustified time delays between the first medical contact and reperfusion. Unjustified time delays did not imply, necessarily, that the time between the first medical contact and reperfusion was > 120 min. As a matter of fact, overall, in 53.2% of the cases the time between the first medical contact and reperfusion was < 120 min, and, among these, excessive time delays were reported in 21.5%. EMS, emergency medical services; pPCI, primary percutaneous coronary intervention.

Differences in reperfusion therapy

pPCI is the treatment of choice for the management of STEMI.[1] The geographical (populations far from pPCI-capable centers) and organizational characteristics (availability of medical service transport with ECG monitorization) across the different AC lead to a variable number of patients be treated with fibrinolysis. A previous analysis of data on the *Codi Infart* in Catalonia revealed that patients treated with fibrinolysis in non- pPCI-capable centers had worse disease progression compared to those transferred to pPCI-capable centers within the first 140 min after diagnosis.[13]

Different time delays to reperfusion

Patient-dependent time delays (from symptom onset to first medical contact) were highly variable. Although the geographic distribution of the population could partially account for these differences, public campaigns should be run to increase awareness on STEMI symptoms and the need for calling out-of-hospital emergency care.[1]

System-dependent time delays (from first medical contact to reperfusion) is much easier to change with organizational measures. Also, it determines prognosis.[14] Time delays to reperfusion depend on whoever is involved in the first medical contact. Therefore, patients treated by emergency medical services—those with the shortest times—showed high variability across the different programs. Better access to these systems for the population would also improve time delays to reperfusion.[15]

European clinical practice guidelines on the management of STEMI describe quality indicators that should be observed by the infarction networks to reduce the time to reperfusion, among these, a single coordination centralized center, interpreting the ECG before arriving at the hospital to achieve diagnosis and activate the system early, the direct transfer of patients to the cath lab without ER or ICU admissions or the follow-up of infarction care times, among other.[1] Our study demonstrated that not all programs meet these recommendations meaning that, in many cases, there is a huge room for improvement. For example, currently, it does not seem reasonable that a significant number of patients who need to be transferred to the pPCI (up to 50% in some cases) wouldn't end up at the cath lab right away. This simple measure can reduce time to reperfusion in 20 min and have a direct impact on prognosis.[16,17]

The presence of unjustified delayed reperfusion times was highly variable across the different AC, as well as the causes for these delays, which is indicative of the characteristics of each AC.

Mortality differences

A study conducted by Cequier et al.[18] analyzed standardized mortality based on the risk of patients with STEMI across different AC from 2003 through 2012 and detected significant differences. However, across this period, not all regions had implemented Infarction Code programs and the rate of pPCI was highly variable. Our study demonstrated that there are still differences in crude mortality that disappear after adjusting for the clinical variables and care network-related variables (location of first medical contact, delay to reperfusion, and management of critically ill patients). We have already mentioned the importance that the first medical contact should be performed by emergency medical services and

Table 4. Mortality analysis in patients treated with primary percutaneous coronary intervention per autonomous community

	Unadjusted hospital mortality	Unadjusted 30-day mortality	Adjusted 30-day mortality
Andalusia	30/563 (5.3)	37/523 (7.1)	6.0 [5.3-6-7]
Aragon	8/127 (6.3)	8/124 (6.5)	5.5 [4.0-6.9]
Principality of Asturias	9/124 (7.3)	10/118 (8.5)	6.7 [5.4-8.0]
Balearic Islands	6/97 (6.2)	6/88 (6.8)	5.0 [3.3-6.7]
Canary Islands	15/179 (8.4)	15/155 (9.7)	7.0 [5.5-8.6]
Cantabria	0/59 (0)	0/59 (0)	0
Castile and Leon	18/296 (6.1)	23/270 (8.5)	8.4 [7.1-9.8]
Castile-La Mancha	9/197 (4.6)	10/191 (5.2)	3.1 [2.3-3.8]
Catalonia	29/854 (3.4)	58/801 (7.2)	6.0 [5.4-6.6]
Extremadura	12/127 (9.5)	16/125 (12.8)	8.1 [6.6-9.5]
Galicia	22/264 (8.3)	28/260 (10.8)	6.8 [5.6-7.9]
La Rioja	1/34 (2.9)	1/33 (3.0)	5.6 [2.3-8.9]
Community of Madrid	14/436 (3.2)	21/421 (5.0)	3.9 [3.3-4.6]
Region of Murcia	21/237 (8.9)	24/226 (10.6)	9.2 [8.0-10.5]
Chartered Community of Navarre	5/45 (11.1)	5/45 (11.1)	9.5 [6.7-12.3]
Basque Country	12/200 (6.0)	16/197 (8.1)	8.9 [7.4-10.4]
Valencian Community	47/526 (8.9)	55/499 (11.0)	10.2 [9.2-11.2]
P	< .001	< .001	.19
Total	258/4365 (5.9)	337/4166 (8.1)	–

Data are expressed as no. (%) or mean [interquartile range].

the measures used to reduce time to reperfusion. Regarding the management of critically ill patients, a study conducted by Sánchez-Salado et al.[19] of 20 000 patients with cardiogenic shock demonstrated that the availability of cardiac surgery intensive care units was associated with a lower mortality rate. Data from this study added to the finding of our registry support the need for expanding the availability of cardiac surgery intensive care units in large volume centers of patients with acute coronary syndrome. In conclusion, the results of mortality study suggest that the organization of the different networks would increase the crude mortality rate seen in some AC.

Limitations

This study has some limitations. In the first place, it is based on self-reported data without external auditing. However, data on interventional cardiology are rather standardized across the world, and the electronic form for data curation was designed to be applied both intuitively and universally. Also, data from Catalonia and Galicia were collected from their official registries, reviewed, and then audited.

Secondly, the profile of patients may have been different across the different AC. To address this limitation and its possible impact on the different crude mortality rates reported, a mortality study was conducted across different AC after adjusting for different clinical variables and care networks. Therefore, some models may be over-adjusted, which is why formal statistical comparisons across AC should be interpreted as cautious as the associations described in any observational trial. The model did not include patients lacking some of the variables included in the model. Table 1 of the supplementary data shows patients discarded from the study for every AC.

Thirdly, patients with STEMI treated outside the infarction networks were not included in this study, although this is probably indicative of a mild selection bias due to its reduced number. Therefore, the greater bias occurs in patients without reperfusion therapy, who, at times, are not covered by these networks. For this reason, these patients were not considered in the mortality analysis. Similarly, patients with myocardial infarction and subacute presentation without emergency reperfusion criteria were not included in the study.

Fourthly, the way of collecting times may have presented some differences between centers and AC. However, since this was a prospective study with previously established definitions, we believe that these differences may have been minimized.

In the fifth place, the data presented date back to 2019. Since then, no big organizational changes have occurred to justify changes in the dynamics of functioning or relevant changes have been made in the European guidelines on the management of STEMI (published back in 2017). Also, in a study conducted during the first wave of the COVID-19 pandemic no differences were seen regarding the type of reperfusion therapy used or time between the first medical contact and reperfusion. However, an increased mortality rate was seen attributed, among other causes, to longer ischemia times.[20]

Finally, this study only included patients for a period of 3 months. However, we think these data can be generalized to what happens in a much larger period.

CONCLUSIONS

This registry showed significant differences in STEMI care across the different Spanish AC regarding incidence rate, the patients' clinical characteristics, reperfusion therapy, time delays to reperfusion, and 30-day crude mortality rate. After adjusting for the clinical characteristics and variables associated with the care network, no differences mortality differences were reported across the different AC.

Standardizing the organization and functioning of Infarction Code networks could correct some of the differences seen in the management of STEMI.

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None whatsoever.

AUTHORS' CONTRIBUTIONS

Drafting of the manuscript: O. Rodríguez-Leor, A.B. Cid-Álvarez, A. Pérez de Prado, and X Rosselló. Process of manuscript revision: all the authors. Statistical analysis: O. Rodríguez-Leor, and X. Rosselló. Database review: O. Rodríguez-Leor, A.B. Cid-Álvarez, and A. Pérez de Prado. Data coordination across the different regional network: all the authors.

CONFLICTS OF INTEREST

A. Pérez de Prado received numerous personal fees from iVascular, Boston Scientific, Terumo, Bbraun, and Abbott Vascular. Á. Cequier received personal fees from Ferrer International, Terumo, Astra Zeneca, and Biotronik. R. Moreno, S. Ojeda, R. Romaguera, and A. Pérez de Prado are associate editors of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The remaining authors did not declare any conflicts of interest associated with the content of this manuscript.

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SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000360.

REFERENCES

1. Ibañez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology. *Eur Heart J.* 2018;39:39:119-177.
2. Cequier A, Pérez de Prado A, Cid-Álvarez AB, et al. Requisitos y sostenibilidad de los programas de ICP primaria en España en el IAMCEST. Documento de consenso de SEC, AEEC y SEMES. *REC Interv Cardiol.* 2019;1:108-119.
3. Ojeda S, Romaguera R, Cruz-González I, Moreno R. Registro español de hemodinámica y cardiología intervencionista. XXIX Informe Oficial de la Asociación de Cardiología Intervencionista de la Sociedad Española de Cardiología (1990-2019). *Rev Esp Cardiol*. 2020;73:927-936.
4. Rodríguez-Leor O, Cid-Álvarez AB, Pérez de Prado A, et al. Análisis de la atención al infarto con elevación del segmento ST en España. Resultados del Registro de Código Infarto de la ACI-SEC. *Rev Esp Cardiol.* 2022;75:669-680.
5. Rodríguez-Leor O, Cid-Álvarez AB, Moreno R, et al. Encuesta sobre las necesidades de los programas de angioplastia primaria en España. *REC Interv Cardiol.* 2020;1:8-14.
6. Instituto Nacional de Estadística. Datos de población de comunidades autónomas. Available online: https://www.ine.es/jaxiT3/Datos.htm?t=2915#!tabs-tabla. Accessed 24 Jan 2022.
7. Bueno H, Rosselló X, Pocock SJ, et al. In-hospital coronary revascularization rates and post-discharge mortality risk in non-ST-segment elevation acute coronary syndrome. *J Am Coll Cardiol.* 2019;74:1454-1461.
8. Rosselló X, Huo Y, Pocock S, et al. Global geographical variations in ST-segment elevation myocardial infarction management and post-discharge mortality. *Int J Cardiol.* 2017;245:27-34.
9. Bueno H, Rosselló X, Pocock S, et al. Regional variations in hospital management and post-discharge mortality in patients with non-ST-segment elevation acute coronary syndrome. *Clin Res Cardiol.* 2018;107:836-844.
10. Alter DA, Austin PC, Tu JV, et al. Canadian cardiovascular outcomes research. Community factors, hospital characteristics and inter-regional outcome variations following acute myocardial infarction in Canada. *Can J Cardiol.* 2005;21:247-255.
11. Bertomeu V, Cequier A, Bernal JL, et al. In-hospital mortality due to acute myocardial infarction. Relevance of type of hospital and care provided. RECALCAR study. *Rev Esp Cardiol.* 2013:66:935-942.
12. Moreno R, Ojeda S, Romaguera R, et al. Actualización de las recomendaciones sobre requisitos y equipamiento en cardiología intervencionista. Documento de consenso de la Asociación de Cardiología Intervencionista y la Asociación de Cardiopatía Isquémica y Cuidados Agudos Cardiovasculares de la Sociedad Española de Cardiología y la Asociación Española de Enfermería en Cardiología. *REC Interv Cardiol*. 2021;3:33-44.
13. Carrillo X, Fernandez-Nofrerias E, Rodriguez-Leor O, et al. Early ST elevation myocardial infarction in on-capable percutaneous coronary intervention centres: in situ fibrinolysis vs. percutaneous coronary intervention transfer. *Eur Heart J.* 2016;37:1034-1040.
14. Terkelsen CJ, Sorensen JT, Maeng M, et al. System delay and mortality among patients with STEMI treated with primary percutaneous coronary intervention. *JAMA*. 2010;304:763-771.
15. Rodríguez-Leor O, Fernández-Nofrerías E, Mauri F, et al. Analysis of reperfusion delay in patients with acute myocardial infarction treated with primary angioplasty based on first medical contact and time of presentation. *Rev Esp Cardiol.* 2011;64:476-483.
16. Rodríguez-Leor O, Fernández-Nofrerías E, Mauri J, et al. Integration of a local into regional primary angioplasty action plan (the Catalan Codi Infart network) reduces time to reperfusion. *Int J Cardiol.* 2013;168:4354-4357.
17. Bagai A, Jollis JG, Dauerman HL, et al. Emergency department bypass for ST-segment-elevation myocardial infarction patients identified with a prehospital electrocardiogram: a report from the American Heart Association Mission: Lifeline program. *Circulation.* 2013;128:352-359.
18. Cequier A, Ariza-Sole A, Elola FJ, et al. Impacto en la mortalidad de diferentes sistemas de asistencia en red para el tratamiento del infarto agudo de miocardio con elevación del segmento ST. La experiencia de España. *Rev Esp Cardiol.* 2017;70:155-161.
19. Sánchez-Salado JC, Burgos V, Ariza-Solé A, et al. Trends in cardiogenic shock management and prognostic impact of type of treating center. *Rev Esp Cardiol.* 2020;73:546-553.
20. Rodríguez-Leor O, Cid-Álvarez AB, Pérez de Prado A, et al. Impact of COVID-19 on ST-segment elevation myocardial infarction care. The Spanish experience. *Rev Esp Cardiol.* 2020;73:994-1002.

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Original article

Neonatal transcatheter pulmonary valve perforation. Evolution from transfemoral to transjugular approach

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ABSTRACT

Introduction and objectives: Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare but serious cyanotic congenital heart disease. Depending on the patient's anatomy, different therapeutic strategies—surgical or trancatheter—can be planned. The objective of this study was to describe the results of transcatheter pulmonary valve perforation in patients with PA/IVS in a single tertiary center, and compare transjugular to transfemoral approach. The need for additional source of pulmonary flow (ductal stenting or systemic-to-pulmonary artery fistula) at follow-up was reviewed to identify possible risk factors associated with this reintervention.
Methods: patients with PA/IVS referred for transcatheter pulmonary valve perforation as first-line therapy from February 2004 through May 2022 were included. Technical procedural details, total procedural and fluoroscopy times, and demographic and echocardiographic data were studied.
Results: A total of 22 patients were included. Procedure was successful in 20 cases (91%). The rate of complications was 2/22 (9%). No deaths were reported. The transjugular and transfemoral approaches were equally safe and effective. The total median procedural (n = 20) and fluoroscopy times (n = 16), however, were shorter in the transjugular compared to the transfemoral approach (85 min vs 156 min, and 31 min vs 62 min, respectively), which reached statistical significance. At follow-up, 8/20 (40%) patients needed additional flow (4 ductal stenting, 4 systemic-to-pulmonary artery shunts). No significant risk factors regarding this reintervention were reported.
Conclusions: Transcatheter mechanical pulmonary valve perforation may be feasible in expert hands and properly selected patients being an attractive alternative to surgery. In our own experience, transjugular approach seems to simplify the procedure, and reduces procedural and fluoroscopy times.

Keywords: Congenital heart defect. Pulmonary atresia. Balloon valvuloplasty. Pulmonary valve. Newborn.

Perforación percutánea de la válvula pulmonar en recién nacidos. Evolución del abordaje transfemoral al transyugular

RESUMEN

Introducción y objetivos: La atresia pulmonar con septo íntegro (APSI) es una cardiopatía congénita cianosante infrecuente que por su gravedad requiere un tratamiento en época neonatal. En función de la anatomía del ventrículo derecho y de la circulación coronaria, se pueden plantear distintas estrategias. El objetivo fue describir los resultados de la perforación valvular pulmonar percutánea de los pacientes con diagnóstico de APSI en un centro terciario. Se comparó el abordaje transfemoral con el transyugular. Se revisó la necesidad de flujo adicional (fístula sistémico-pulmonar o *stent* ductal) en el seguimiento, procurando identificar posibles factores de riesgo asociados a esta reintervención.
Métodos: Se incluyeron todos los pacientes con APSI tratados con perforación percutánea de la válvula pulmonar como primera opción terapéutica desde febrero de 2004 hasta mayo de 2022. Se estudiaron los detalles técnicos del cateterismo, los tiempos de procedimiento y de escopia, y variables demográficas y ecocardiográficas.
Resultados: Se incluyeron 22 pacientes y el procedimiento fue exitoso en 20 (91%). Se presentaron complicaciones en 2 pacientes (9%). No hubo fallecimientos. Los abordajes transyugular y transfemoral mostraron una eficacia y una seguridad parecidas. Los tiempos medianos de procedimiento (n = 20) y de escopia (n = 16) fueron menores en los pacientes con acceso transyugular que en aquellos con acceso transfemoral (85 frente a 156 y 31 frente a 62 minutos, respectivamente), con significación estadística. En el seguimiento, 8 pacientes (40%) necesitaron flujo adicional (4 *stent* ductal y 4 fístula sistémico-pulmonar). No se encontró ningún factor asociado significativamente a esta reintervención.

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Conclusiones: La perforación percutánea de la válvula pulmonar puede ser factible en manos expertas y en pacientes bien seleccionados, y representa una alternativa atractiva a la cirugía. En nuestra experiencia, el abordaje transyugular parece simplificar el procedimiento, reduciendo los tiempos de intervencionismo y de escopia.

Palabras clave: Cardiopatía congénita. Atresia pulmonar. Valvuloplastia con balón. Válvula pulmonar. Recién nacido.

Abbreviations

CTO: chronic total coronary occlusion. **PA/IVS:** pulmonary atresia with intact ventricular septum. **PV:** pulmonary valve. **RV:** right ventricle. **TV:** tricuspid valve.

INTRODUCTION

Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare cyanotic congenital heart disease, that can exhibit a wide array of clinical presentations.[1-8] It accounts for < 1% of all congenital heart defects, and its anatomical variability involves a complex decision-making process.[9] Some procedures during the neonatal period are necessary to provide a reliable source of pulmonary blood flow.[3,10,11] Patients with severe right ventricular (RV) hypoplasia or a RV-dependent coronary circulation (some ventricular areas are exclusively perfused from the RV cavity) should be eligible for univentricular heart physiology. In contrast, patients without RV-dependent coronary circulation, mild or moderate RV hypoplasia and membranous pulmonary atresia can be elilgible for transcatheter pulmonary valve (PV) perforation to achieve biventricular circulation.[1,4,5,8,10-18] Overall, over the past 2 decades, we have been seeing a transition from surgical RV decompression to transcatheter approach, the latter being associated with a lower mortality rate.[7] Nevertheless, thorough patient selection seems crucial to obtain good results.[17,19,20]

In the 90s, several techniques were described to perforate the atretic PV like laser, radiofrequency or puncture using the stiff end of a guidewire.[2-4,10-12,14,15,17,21] Currently, however, laser has become obsolete due to its high cost, bulky equipment, and risk of retinal damage.[12,22] Although radiofrequency seems like the method most commonly used, mechanical perforation with the stiff end of a coronary guidewire or a chronic total coronary occlusion (CTO) coronary guidewire can be a promising alternative when the former is not available or is too expensive.[8,12,20]

Whichever technique was used, complications were common in the early era. The growing experience and the continuous technical improvement, however, have allowed us to contemplate the percutaneous perforation of the PV as a first-line option for neonates with PA/IVS.[4,5,11,12,16-18] Also, we should mention that establishing antegrade pulmonary flow early through the atretic valve may increase the chances of growing for the RV.[1,3,8,17,23] Furthermore, the transcatheter procedure enables RV decompression, thus avoiding open heart surgery in the neonatal period.

The objective of this study is to describe the results of neonatal transcatheter PV perforation with PA/IVS in a single tertiary center, and compare both the transjugular and transfemoral approaches.

METHODS

This study was approved by Vall d'Hebron Hospital ethics committee (Barcelona) in compliance with the Declaration of Helsinki. Inform consent from the patients' parents or legal guardians was obtained before publishing this manuscript.

Patients with PA/IVS treated with transcatheter perforation from February 2004 through May 2022 were included. Those with RV-dependent coronary circulation, unipartite RV, muscular pulmonary atresia, severe hypoplastic RV (z-score of tricuspid annulus < -5) or severe Ebstein's disease were excluded.

Procedures were divided into 2 groups depending on which venous access—femoral or jugular—was used. Demographic, pre- and postoperative echocardiographic variables (PV and tricuspid valve [TV] z-score values, RV morphology), and procedural data were described and compared between the 2 groups. Technical procedural details and complications were also briefly described. We tried to identify risk factors associated with the need for an additional procedure to provide pulmonary blood flow (fistula, ductal stenting). The whole study was divided into 2 periods, from 2004 through 2011 (first period) and from 2012 through 2022 (second period) due to the existence of a new first operator and the selection of transjugular approach as the first option.

All procedures were performed under general anesthesia and mechanical ventilation. Absence of RV-dependent coronary circulation was assessed in all cases through right ventriculography (figure 1A). A 4F Judkins right catheter (via femoral access) or a C1/C3 Cobra catheter (via jugular access) were used and inserted into the right ventricle outflow tract below the atretic PV. Afterwards, using different 0.014 in CTO guidewires the PV was mechanically perforated. Thereafter, a 0.014 in microcatheter was advanced and an angiography performed in the pulmonary tree to confirm proper position (figure 1B). Unfrequently, the guidewire didn't achieve the pulmonary trunk on the first attempt. Guidewire and microcatheter were removed uneventfully at this step of the procedure, and another attempt was made until the pulmonary trunk was reached. Once the proper location of the guidewire was confirmed, the CTO guidewire was exchanged for an BMW guidewire (Abbott Vascular, United States) followed by progressive balloon dilatations of the PV to improve pulmonary flow (figure 1C). Finally, a right ventriculography was performed to discard the presence of complications and proper flow across the PV (figure 1D).

Indications for additional source of pulmonary blood flow (systemic-to-pulmonary artery fistula first—until 2011—and ductal stenting later) were failed prostaglandin E1 withdrawal with excessive cyanosis (hemoglobin saturation < 70%) 1 or 2 weeks after the procedure.

Statistical analysis

Descriptive analysis of data was expressed as median values and interquartile range (IQR) (25^{th}-75^{th} percentile) for qualitative,

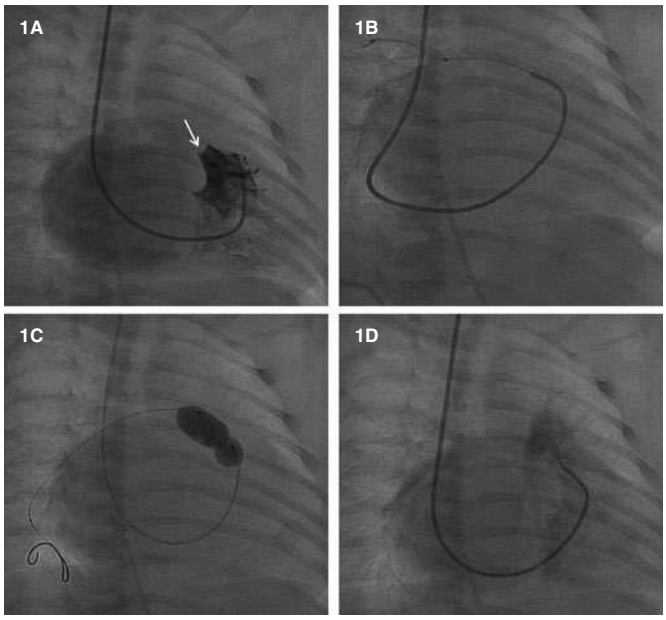

Figure 1. Transcatheter atretic pulmonary valve perforation. **A:** right ventriculography showing atretic pulmonary valve (white arrow) and no coronary sinusoids. **B:** microcatheter-based angiography showing proper positioning inside the right pulmonary artery. **C:** pulmonary valve valvuloplasty. **D:** right ventriculography showing flow towards the pulmonary artery without complications.

dichotomic or high dispersion variables, and as mean values with standard deviation (SD) for quantitative continuous variables (weight and gestational weeks). Fischer's exact test was used to look for possible associations between the binary variables. *P* values < .05 were considered statistically significant

Statistical analysis was performed using SPSS (statistical package for social sciences) version 20.0 (Illinois, United States).

RESULTS

A total of 22 patients were included, 13 of whom were women (59%). The mean gestational age was 38.3 weeks (+/- 2.9), and the mean weight, 2.96 kg (+/- 0.62).

Before the procedure, the median PV and TV z-scores for the whole sample were -1.2, (n = 22; IQR, -2.01 - -0.25) and -2.0 (n = 21; IQR, -3- -0.65), respectively. All patients but 2 were categorized as tripartite RV and 2 as bipartite with a hypoplastic trabecular part.

Regarding the transcatheter venous access route, initially, the transjugular and transfemoral groups included 13 and 9 patients, respectively. In 3 transfemoral cases, however, the approach had to be changed for the transjugular one due to catheter instability or impossibility to perforate the valve. Therefore, the definitive transjugular and transfemoral groups included 16 and 6 patients, respectively. All transfemoral (n = 6) and 4/16 transjugular cases were performed within the first period while the remaining 12 transjugular cases were performed within the second period.

The median age of the whole sample when the procedure was performed was 1 day of life (1-3). The ratio between the maximum balloon diameter and pulmonary annulus went from 0.8 to 1.45. No peri- or postoperative deaths were reported. The overall procedural success rate was 91% (20/22) [15/16 (94%) and 5/6 (83%) for transjugular and transfemoral groups, respectively]. Data on all successful patients (n = 20), and the comparison between transjugular and transfemoral group are shown on table 1.

Comparison between successful transfemoral and transjugular cases

The procedural duration of the 3 cases that crossed from one therapy to the other was considered from the moment transjugular approach was decided (and transfemoral dropped). Fluoroscopy time of these 3 cases was not estimated since we had no way of knowing what the exact fluoroscopy time of transjugular approach really was. There was also one missing piece of information in this variable. Therefore, the overall sample for fluoroscopy time was 16 (20 successful cases—3 cases crossed from one therapy to the other—1 missing data case). As shown on table 1, the variables procedural duration and fluoroscopy time were significantly shorter in the transjugular group. A residual gradient ≤ 20 mmHg (n = 18) measured invasively prevailed in the transjugular group since 15 out of these 18 patients were from this group whereas patients with an invasive gradient > 20 mmHg (n = 2) were from the transfemoral group.

Complications and failed cases

The procedure failed in 2/22 cases (9%). One transfemoral procedure due to right ventricular outflow tract perforation with a significant cardiac hematoma (the patient was urgently treated with surgical valvotomy). In this patient, misjudging the CTO guidewire position—actually located outside the pulmonary tree—triggered balloon dilatation in an incorrect location, thus causing hemopericardium. The other failed case was transjugular due to the impossibility of perforating the valve for being very thick and hypoplastic (surgical valvulotomy and systemic-to-pulmonary artery shunt were performed 6 days later).

No deaths were reported, and the rate of complications was 2/22 (9%). Aside from the significant cardiac hematoma (first period), the other complication occurred in the transjugular approach [atrial flutter that required electrical cardioversion (second period)].

We did not find any factors (gestational week < 37, weight < 2.7kg, TV or PV annulus < -2.0, venous access) associated with complications.

Follow-up and reintervention of the successful cohort

Figure 2 shows a diagram on the management and reintervention rates of the entire cohort.

The 2 failed cases sent to surgery were excluded from the follow-up.

The median follow-up was 9.39 years (3.97-11.94) [6.61 (3.67-10.29) and 13.9 (11.66-16.67) for the transjugular and transfemoral groups, respectively]. Of note, 10/20 patients (50%) were followed over 10 years. At follow-up, 10/20 patients (50%) needed some type of reintervention (4 ductal stenting, 4 systemic-to-pulmonary (SP) artery shunts, and 2 re-valvuloplasties) for a median of 12 days (5.2-30). The median time for using an additional flow source (4 SP artery shunts, 4 ductal stenting) was 7.5 days (from the procedure day), 3.0 days for SP fistula (0.87-13.75), and 13.5 days for ductal stenting (6.25-18.5). During the 2004-2011 period all patients who needed additional source intervention underwent a SP shunt (n = 4) whereas from 2012 through 2022 patients underwent a ductal stenting (n = 4) following the new hospital policy.

Table 1. Comparison between transjugular and transfemoral group (successful cases)

Approach	Global	Transjugular	Transfemoral	*P*
Succesful cases (n)	20	15	5	–
Procedural time (min)[a]	105 (63-143.8)	85 (53-130)	156 (120.5-220)	
Duration < 140 min	14 (70%)	13	1	**.01**
Duration ≥ 140 min	6 (30%)	2	4	
Fluoroscopy time (min); n = 16[b]	35.6 (20.6-57.1) n = 16	31.2 (19-53.4) n = 11	62.5 (25.5-80) n = 5	
Fluoroscopy < 60 min	13/16 (81%)	11	2	**.02**
Fluoroscopy ≥ 60 min	3/16 (19%)	0	3	
Balloon/valve ratio	1.24 (1.11-1.33)	1.2 (1.1-1.28)	1.35 (1.26-1.4)	
Invasive residual gradient ≤ 20 mmHg	18 (90%)	15	3	**.05**
Invasive residual gradient > 20 mmHg	2 (10%)	0	2	
Complications; n = 20	1 (5%)	1/15	0/5	.75
Echocardiographic assessment of PS < 25 mmHg; n = 19[c]	11/19 (58%)	8/15	3/4	.43
Echocardiographic assessment of PR (mod/sev); n = 19[c]	15/19 (79%)	11/15	4/4	.35
Need for AFS	8 (40%)	5/15	3/5	.3
DS	4	4/5	0/3	
Fistula	4	1/5	3/3	
Need of re-valvuloplasty	4 (20%)	3/15	1/5	.72
Biventricular circulation	18 (90%)	14/15	4/5	.45
Circulation 1 and 1/2	2 (10%)	1/15	1/5	

AFS, additional flow source; DS, ductal stenting; min, minutes; PR, pulmonary regurgitation; PS, pulmonary stenosis.
[a] Procedural time of the 2 failed cases (transfemoral and transjugular) were 146 min and 177 min, respectively.
[b] Fluoroscopy time, n = 16 (20 successful procedures—3 crossed from one therapy to the other—1 procedure with missing data).
[c] Echocardiographic assessment of PS < 25 mmHg and *PR* (mod/sev); n = 19 (20-1 patients with missing data).
Values expressed as median and interquartile range.

The median time of re-valvuloplasty as first reintervention (n = 2) was 4.4 months. Another 2 patients required re-valvuloplasty 3 and 9.5 months after a SP shunt and ductal stenting, respectively. Three of the 10 patients who required some reintervention were from the transfemoral group and 7 from the transjugular one. Table 2 compares patients who did not need (n = 12) or who did need (n = 8) an additional source of pulmonary blood flow. An association (P = .05) was seen between the RV/systemic pressure ratio < 150% before the procedure (n = 7) and the need for additional source intervention later since 5/7 patients (71%) with ratios < 150% and only 3/13 (23%) patients with ratios > 150% needed it.

Overall, 18/20 (90%) patients achieved biventricular circulation, and 2/20 (10%) a 1.5 ventricle repair (bidirectional superior cavo-pulmonary anastomosis surgery for right ventricular unloading) at a median time of 21.7 months after the index transcatheter procedure. One of these 2 patients were from the transfemoral group and the other from the transjugular group. No study patient underwent univentricular circulation.

DISCUSSION

In patients with PA/IVS and proper anatomy, decompressing the RV with early transcatheter PV perforation may help promote the RV growth and functional development, and facilitate the growth of pulmonary arteries, thus enhancing the options to achieve a biventricular circulation.[1,3,17,19,21,24] In this setting, the most frequently reported approach until now has been the transfemoral one.[4,5,8,13,15,19,20,23-25]

Although with a very modest sample (n = 22), this study is, as far as the authors know, the first to describe the use of transjugular access to perforate the PV in neonates with PA/IVS. Therefore, it is the first one to compare the transjugular and transfemoral approaches.

Compared to other case series where the method to perforate the valve was mixed,[1,2,4,11,25] the method of this study was always mechanical perforation using a CTO coronary guidewire.

The rates of success associated with performing mechanical PV perforation with CTO or other coronary guidewires are between 73% and 100%.[5,10,19] Overall, the success rate of our cohort was 91% (20/22). The failed transfemoral case was due to perforation and dilatation in an incorrect place of the right ventricular outflow tract whereas the transjugular one was probably due to improper case selection since the anatomy seen in the cath lab was worse compared to the one expected in the echocardiography. The annulus and subvalvular area were more hypoplastic, and the membrane

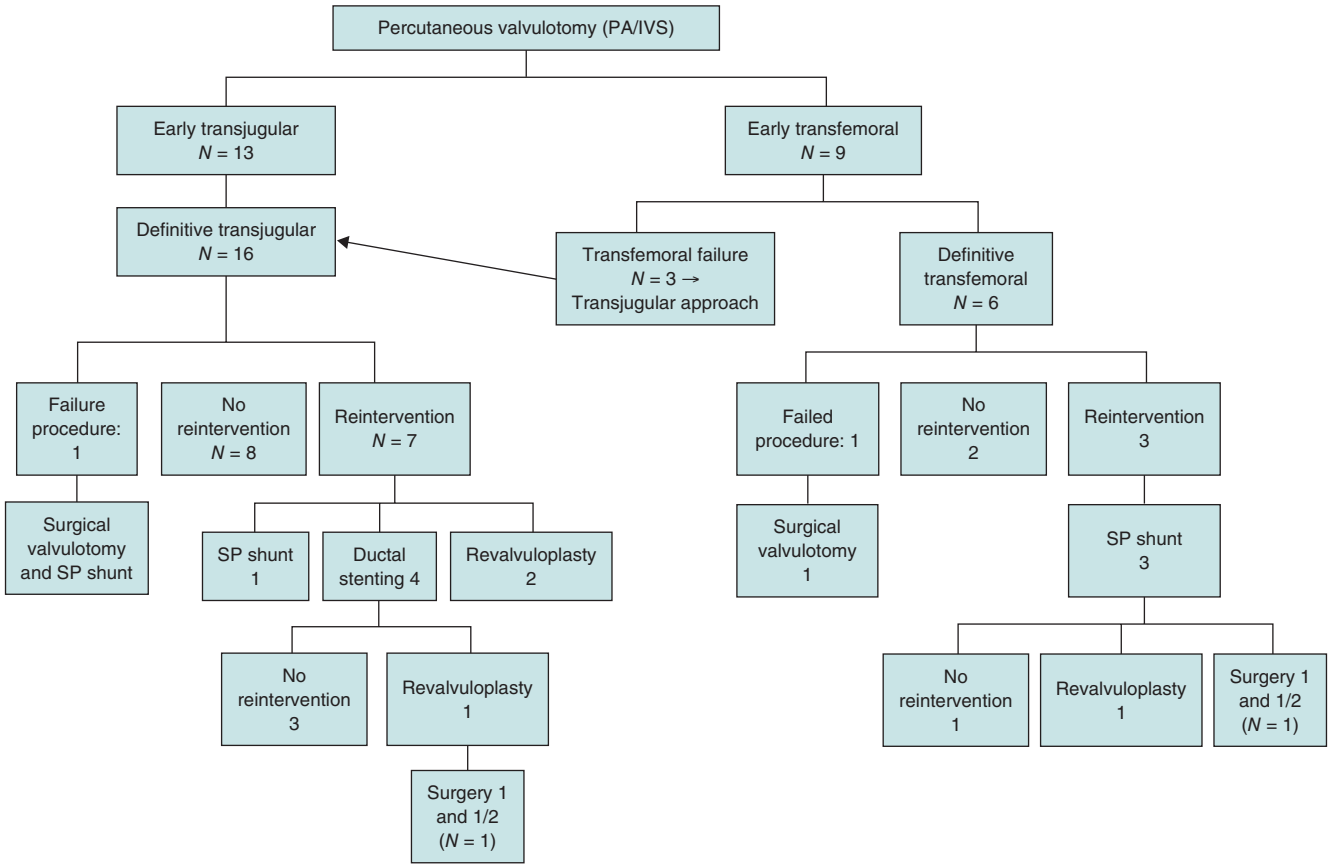

Figure 2. Management and reintervention of the whole sample. PA/IVS, pulmonary atresia with intact ventricular septum; SP, systemic-to-pulmonary artery.

Table 2. Comparison between successful cases requiring or not additional flow

Additional flow source (AFS)	Global	No need for AFS	Need for AFS	*P* (Fischer's exact test)
Global (n)	20	12	8	–
GW ≤ 37	5 (25%)	4	1	.31
Weight < 2.7 kg	4 (20%)	2	2	.53
PV z-score pre-flow < -2.0	5 (25%)	2	3	.3
TV z-score pre-flow < -2.0	10 (50%)	6	4	.68
RVP/systemic ratio ≥ 150%	13 (65%)	10	3	.05
RVP/systemic ratio < 150%	7 (35%)	2	5	
Residual echocardiographic gradient at discharge (≥ 25 mmHg); n = 19	8/19 (42%)	5	3	.66
PR at discharge (mod/sev); n = 19	15/19 (79%)	10	5	.48
PR at discharge (min-mild); n = 19	4/19 (21%)	2	2	

AFS, additional flow source; GW, gestational week; kg, kilograms; PR, pulmonary regurgitation; min, minimum; mod, moderate; sev, severe; PV, pulmonary valve; RVP, right ventricular pressure; TV, tricuspid valve.

was thick at PV level. These findings rendered catheter maneuvers cumbersome. Based on this case and other studies, proper case selection is key for successful procedures.[1,2,14,15,19,20,24]

Percutaneous PV perforation involves significant risks including RV or pulmonary trunk perforation.[16] Some authors consider mechanical perforation with a coronary guidewire has a higher risk compared to using laser or radiofrequency procedures.[10,12,19,20] Nevertheless, the smaller diameter of the CTO guidewire and its microcatheter would add an advantage in relation to larger diameters of the RF guidewire (0.016 in) and microcatheter (0.024 in), thus causing a smaller injury usually without significant consequences if the guidewire is not in the correct place.[12] Moreover, CTO guidewires seem to provide increased catheter stability, and advanced torquability and maneuverability to allow more accurate and controlled perforations.[12,19,20]

As far as the authors know, ours is one of the largest series of neonates with PA/IVS using exclusively mechanical PV perforation with CTO coronary guidewire. Overall, we reported 1/22 (4,5%) cases of significant right ventricular outflow tract perforation due to balloon dilatation. When radiofrequency is unavailable or unsuccessful, the mechanical PV perforation using CTO coronary guidewires may be an attractive alternative in view of its penetration capabilities and reduced cost although it can be technically challenging.[8,12,19,20]

Comparison between the transfemoral and transjugular groups

As far as the authors know, there is no previous comparative studies between the 2 different approaches in the medical literature currently available. Therefore, according to our observations of the overall procedural time, transjugular procedures were faster compared to transfemoral ones (85 min vs 156 min). This was associated with shorter fluoroscopy times in the transjugular group (31 min vs 62 min). Based on our own experience, the transjugular approach with a Cobra catheter seems to bring good stability, allow better positioning under PV leaflets, and greater support to perforate the atretic valve. Aside from the cited reasons, time differences between the 2 groups can also be due to the learning curve since all transfemoral cases (n = 6) were performed within the first period while 12/16 transjugular cases were performed within the second one. Also, the systematic use of the echography to canalize the central venous access since 2018 (n = 5) can also have contributed, in part, to the procedural time differences seen.

Need for additional flow source, re-valvuloplasty, and follow-up

The rate of reinterventions reported in several case series is still noticeable (from 30% to 72%). They seem to be mainly associated with the increased pulmonary blood flow.[4,17,18,25] In our study and among the successful procedures, 8 out of 20 patients (40%) needed additional flow source interventions, a percentage slightly lower compared to the one reported by Kim YH, Cho MJ or Hasan.[5,10,11] A certain trend—that almost reached statistical significance (P = .05)—was seen between the RV/systemic pressure ratio < 150% before the procedure (n = 7) and the need for further additional flow source intervention since 5/7 (71%) patients with ratios < 150% needed an extra flow source compared to only 3/13 (23%) patients with ratios > 150%. This observation could show that these right ventricles that were more dysfunctional and less capable of generating pressure could not provide an adequate antegrade pulmonary flow after the procedure. No other variables were associated with the need for an additional flow source intervention. In contrast, other studies reported lower tricuspid z-score values as a risk factor for additional flow source interventions.[11,13,15,18,23] Also, Wang et al. reported smaller PV diameters (median z-score of -2.11) and higher echocardiographic gradients 1 month after the procedure as risk factors for reintervention.[6]

Noteworthy, the median follow-up of our patients was 9.39 years (3.97-11.94). At follow-up, 10/20 patients (50%) did not require any type of reintervention, a higher number compared to the one published by Hasan (7/26, 27%), Schwartz (6/21, 29%) or Chen (7/36, 19%).[11,13,25]

Regarding the successful group (n = 20) all patients but 2 achieved biventricular circulation (90%), a percentage similar to the data published by Schwartz (18/19, 95%) or Chen (26/31 84%) series.[13,25] Our 2 cases with non-biventricular circulation had a TV z-score of -3 but a normal PV z-score (-1.3 and +1.5, respectively). Chubb et al. reported that patients with early smaller TV and PV z-scores were less likely to achieve biventricular circulation.[4] Yoldaş reported PV z-score values > -1.7 and TV z-core values > -1 as good predictors of biventricular circulation in 31 neonates with PA/IVS treated with radiofrequency PV perforation.[18]

Limitations

The small sample of patients with PA/IVS from a single center limits the power to draw conclusions. Also, given the study retrospective nature, the definitive 2 groups (transjugular and transfemoral) were not balanced (16 vs 6 patients) since the transfemoral approach failed in 3 of these patients and had to be changed. This imbalance limits the inter-group comparison and prevents drawing more solid conclusions.

In addition, all transfemoral cases were performed within the first period, thus implying a potential "period time" bias also associated with the learning curve and the effect of evolving improvements in procedural materials and technique like the systematic echography-guided vessel puncture from 2018 or or the change of first option for additional flow source (ductal stenting instead of Blalock Taussig shunt) from 2012 through 2022.

CONCLUSIONS

Transcatheter mechanical PV perforation in patients with PA/IVS may be feasible in expert hands and is a reasonable alternative to heart surgery. Proper case selection appears to be key for transcatheter success. In our own experience, compared to the transfemoral approach, the transjugular one seems to simplify the procedure by reducing procedural and fluoroscopy times. However, new and larger prospective studies would be necessary to corroborate these findings.

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AUTHORS' CONTRIBUTIONS

M. Figueras Coll: study design and idea, data curation, image acquisition, statistical analysis, drafting of the manuscript, and final approval of the version that will be published eventually. He takes full responsibility for all aspects of this manuscript. A. Fidalgo García: study designa an idea, statistical analysis, collaboration drafting the manuscript, and final approval of the version that will be published eventually. He takes full responsibility for all aspects of this manuscript. G. Martí Aguasca: study design, image provision, collaboration drafting the manuscript, critical review of its content and intellectual interest, and final approval of the version that will be published eventually. He takes full responsibility for all aspects of this manuscript. P. Betrián Blasco: study idea and design, image provision, collaboration drafting the manuscript, critical review of its content and intellectual interest, and final approval of the version that will be published eventually. He takes full responsibility for all aspects of this manuscript.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THE TOPIC?

- Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare but serious cyanotic congenital heart disease. Over the past 2 decades, we have seen a move away from surgical right ventricular decompression to a more transcatheter-centered approach that has reduced mortality. However, not all cases with PA/IVS are eligible for transcatheter perforation. Therefore, proper case selection remains key for procedural success. In patients with no right ventricular dependent coronary circulation, mild or moderate RV hypoplasia and membranous (not muscular) pulmonary atresia, transcatheter PV perforation may be a valuable therapeutic option to achieve biventricular circulation.

WHAT DOES THIS STUDY ADD?

- As far as the authors know, this study is the first one to describe transjugular access to perforate the pulmonary valve in neonates with PA/IVS, and the proper anatomy. Also, it is the first to compare the results of transfemoral vs transjugular approach. Based on our own experience, the transjugular approach has proven safe and effective, simplifies the procedure, and reduces interventional and fluoroscopy times.

REFERENCES

1. Humpl T, Söderberg B, McCrindle BW, et al. Percutaneuos balloon valvotomy in pulmonary atresia with intact ventricular septum: impact on patient care. *Circulation.* 2003;108:826-832.
2. Agnoletti G, Piechaud JF, Bonhoeffer P, et al. Perforation of the atretic pulmonary valve. Long-term follow-up. *J Am Coll Cardiol.* 2003;41:1399-1403.
3. Qureshi SA. Catheterization in neonates with pulmonary atresia with intact ventricular septum. *Catheter Cardiovasc Interv.* 2006;67:924-931.
4. Chubb H, Pesonen E, Sivasubramanian S, et al. Long-term outcome following catheter vavlotomy for pulmonary atresia with intact ventricular septum. *J Am Coll Cardiol.* 2012;59:1468-1476.
5. Kim YH. Pulmonary valvotomy with echocardiographic guidance in neonates with pulmonary atresia and intact ventricular septum. *Catheter Cardiovasc Interv.* 2015;85:E123-8.
6. Wang Q, Wu YR, Zhang LN, et al. Evaluating the risk factors of reintervention of neonates with PA/IVS and CP/IVS after PBPV as initial intervention method. *J Cardiol.* 2016;68:190-195.
7. Wright LK, Knight JH, Thomas AS, Oster ME, St Louis JD, Kochilas LK. Long-term outcomes after intervention for pulmonary atresia with intact ventricular septum. *Heart.* 2019;105:1007-1013.
8. Kamalı H, Tanıdır İC, Erdem A, Sarıtaş T, Güzeltaş A. The Use of Chronic Total Occlusion (CTO) Wires for Perforation of Atretic Pulmonary Valve; Two Centers Experience. *Pediatr Cardiol.* 2021;42:1041-1048.
9. Li QZ, Cao H, Chen Q, Zhang GC, Chen LW, Chen DZ. Balloon valvuloplasty through the right ventricle: another treatment of pulmonary atresia with intact ventricular septum. *Ann Thorac Surg.* 2013;95:1670-1674.
10. Cho MJ, Ban KH, Kim MJ, Park JA, Lee HD. Catheter – based treatment in patients with critical pulmonary stenosis or pulmonary atresia with intact ventricular septum: a single institute experience with comparison between patients with and without additional procedure for pulmonary flow. *Congenit Heart Dis.* 2013;8:440-449.
11. Hasan BS, Bautista-Hernandez V, Mc Elhinney DB, et al. Outcomes of transcatheter approach for initial treatment of pulmonary atresia with intact ventricular septum. *Catheter Cardiovasc Interv.* 2013; 81:111-118.
12. Alwi M, Budi RR, Mood MC, Leong MC, Samion H. Pulmonary atresia with intact septum: the use of Conquest Pro coronary guidewire for perforation of atretic valve and subsequent interventions. *Cardiol Young.* 2013;23:197-202.
13. Schwartz MC, Glatz AC, Dori Y, Rome JJ, Gillespie MJ. Outcomes and predictors of reintervention in paitents with pulmonary atresia and intact ventricular septum treated with radiofrequency perforation and ballon pulmonary valvuloplasty. *Pediatr Cardiol.* 2014;35:22-29.
14. El Shedoudy S, El-Doklah E. Transcatheter perforation of atretic pulmonary valve by the stiff end of a coronary wire in neonates with pulmonary atresia with intact ventricular septum: A solution in developing countries. *J Saudi Heart Assoc.* 2018;30:222-232.
15. Hascoët S, Borrhomée S, Tahhan N, et al. Transcatheter pulmonary valvulplasty in neoantes with pulmonary atresia and intact ventricular septum. *Arch Cardiovasc Dis.* 2019;112:323-333.
16. Asnes JD, Fahey JT. Novel catheter positioning technique for atretic pulmonary valve perforation. *Catheter Cardiovasc Interv.* 2008;71:850-852
17. Morgan GJ, Narayan SA, Goreczny S, et al. A low threshold for neonatal intervention yields a high rate of biventricular outcomes in pulmonary atresia with intact ventricular septum. *Cardiol Young.* 2020;30:649-655.
18. Yoldaş T, Örün UA, Doğan V, et al. Transcatheter radiofrequency pulmonary valve perforation in newborns with pulmonary atresia/intact ventricular septum: Echocardiographic predictors of biventricular circulation. *Echocardiography.* 2020;37:1258-1264.
19. Haddad RN, Saliba Z. Optimal management of pulmonary atresia with intact ventricular septum in a developing country: the art of pulmonary valve mechanical perforation in the era of CTO hardware. *Am J Cardiovasc Dis.* 2021;11:21-28.
20. Bakhru S, Marathe S, Saxena M, et al. Transcatheter pulmonary valve perforation using chronic total occlusion wire in pulmonary atresia with intact ventricular septum. *Ann Pediatr Cardiol.* 2017;10:5-10.
21. Haddad RN, Hanna N, Charbel R, Daou L, Chehab G, Saliba Z. Ductal stenting to improve pulmonary blood flow in pulmonary atresia with intact ventricular septum and critical pulmonary stenosis after balloon valvuloplasty. *Cardiol Young.* 2019;29:492-498.
22. Rosenthal E, Qureshi SA, Chan KC, et al. Radiofrequency-assisted balloon dilatation in patients with pulmonary valve atresia and an intact ventricular septum. *Br Heart J.* 1993;69:347-351.
23. Marasini M, Gorrieri PF, Tuo G, et al. Long-term results of cathter-based treatment of pulmonary atresia and intact ventricular septum. *Heart.* 2009;95:1520-1524.
24. Rathgeber S, Auld B, Duncombe S, Hosking MC, Harris KC. Outcomes of radiofrequency perforation for pulmonary atresia and intact ventricular septum: A single-centre experience. *Pediatr Cardiol.* 2017;38:170-175.
25. Chen RHS, K T Chau A, Chow PC, Yung TC, Cheung YF, Lun KS. Achieving biventricular circulation in patients with moderate hypoplastic right ventricle in pulmonary atresia intact ventricular septum after transcatheter pulmonary valve perforation. *Congenit Heart Dis.* 2018;13:884-891.

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Debate: Revascularization of non-culprit lesions in ACS: physiology, OCT-guided or both? Perspective from physiology

A debate. Revascularización de lesiones no culpables en SCA. ¿Guiada por fisiología, por OCT o por ambas? Perspectiva desde la fisiología

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Question: What kind of evidence supports the use of the pressure guidewire for the management of nonculprit lesions in patients with multivessel disease? Can you explain to us the controversy surrounding the results of the most recent clinical trials compared to the former ones?

Answer: I would like to start by contextualizing the change of paradigm we've been experiencing regarding myocardial revascularization. In controlled clinical trials of stable coronary artery disease, compared to optimal medical therapy, unfortunately, myocardial revascularization—the percutaneous one (PCI) in particular—has not been able to reduce clinical events whether angiography-guided (COURAGE and BARI 2D trials) or guided by non-invasive ischemia detection studies (ISCHEMIA trial).[1] 1It is hard to believe that although there is a significant correlation between the degree of ischemia documented non-invasively and the risk of adverse events, revascularization based on the information that, as interventional cardiologists, we collecrt from non-invasive studies doesn't lead to better clinical outcomes compared to non-revascularizing the patient leaving him with ischemia and on optimal medical therapy. Here's where the use of the pressure guidewire (PG) during the procedure (and possibly its angiographic alternatives) seems to lead to a different outcome. Currently, 3 randomized clinical trials are being conducted—2 of them in patients with acute coronary syndrome (ACS)—comparing the clinical events associated with PG- and optimal medical therapy-guided myocardial revascularization alone. A recent metanalysis revealed that, compared to optimal medical therapy, PG-guided myocardial revascularization reduces the risk of cardiac death an infarction significantly at 5 years.[2] We should mention that this is a high-quality metanalysis that only included randomized clinical trials and «hard» events in its primary outcome. Also, unlike the ISCHEMIA trial that reported more early events associated with revascularization, fewer events were also documented in the PG arm from the beginning of follow-up and, as years went by, this event difference has grown favorable to revascularization. This and other information suggest that the PG allows us to select more accurately compared to angiography the segments of epicardial arteries where the benefits of PCI exceed risks.[3,4] This evidence has changed the clinical practice guidelines that now recommend the use of the PG for the lack of previous evidence of ischemia and when the use of revascularization is under consideration. However, although this recommendation has been effective for years, the clinical use of PG is still low worldwide.

Recently, some PG studies have shown neutral or negative results: the FUTURE, RIPCORD 2, FAME 3, and the FLOWER-MI.[4] Without smearing the effort made by the investigators, I'll try to share my view on these trials.

The FUTURE trial randomized patients with and without ACS and 2- or 3-vessel disease to routine or PG-guided revascularization.[3,4] The study was interrupted by the safety committee after only 54% of the entire sample was recruited and due to an increased overall mortality rate reported in the PG group. It is always difficult to interpret a study without statistical potential due to the sample size. However, the lack of differences in infarction and cardiac death makes it hard to explain how the PG can increase overall mortality through non-cardiac ways. Also, upon decision by the investigators, over 20% of negative lesions according to the PG were revascularized, which increased the number of procedures performed and stents used in the PG arm. This dropped the rate of revascularization down to 12.6% when, overall, in PG studies where a lower rate of stenting (30%) is often reported.

The RIPCORD-2 included 1100 patients with stable symptoms or ACS without ST-segment elevation randomized to angiography-guided revascularization or systematic use of the PG. The study concluded that the systematic use of the PG did not improve quality of life or reduced costs compared to the angiography-guided PCI.

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It's surprising to see how the PG was used in this study since, per protocol, PGs were used in all the arteries even in the absence of visible atherosclerosis. In my opinion, this is a complete game changer from the clinical use of PG, prolongs time, and increases risk without a clear justification. We still don't know if this proposal of using PG could be associated with the increased number of events seen at 1 year in the PG arm—close to 9%—which was high compared to many other PG studies. However, statistically, it was similar to the one seen in the angiography-guided PCI group of the same study.

There is nothing controversial about the FAME 3, I think. For years, we've been seeing the same slide in several meetings showing how the PG-related number of events from the FAME trial was similar to the number of events reported in the surgical arm of the SYNTAX trial. That's the origin of the FAME 3 that compared—with a non-inferiority design—PG-guided surgical to percutaneous revascularization for the management of 3-vessel disease. It was a disappointment to see that the PG-guided PCI is not inferior to surgery even accepting a large non-inferiority margin of 45%. Although the use of intracoronary imaging was low in the FAME 3, it's not easy to think of an image-guided PCI study reaching non-inferiority compared to surgery given the results of the recent FLAVOUR trial that assessed PG- vs intracoronary ultrasound-guided PCI. Similar clinical outcomes were seen with both strategies at the expense of a 30% increase in the number of stents from the image group.[5] We hope that, in the future, it'll tell us if the interventional strategy included in the SYNTAX II cohort (combining an optimal selection of patients with PG- and intracoronary imaging-guided PCI including total occlusions) is non-inferior to surgery in a controlled clinical trial.

Last but not least, the FLOWER MI trial.[6] In my opinion, it is the only one that suggests, in a convincing way, that safety is lower when decisions are based on PGs in patients with ST-segment elevation acute coronary syndrome (STEACS). In the FLOWER MI, a total of 1171 patients with STEACS were randomized to receive angiography- or PG-guided total revascularization after treating the culprit artery. Although the 1-year cumulative rate of the primary event did not change between both arms, a statistically non-significant increase in the risk of infarction (77% in the PG arm) was reported. Also, the estimated cut-off of the effect for the primary endpoint suggests PG-related damage and no benefit. Still, the accuracy of this effect estimate is low and non-significant.

Q.: What kind of evidence supports the use of the PG in nonculprit lesions of an ACS? Do you think it's strong enough to recommend it?

A.: Currently, 2 large metanalyses are being conducted including the evidence available on the use of PGs in nonculprit lesions, which is large. The first one conducted by Cerrato et al.[3] of 8579 patients from 5 different cohorts, 6461 of whom had stable symptoms and 2118 ACS.[3] A larger number of events was seen in the group of patients with PG-guided delayed revascularization with ACS compared to the group of patients in stable condition. However, and significantly, patients with ACS treated with PCI had more events compared to patients with ACS and PG-guided delayed treatment. This study suggests that safety of PG-guided delayed PCI depends on the clinical presentation being safer with stable symptoms compared to ACS. Also, that treating nonculprit lesions doesn't reduce the chances of events compared to delaying the procedure unlike what the FLOWER-MI reported. We should mention that this metanalysis could not distinguish STEACS from other forms of ACS, which is why it should be interpreted in detail.

The second metanalysis is important because it compares all randomized clinical trials currently available on 3 strategies for nonculprit lesion revascularization proposed for patients with STEACS: culprit lesion only revascularization, angiography- and PG-guided total revascularization.[4] A total of 8195 patients from 11 randomized clinical trials were included. It was reported that in patients with multivessel disease and STEACS, angiography- or PG-guided total revascularization is associated with a lower rate of adverse events compared to the strategy of revascularizing the culprit lesion only. Also, the PG-guided strategy was associated with a non-significant increased risk of adverse events of 23% (95% confidence interval, 0.78-1.94) compared to the angiography-guided total revascularization strategy. Therefore, in the management of STEACS, angiography-guided total revascularization strategy is far more superior compared to the culprit lesion-only revascularization and similar to PG-guided revascularization. However, the effect estimate of the last comparison is favorable to the total angiography strategy.

Q.: Are there any differences based on the type of ACS with or without ST-segment elevation?

A.: This is not an easy question to answer because most studies report combined data of ACS without stratifying STEACS and NSTEACS.[2,3,4] What we know so far is that the current evidence that has generated controversy comes specifically from patients with STEACS. This is consistent with the maturity of multiple lines of research that suggest that the nonculprit lesions of patients with STEACS behave more aggressively compared to the same lesions in patients with stable symptoms. We should remember that, overall, PG-related non-significant lesions in stable disease are responsible for 3% to 4% of clinical events per year while contemporary stents are responsible for an annual 6%. Therefore, if treated, we could be inducing damage. However, non-significant lesions according to the PG in patients with STEACS seem to cause more events—with rates close to 8%—like a substudy of the FLOWER-MI suggests.[7] Therefore, any procedure performed here may be associated with more benefits than risks. Therefore, the utility of PG specifically in STEACS seems lower. Finally, we should mention that the results of the COMPLETE and FLOWER MI trials cannot be extrapolated to the STEACS setting. Also, there are many more studies supporting the utility of the PG in this scenario. Therefore, until future studies with robust designs analyze the safety profile of PG to treat NSTEACS, we won't be able to determine whether safety is closer to the one reported in the stable context or discretely lower, as in the case of STEACS.

Q.: Are there any differences based on the type of index, whether hyperemic or not?

A.: The differences between hyperemic and non-hyperemic indexes does not seem to be very significant from the clinical standpoint. However, when we migrate from clinical trials to physiological indexes (that report, in small series, their findings from combined measurements of pressure and intracoronary flow) it's hard to determine what indexes are better diagnostic tool in the ACS setting since results are controversial. Therefore, there seems to be greater scientific consensus recognizing a transient fatigue of hyperemic response compared to recognizing significant changes to the baseline conditions. This transient fatigue of hyperemic response is characterized by a reduced coronary flow reserve and an increased coronary fractional flow reserve, a situation that could clinically produce more false negatives with hyperemic compared to non-hyperemic indexes.[8] Despite of all this, currently, there are no solid arguments to prefer hyperemic over non-hyperemic indexes.

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CONFLICTS OF INTEREST

M. Echevarría-Pinto is speaker and proctor for manufacturers of pressure guidewires (BSC, Abbot, and Philips).

REFERENCES

1. Mavromatis K, Boden WE, Maron DJ, et al. Comparison of Outcomes of Invasive or Conservative Management of Chronic Coronary Disease in Four Randomized Controlled Trials. *Am J Cardiol*. 2022;185:18-28.
2. Zimmermann FM, Omerovic E, Fournier S, et al. Fractional flow reserve-guided percutaneous coronary intervention vs. medical therapy for patients with stable coronary lesions: meta-analysis of individual patient data. *Eur Heart J*. 2019;40:180-186.
3. Cerrato E, Mejía-Rentería H, Dehbi HM, et al. Revascularization Deferral of Nonculprit Stenoses on the Basis of Fractional Flow Reserve: 1-Year Outcomes of 8,579 Patients. *JACC Cardiovasc Interv*. 2020;13:1894-1903.
4. Elbadawi A, Dang AT, Hamed M, et al. FFR- Versus Angiography-Guided Revascularization for Nonculprit Stenosis in STEMI and Multivessel Disease: A Network Meta-Analysis. *JACC Cardiovasc Interv*. 2022;15:656-666.
5. Koo BK, Hu X, Kang J, et al. Fractional Flow Reserve or Intravascular Ultrasonography to Guide PCI. *N Engl J Med*. 2022;387:779-789.
6. Puymirat E, Cayla G, Simon T, et al. Multivessel PCI Guided by FFR or Angiography for Myocardial Infarction. *N Engl J Med*. 2021;385:297-308.
7. Denormandie P, Simon T, Cayla G, et al. Compared Outcomes of ST-Segment-Elevation Myocardial Infarction Patients With Multivessel Disease Treated With Primary Percutaneous Coronary Intervention and Preserved Fractional Flow Reserve of Nonculprit Lesions Treated Conservatively and of Those With Low Fractional Flow Reserve Managed Invasively: Insights From the FLOWER-MI Trial. *Circ Cardiovasc Interv*. 2021;14:e011314.
8. van der Hoeven NW, Janssens GN, de Waard GA, et al. Temporal Changes in Coronary Hyperemic and Resting Hemodynamic Indices in Nonculprit Vessels of Patients With ST-Segment Elevation Myocardial Infarction. *JAMA Cardiol*. 2019;4:736-744.

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Debate. Revascularization of nonculprit lesions in ACS: physiology or OCT-guided or both? Perspective from imaging

A debate. Revascularización de lesiones no culpables en SCA. ¿Guiada por fisiología, por OCT o por ambas? Perspectiva desde la imagen

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Question: What is the benefit of intravascular imaging modalities—specifically the optical coherence tomography (OCT)—in the context of nonculprit lesions of an acute coronary syndrome (ACS)?

Answer: The publications of the COMPLETE and FLOWER MI clinical trials has changed the management of nonculprit lesions tremendously in patients with ACS jeopardizing the role of the pressure guidewire guiding the revascularization of these lesions.[1,2] In the COMPLETE trial, angiography-guided complete revascularization reduced the rates of death and infarction compared to the optimal medical therapy (OMT).[1] We should mention that over 80% of the lesions included had an angiographic percent diameter stenosis ≥ 70%.[1] In the FLOWER MI trial that included less severe nonculprit lesions, pressure guidewire-guided complete revascularization reduced the number of lesions treated (45% fewer lesions) compared to angiography-guided complete revascularization with a similar rate of events in both strategies.[2] However, a subanalysis of the group of patients treated with pressure guidewire guidance revealed that patients with fractional flow reserve (FFR) values ≤ 0.80 (stented according to protocol) had fewer events compared to patients with FFR values > 0.80 (treated with OMT).[3] This has aroused controversy regarding the utility of the pressure guidewire in this context. Probably the reason why the FFR has such a low negative predictive value is the lack of information on the composition of the plaque of the target lesion. In a subanalysis of the COMPLETE trial where nonculprit lesions were treated with OCT, it was reported that > 35% of the lesions with stenosis ≥ 70% were classified as vulnerable plaques compared to 25% of intermediate lesions (stenosis between 50% and 69%).[4]

Vulnerable plaques include a high lipidic content and are covered by a thin fibrous layer (≤ 65 µm according to pathological anatomy, which corresponds to ≤ 80 µm according to OCT if the axial resolution of this technique is taken into consideration).[5] According to the PROSPECT clinical trials, the use of intracoronary ultrasound and infrared spectroscopy can detect vulnerable plaques in nonculprit coronary arteries in patients with ACS, and the former are associated with a high risk of triggering ACS at 4-year follow-up (up to 18% if they had a minimum lumen area and a large plaque burden).[6,7]

The role of OCT to detect vulnerable plaques in nonculprit lesions of ACS is still to be elucidated. However, since this intravascular imaging modality provides the highest resolution of all, it is probably the best imaging modality to assess the morphological characteristics of these lesions, particularly if they show signs of vulnerability.

Q.: How would you introduce the OCT in the assessment protocol of these lesion in relation to the pressure guidewire?

A.: In my opinion, the use of diagnostic intracoronary imaging modalities (whether with guidewire pressure or intravascular images) in severe nonculprit lesions (with percent diameter stenosis ≥ 70%) is not currently justified. Like I said before, severe nonculprit lesions on the angiography have high chances of being vulnerable plaques and, if untreated, are associated with a larger number of adverse events.[1,4] As a matter of fact, with a level of evidence IA, the recent clinical practice guidelines from the American College of Cardiology and the American Heart Association published following the COMPLETE and FLOWER-MI trials recommend the revascularization of nonculprit lesions of ST-segment elevation ACS (STEACS) with percent diameter stenosis ≥ 70% on the angiography.[8]

However, the role these diagnostic intracoronary imaging modalities play in intermediate lesions (stenosis between 40% and 69%) or even in angiographic segments without overt angiographic lesion is still to be elucidated. An early assessment of intermediate

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lesions with FFR through pressure guidewire allows us to select those lesions that, *per se*, trigger ischemia. According to former studies on this type of intermediate lesions, nearly 45% of them show FFR values ≤ 0.80 and, therefore, have an indication for revascularization.[2,9] As a matter of fact, the positive predictive value of FFR values ≤ 0.80 is not discussed here, and the management of lesions with pathological FFR values is currently backed by the routine clinical practice guidelines with a level of evidence IA.[8,10] In my opinion, the utility of the OCT should be reviewed in lesions that don't trigger ischemia (like lesions with FFR values > 0.80) and when the management of nonculprit lesions is purely preventive.

Up until now, only 1 study has assessed the preventive treatment of nonculprit lesions with characteristics of vulnerability. The PROSPECT-ABSORB trial randomized nonculprit lesions with characteristics of vulnerability on the intravascular echocardiography to receive bioresorbable stents or OMT. In this trial, the preventive treatment of vulnerable plaques reduced the rates of events compared to treatment although the study was not designed to compare clinical events.[11]

Q.: In your opinion, what will the future bring, new protocols combined? maybe new techniques?

A.: The risk associated with a vulnerable plaque in patients with multivessel ACS is currently under study and discussion. After an infarction, over 50% of the ischemic events described at follow-up are due to nonculprit lesions.[7] The Spanish Society of Cardiology Working Group on Intracoronary Diagnosis of the Interventional Cardiology Association has inspired a randomized clinical trial that will include over 40 Spanish centers. The VULNERABLE trial (NCT 05599061) will study nearly 2500 patients with STEACS and angiographically intermediate nonculprit lesions (angiographic percent diameter stenosis between 40% and 69%). Per protocol, these lesions will be studied in an elective procedure different from the index procedure with which the culprit lesion was treated successfully. All eligible lesions will be interrogated using the pressure guidewire, and those with pathological FFR values (≤ 0.80) will be stented and considered a selection failure (it is estimated that nearly 40% of the lesions studied). The remaining lesions (1500 approximately) with FFR values > 0.80 will be studied with the OCT looking for characteristics of vulnerability. Lesions without these characteristics (an estimate of 900 lesions) will be treated with OMT and periodically followed to assess adverse events (within the VULNERABLE Registry). Finally, the study will include a total of 600 lesions with negative FFR but with characteristics vulnerability on the OCT that will be randomized (1:1) to stenting or OMT (within the VULNERABLE clinical trial). The follow-up period scheduled for both registry patients and the clinical trial is 4 years. This is the first trial ever conducted with statistical power to assess the clinical effectiveness of preventive stenting of nonculprit lesions with characteristics of vulnerability according to the OCT.

Q.: How would you bring together the concepts of vulnerable plaque and vulnerable patient?

A.: In my opinion, patients with ACS have 3 different problems occurring simultaneously. First, like I mentioned before, they have a type of aggressive atherosclerosis with significant plaque burden and characteristics of vulnerability.[4] Second, patients with ACS have a higher degree of microvascular dysfunction, not only in the infarct-related artery but also in other nonculprit arteries.[12] Pancoronary microvascular dysfunction is probably associated with a higher sensitivity to the chronic ischemia due to epicardial obstructive coronary lesions and the inability to create collateral circulation in the presence of a new acute complete obstruction (therefore associated with a higher risk of infarction). And third, patients with ACS have elevated inflammatory markers, more platelet reactivity, and more thrombogenicity compared to chronic patients.[13] As a matter of fact, anti-inflammatory treatments have proven capable of reducing adverse events in patients with ACS.[14]

Therefore, patients with ACS have anatomical, functional, and systemic inflammatory-thrombotic characteristics that clearly separate them from chronic patients. This differentiation is mainly based on a higher risk of new thrombotic events in the future. Some, actually, call them «vulnerable patients». The management of these «vulnerable» patients should address these 3 problems at the same time. Therefore, therapeutic advances are necessary to reduce the plaque burden and stabilize vulnerable plaques. Also, antiplatelet therapies to reduce ischemic risk, at least, until most vulnerable plaques have stabilized, and eventually therapies to reduce systemic inflammation and, probably, improve the endothelial function of these patients.

The role of preventive angioplasty with stenting in vulnerable plaques is still to be elucidated. Undoubtedly, one of the dilemmas we'll have to elucidate in the future is whether to choose intensive medical therapy with new drugs capable of stabilizing vulnerable plaques or «stabilization sealing» of neointimal tissue layer induced by stenting plus OMT.

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CONFLICTS OF INTEREST

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REFERENCES

1. Mehta SR, Wood DA, Storey RF, et al. Complete Revascularization with Multivessel PCI for Myocardial Infarction. *N Engl J Med.* 2019;381:1411-1421.
2. Puymirat E, Cayla G, Simon T, et al. Multivessel PCI Guided by FFR or Angiography for Myocardial Infarction. *N Engl J Med.* 2021;385:297-308.
3. Denormandie P, Simon T, Cayla G, et al. Compared Outcomes of ST-Elevation Myocardial Infarction Patients with Multivessel Disease Treated with Primary Percutaneous Coronary Intervention and Preserved Fractional Flow Reserve of Non-Culprit Lesions Treated Conservatively and of Those with Low Fractional Flow Reserve Managed Invasively: Insights from the FLOWER MI trial. *Circ Cardiovasc Interv.* 2021;14:e011314.
4. Pinilla-Echeverri N, Mehta SR, Wang J, et al. Nonculprit Lesion Plaque Morphology in Patients With ST-Segment-Elevation Myocardial Infarction: Results From the COMPLETE Trial Optical Coherence Tomography Substudys. *Circ Cardiovasc Interv.* 2020;13:e008768.
5. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol.* 2006;47:C13-18.
6. Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med.* 2011;364:226-235.
7. Erlinge D, Maehara A, Ben-Yehuda O, et al. Identification of vulnerable plaques and patients by intracoronary near-infrared spectroscopy and ultrasound (PROSPECT II): a prospective natural history study. *Lancet.* 2021;397:985-995.
8. 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.
9. Koo BK, Kang J, Wang J. Fractional Flow Reserve or Intravascular Ultrasound for PCI. Reply. *N Engl J Med.* 2022;387:2099.
10. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2019;40:87-165.

11. Stone GW, Maehara A, Ali ZA, et al. Percutaneous Coronary Intervention for Vulnerable Coronary Atherosclerotic Plaque. *J Am Coll Cardiol.* 2020; 76:2289-2301.
12. van de Hoef TP, Bax M, Meuwissen M, et al. Impact of coronary microvascular function on long-term cardiac mortality in patients with acute ST-segment-elevation myocardial infarction. *Circ Cardiovasc Interv.* 2013;6:207-215.
13. Matsuo K, Ueda Y, Nishio M, et al. Thrombogenic potential of whole blood is higher in patients with acute coronary syndrome than in patients with stable coronary diseases. *Thromb Res.* 2011;128:268-273.
14. Tardif JC, Kouz S, Waters DD, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. *N Engl J Med.* 2019;381: 2497-2505.

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Early experience with the FlowTriever thrombectomy system to treat pulmonary embolism

Experiencia inicial de trombectomía con FlowTriever en embolia aguda de pulmón

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To the Editor,

Catheter-directed therapy is indicated in high-risk patients (PE-HR) to treat pulmonary embolism (PE) when systemic thrombolysis is contraindicated or has failed (indication IIA, C). Also, as a bailout therapy in intermediate/high-risk patients (PE-IHR) with hemodynamic impairment as an alternative to systemic thrombolysis (indication IIA, C).[1] However, clinical practice guidelines do not specify which is the optimal catheter-directed therapy that should be used. It can be local thrombolysis that consists of the direct infusion of variable doses (around 20% of systemic dose) of thrombolytic drugs (alteplase or tenecteplase) into the pulmonary artery (intra-thrombus) or else mechanical thrombectomy with direct aspiration catheter that consists of thrombus extraction (with or without previous fragmentation). Finally, a mechanical-pharmacological strategy with both techniques combined can be used sequentially.[2]

This is the early experience of mechanical thrombectomy with direct aspiration using the FlowTriever retrieval/aspiration system (Inari, United States) of 4 Spanish and Portuguese centers. The Hospital Clínico San Carlos ethics committee approved the registry and obtained the participants' written informed consent. The FlowTriever is a 24-Fr thrombus aspiration system with an oversized tube and accessories to optimize thrombus extraction.[3,4] These are 3 cases of PE-HR with contraindication for systemic thrombolysis and 7 cases of PE-IHR treated at centers experienced in catheter-directed therapy, but not with this specific device, whose distribution in these countries started back in 2022. Clinical and procedural characteristics are shown on table 1. Procedure was performed on a mean of 25.7 ± 23 hours since diagnosis. Procedures were successful in 100% of the cases (defined as catheter navigation towards the pulmonary artery with extraction of thrombotic material and no procedural deaths or complications reported) with obtention of abundant thrombus as shown on figure 1. Drug therapy consisted of low molecular weight heparin in 4/10 cases, sodium heparin in 4/10 cases, and no anticoagulation in 2. Fibrinolytic agents were not used in any patients. Access route was femoral in all the cases (24-Fr) with vascular closure in 4/10 (1 Perclose Proglide Abbott Vascular device, United States), figure-of-eight suture in 4/10, and manual compression in 2/10. No vascular access complications were reported. Hemodynamic parameters improved after the procedure as shown on table 1. The volume of blood drawn is significant, and 2/3 of the patients from the PE-HR group required transfusion during admission. Probably after the learning curve the volume should be smaller (in the FLASH cohort, the mean volume was 255 mL.[4]) Additionally, the FlowTriever system has a

Table 1. Clinical and procedural data

Preoperative clinical data (N = 10)		
Age	57.3 ± 16.1	
Woman	60%	
Past medical history of VTED	30%	
Elevated troponin levels	100%	
Venous lactate at admission (mmol/L)	3.01 ± 1.9	
Inotropic support	60%	
Ultrasound and hemodynamic parameters	**Pre-CDT**	**Post-CDT**
RV/LV ratio > 0.9	100%	20%
TAPSE	12.6 ± 3.5	19 ± 34
Systemic systolic pressure	107 ± 24	138 ± 23
Heart rate (bpm)	114 ± 16	95 ± 11
Pulmonary systolic pressure (mmHg)	51 ± 8	37 ± 12
Other procedural data		
Contrast (mL)	156 ± 77	
Aspirated volume (mL)	396 ± 167	
Procedural time (min)	126 ± 52	

CDT, catheter-directed therapy; LV, left ventricle; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; VTED, venous thromboembolic disease.

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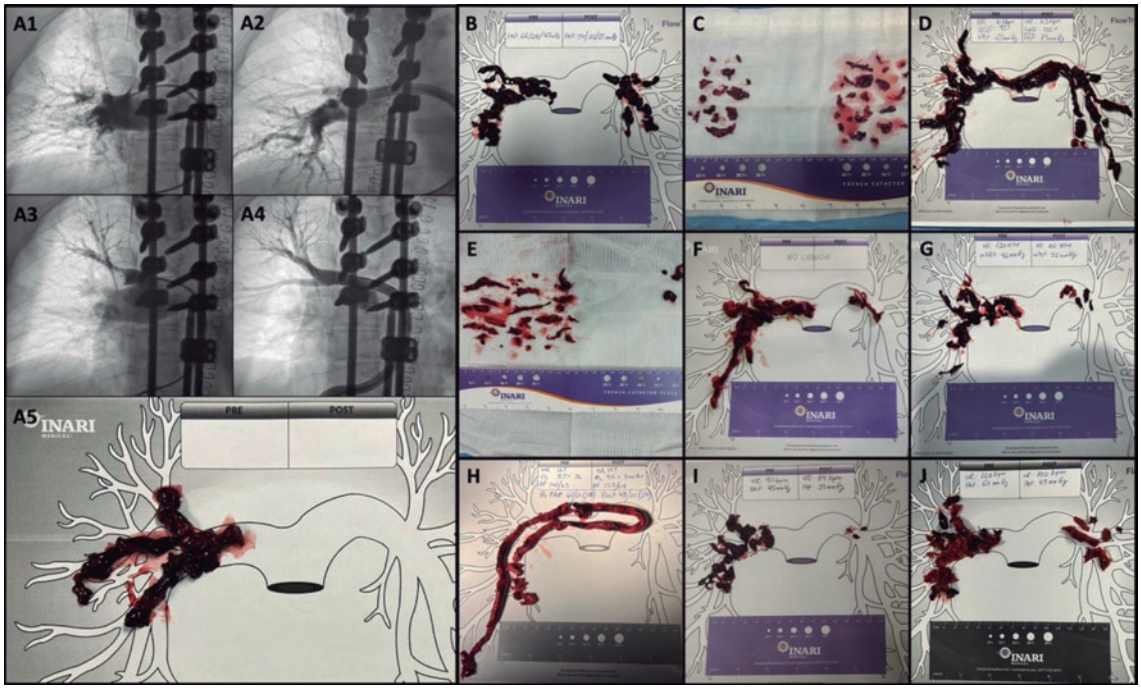

Figure 1. **A:** case #1 from Hospital General Universitario Gregorio Marañón. Sub-selective angiographies before **(A1/A3)** and after **(A2/A3)** the catheter-directed therapy, and material obtained **(A5). B** to **D:** material obtained in the cases from Hospital General Universitario Gregorio Marañón. **E** and **F:** cases from Hospital Clínico San Carlos. **G** and **H:** cases from Hospital La Paz. **I** and **J:** cases from Centro Hospitalar de Lisboa Ocidental.

filter capable of returning most of the aspirated blood— thrombus-free—back to the patient. However, this version is still not available in Europe.

The composite endpoint of major adverse events used in large registries consists of device-related death, major bleeding (Bleeding Academic Research Consortium type ≥ 3b) or procedure or device-related adverse events.[4] In our case series 1 major adverse event in 1 procedure was reported: a stroke within the first 24 hours after the procedure due to paradoxical embolism. The presence of patent foramen ovale was confirmed during the procedure due to the crossing of the guidewire towards the left atrium. It is not possible to determine whether the embolism could have been triggered by the manipulation with the guidewire inside the atrium or whether it could have happened spontaneously. The patient recovered and was discharged 9 days after the procedure. Among the cases of PE-HR, 1 patient improved rapidly, and a second one remained in shock with distributive component in the immediate postoperative setting (< 24 h) and improved late with hospital discharge. The third one was admitted after an out-of-hospital cardiac arrest and died due to post-anoxic encephalopathy (the only case of in-hospital death considered unrelated to the procedure). Therefore, mortality 1/3 in the PE-HR and PE-IHR groups was 1/3 and 0/7, respectively. No additional adverse events or readmissions have been reported at 30-day follow-up in any of the patients.

Early diagnosis, risk stratification, and knowledge of these invasive therapies performed by interventional radiologists or cardiologists can contribute to improving the patients' prognoses. Coordination from response teams to PE to optimize workflow and the decision-making process is of paramount importance.[1] Reproducibility, efficacy and, safety are always sought at the dawn of interventional techniques. In a meta-analysis of ultrasound-facilitated local thrombolysis of 2135 patients, efficacy was described as reduced radiographic thrombus loads and ventricular diameters with rates of major bleeding > 5.4%.[5] In contemporary studies on mechanical thrombectomy with aspiration with specific devices, a similar efficacy has been described. However, the rates of major bleeding are lower: 1.7% with the Indigo system (Penumbra, United States) in 119 patients,[6] and 1.2% with the FlowTriever system (Inari, Estados United States) in 250 patients.[4] Therefore, since comparative studies like the PEERLESS trial (NCT05111613) are lacking, mechanical thrombectomy with aspiration seems to offer similar results with a lower bleeding risk. Our early experience with the device confirms that the proper description of the technique and proctoring training during the case can shorten the learning curve significantly. In this early experience, we managed to replicate the results of efficacy and safety previously reported with this promising device for the interventional management of PE.

FUNDING

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AUTHORS' CONTRIBUTIONS

P. Salinas: study idea, supervision, investigation, formal analysis, and drafting of the original manuscript. M.E. Vázquez-Álvarez: investigation, data management, review, and edition of the manuscript. A. Jurado-Román: investigation, data management, review, and edition of the manuscript. S. Leal: investigation, data management, review, and edition of the manuscript. M. Huanca: investigation, data management, review, and edition of the manuscript.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J*. 2020;41:543-603.
2. Salinas P. A debate: Terapia farmacológica o invasiva en la tromboembolia pulmonar aguda. Perspectiva del intervencionista. *REC Interv Cardiol*. 2022;4:240-242.
3. Salinas P, Real C, Fernández-Ortiz A. Tromboaspiración con sistema FlowTriever en embolia pulmonar aguda. *Med Clin*. 2022;159:154.
4. Toma C, Bunte MC, Cho KH, et al. Percutaneous mechanical thrombectomy in a real-world pulmonary embolism population: Interim results of the FLASH registry. *Catheter Cardiovasc Interv*. 2022;99:1345-1355.
5. Pei DT, Liu J, Yaqoob M, et al. Meta-Analysis of Catheter Directed Ultrasound-Assisted Thrombolysis in Pulmonary Embolism. *Am J Cardiol*. 2019;124:1470-1477.
6. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. *JACC Cardiovasc Interv*. 2021;14:319-329.

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First experience in Spain with PiCSO therapy in patients with acute myocardial infarction

Primera experiencia en España con el sistema PiCSO en pacientes con infarto agudo de miocardio

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To the Editor,

Myocardial infarction is the leading cause of morbidity and mortality in our setting. Percutaneous coronary intervention has improved the prognosis of patients with ST-segment elevation myocardial infarction (STEMI).[1] However, there is a subgroup of patients who suffer from suboptimal myocardial reperfusion with appearance of myocardial fibrosis, ventricular dysfunction, and development of heart failure.[2]

Recently, several pharmaceutical and procedural strategies have been developed to improve these results.[3] The PiCSO system (Pressure-controlled intermittent coronary sinus occlusion) developed by Miracor Medical SA, Belgium consists of a balloon catheter to occlude the coronary sinus periodically:

1) During the occlusion stage (5 to 15 s), venous flow is redistributed from well perfused areas towards ischemic regions through the formation of collateral circulation. Also, through an increased venous systolic pressure, the plasma skimming phenomenon allows better perfusion of venules with oxygen-and-metabolite-rich plasma.

2) During the release stage (3 to 4 s) the dramatic drop of venous pressure creates a gradient that ends up clearing all thrombotic debris, toxic metabolites, and myocardial edema.

3) These pressure variations can induce mechanotransduction by activating vascular cells and releasing growth factors, vasodilator substances, and microRNA into microcirculation (figure 1).

The PiCSO system has proven capable of improving microvascular function and reducing the infarction size in non-randomized clinical trials of patients with high-risk anterior STEMI.[4] As a matter of fact, it was granted the CE marking in 2020 with a clinical indication for the management of anterior STEMI with < 12-hour evolution and early TIMI grade 0-1 flow (Thrombolysis in Myocardial Infarction) and culprit lesion in the proximal or middle segments of the left anterior descending coronary artery. We wish to use this scientific letter to share our experience with this novel device in 2 case reports. The patients' informed consent was obtained, and the study was approved by the ethics committee according to the principles set forth in the Declaration of Helsinki.

The first case is a 83-year-old man without a past medical history of interest with thoracic pain and anterior ST-segment elevation of 3 mm in V1-V4 on the electrocardiogram. The coronary angiography revealed the presence of an acute thrombotic occlusion in the proximal segment of the left anterior descending coronary artery with early TIMI grade-0 flow (figure 2A). Thrombus aspiration and drug-eluting stent implantation led to TIMI grade-3 flow after 115 min of total ischemia (figure 2B). Since this was a large anterior STEMI

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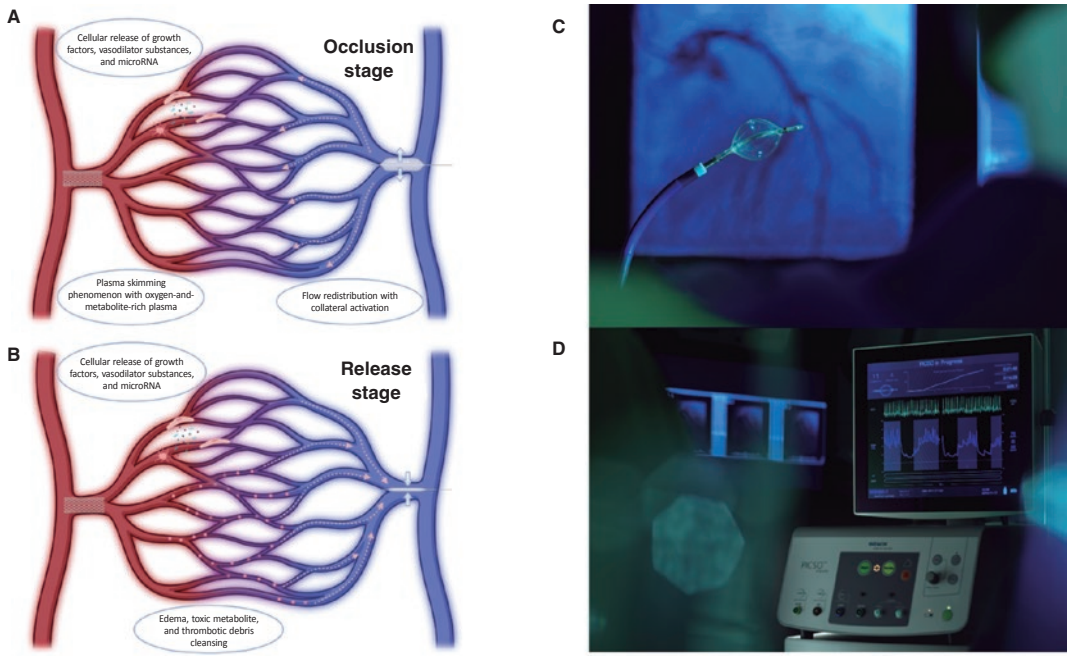

Figure 1. Representation of the mechanism of action of the PiCSO system in the occlusion (**A**) and release stages (**B**). The PiCSO system includes a balloon catheter (**C**) connected to a console (**D**) to automatically occlude the coronary sinus intermittently.

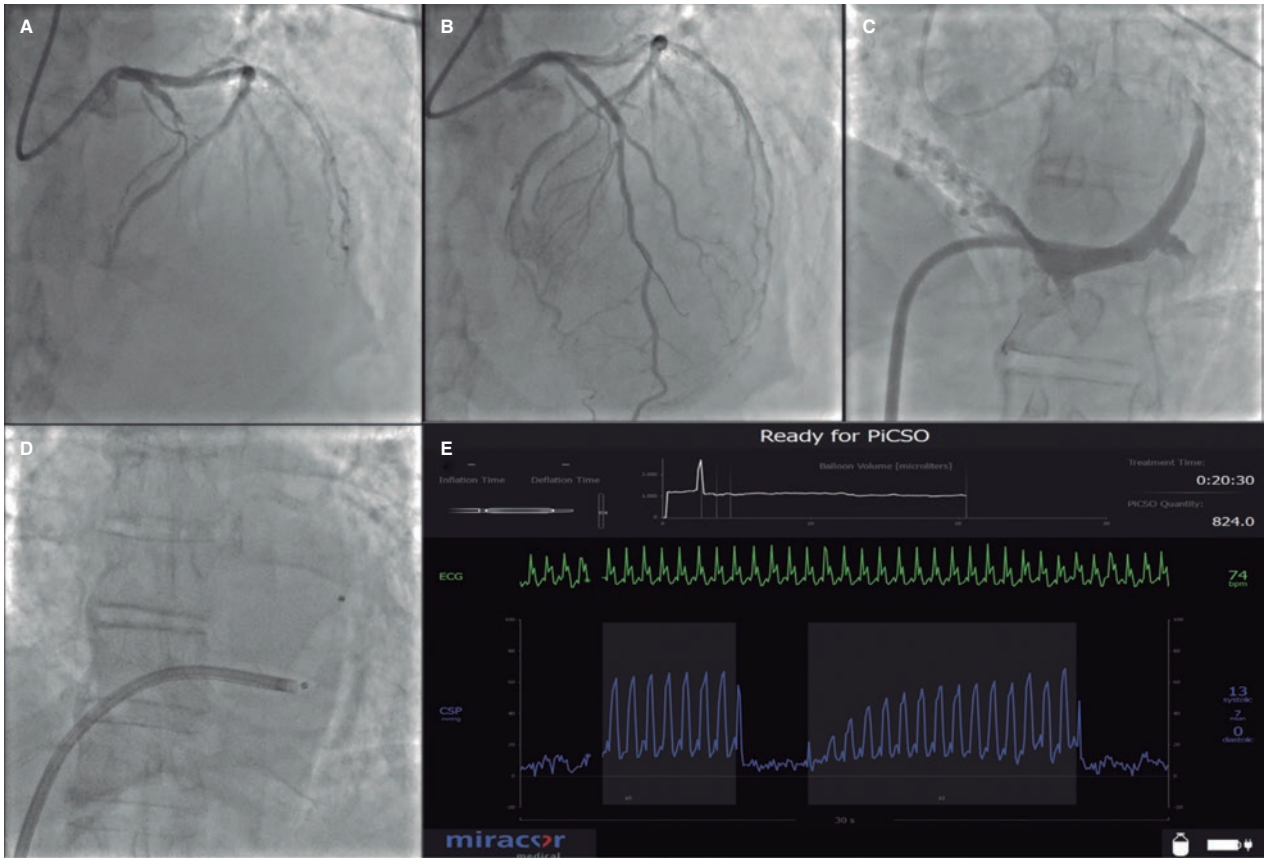

Figure 2. Coronary angiography showing an acute thrombotic occlusion in the proximal left anterior descending coronary artery (**A**). Coronary flow recovery after thrombus aspiration and stenting (**B**). Afterwards, via right femoral vein (12-Fr), a 8.5-Fr Destino Reach introducer sheath (Oscor, United States) was used for cannulation (**C**) and the PiCSO balloon catheter was implanted in the coronary sinus (**D**). The console (**E**) shows charts with information on coronary sinus pressures and an algorithm to estimate the dose of PiCSO in mmHg—which is a reference of the performance of PiCSO—based on inflation time, the coronary sinus maximum pressure in systole and diastole, and the mean pressure during the release stage.

with early TIMI grade-0 flow, right femoral venous access, cannulation (figure 2C), and PiCSO balloon catheter implantation in the coronary sinus were used (figure 2D) with a 21 min therapy time, and PiCSO doses of 824 mmHg (values > 800 mmHg are advised since they are associated with a reduced infarction size in former studies)[4] (figure 2E). The first electrocardiogram revealed a left ventricular ejection fraction (LVEF) of 30% with peak troponin levels of 197 419 ng/L. The patient was discharged without any signs of angina or heart failure and a LVEF of 35% to 40% at 7 days.

The second case was a 67-year-old man, active smoker, who had sustained a cardiac arrest due to ventricular fibrillation with recovered circulation 25 min after starting cardiopulmonary resuscitation. The electrocardiogram confirmed the presence of anterior ST-segment elevation of 20 mm in V1-V4, and the coronary angiography the presence of acute thrombotic occlusion in the middle segment of the left anterior descending coronary artery (TIMI grade-0 flow). Thrombus aspiration and drug-eluting stent implantation led to TIMI grade-3 flow (total ischemia time, 120 min). Since this was also a high-risk anterior STEMI, it was decided to implant the PiCSO system in the coronary sinus via right femoral vein with a 20 min therapy time and a PiCSO dose of 830 mmHg. The first electrocardiogram showed a LVEF of 35% and peak troponin levels of 63 141 ng/L. The patient neurological and cardiologic progression was good. The patient's LVEF was 55% 10 days after the infarction.

The PiCSO system is a safe and easy to implement tool in the management of STEMI. However, PiCSO will have to demonstrate its efficacy in ongoing randomized trials.

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AUTHORS' CONTRIBUTIONS

S. Brugaletta, and P. Vidal-Calés participated in the manuscript idea, design, and data analysis. O Abdul-Jawad Altisent, F. Spione, V. Arévalos, and M.Sabaté reviewed and edited the manuscript.

CONFLICTS OF INTEREST

None reported.

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REFERENCES

1. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39:119-177.
2. Stone GW, Selker HP, Thiele H, et al. Relationship Between Infarct Size and Outcomes Following Primary PCI: Patient-Level Analysis From 10 Randomized Trials. *J Am Coll Cardiol.* 2016;67:1674-1683.
3. Vidal-Calés P, Cepas-Guillén PL, Brugaletta S, Sabaté M. New Interventional Therapies beyond stenting to Treat ST-Segment Elevation Acute Myocardial Infarction. *J Cardiovascular Dev Dis.* 2021;8:100.
4. De Maria GL, Alkhalil M, Borlotti A, et al. Index of microcirculatory resistance-guided therapy with pressure-controlled intermittent coronary sinus occlusion improves coronary microvascular function and reduces infarct size in patients with ST-elevation myocardial infarction: the Oxford Acute Myocardial Infarction - Pressure-controlled Intermittent Coronary Sinus Occlusion study (OxAMI-PICSO study). *EuroIntervention.* 2018;14:e352-e359.

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Coronary thrombus after cannabis consumption: the important role of intracoronary imaging modalities

Trombo coronario tras consumo de cannabis: la importancia de la imagen intracoronaria

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To the Editor,

Acute myocardial injury in young adults may be a challenging finding. Although coronary artery disease associated with traditional cardiovascular risk factors is possible, other etiologies like the use of recreational drugs, myocarditis, coronary embolism, spontaneous coronary artery dissection or coronary vasospasm should be considered as well.[1] Intracoronary imaging modalities provide diagnostic information added to invasive coronary angiography on coronary lesion features, and are useful to guide percutaneous coronary interventions.[2]

This is the case of a 29-year-old male patient with a history of smoking. His family history included coronary artery disease, but not at a young age. The patient presented to the emergency room with signs of acute chest pain radiating down his left arm the morning following a night of heavy alcohol and cannabis consumption.

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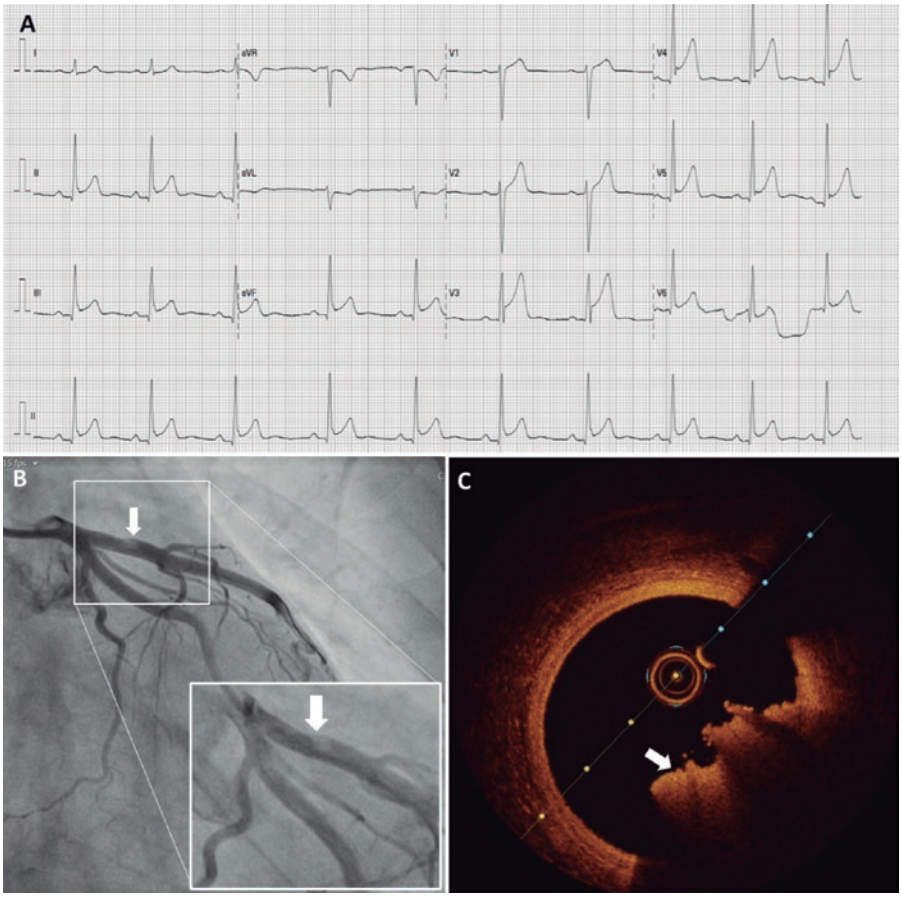

Figure 1. A: first 12-lead electrocardiogram. **B:** invasive coronary angiography of left main coronary artery with zoomed-in image of the filling defect. **C:** optical coherence tomography imaging of the same lesion showing a red thrombus.

The 12-lead electrocardiogram revealed sinus rhythm, heart rate of 60 beats per minute, and slight and diffuse ST-segment elevation (figure 1A). Blood biochemistry analysis revealed elevated troponin I levels (37.6 ng/mL; normal values < 0.045 ng/mL). The transthoracic echocardiogram revealed the presence of preserved left ventricular systolic function with normal heart wall motion kinetics, and no evidence of structural heart disease.

Although the early suspected diagnosis was myopericarditis, and the patient was already pain-free, he was referred for elective invasive coronary angiography—via right radial artery—24 hours after hospital admission. We first visualized a dominant right coronary artery with no significant disease. Afterwards, the left main coronary artery angiography showed no significant disease on either the left main or circumflex arteries, but a small filling defect in the proximal segment of the left anterior descending coronary artery causing no flow restriction (figure 1B). To better characterize the lesion, an intracoronary imaging modality—optical coherence tomography—was prescribed (video 1 of the supplementary data). In the corresponding area of the filling defect, we observed a red thrombus that prevented the evaluation of a possible underlying atherosclerotic plaque (figure 1C; minimum lumen area of 9.5 mm^2 (reference, 12.6 mm^2).

After these findings, the diagnosis of acute coronary syndrome was assumed. Therefore, since no percutaneous coronary intervention was ever performed, the patient remained on triple antithrombotic therapy (acetylsalicylic acid, 100 mg; ticagrelor, 90 mg twice a day, and enoxaparin 1 mg/Kg twice a day). Reassessment with invasive coronary angiography was scheduled in a 7-day interval.

By the time of the second left main coronary artery angiography, no filling defect was seen on the proximal segment of the left anterior descending coronary artery (figure 2A). To confirm the improved status of the lesion, reassessment with optical coherence tomography was also performed (video 2 of the supplementary data). This time, we observed a fibroadipose atherosclerotic plaque with no signs of instability with some reminiscent thrombus on the surface of the plaque (figure 2B). The lesion mechanism was thought to be definite plaque erosion (according to the classification by Kolte et al.[3]). The patient was successfully discharged on dual antiplatelet therapy and behavioral restriction regarding drug consumption.

It has been established that cannabis exerts pathophysiological effects on the cardiovascular system.[4] There is a growing number of case reports describing adverse cardiovascular events, specifically, cannabis-induced myocardial infarction. As this situation is most frequently reported in young individuals, it may go unnoticed and, consequently, untreated. Intracoronary imaging modalities play a key role in the definition of the mechanism behind coronary lesions—whether atherosclerotic or not—in patients with suspected acute coronary syndrome/myocardial infarction with non-obstructive coronary arteries.[2] Reassessment after some time of triple antithrombotic therapy may also contribute to clarify the mechanism as the artery lumen may be thrombus-free.

Informed consent and authorization to publish these figures and videos were obtained from the patient.

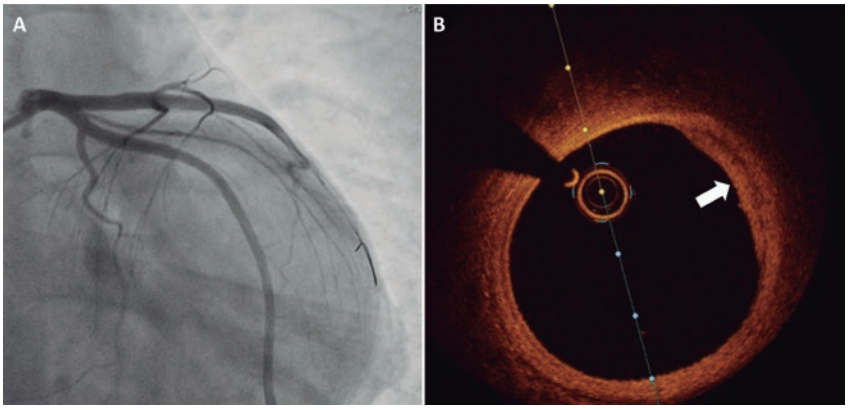

Figure 2. A: reassessment with invasive coronary angiography no longer showing the previous filling defect on the proximal segment of the left anterior descending coronary artery. **B:** optical coherence tomography of this region revealing a fibroadipose atherosclerotic plaque without signs of instability.

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AUTHORS' CONTRIBUTIONS

All authors contributed to the genesis of this manuscript, were involved and approved its submission.

CONFLICTS OF INTEREST

None reported.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000356.

REFERENCES

1. Gulati R, Behfar A, Narula J, et al. Acute Myocardial Infarction in Young Individuals. *Mayo Clin Proc*. 2020;95:136-156.
2. Aparisi Á, Cubero-Gallego H, Tizón-Marcos H. Intracoronary imaging: review and clinical use. *REC Interv Cardiol*. 2022;4:228-237.
3. Kolte D, Yonetsu T, Ye JC, et al. Optical Coherence Tomography of Plaque Erosion: JACC Focus Seminar Part 2/3. *J Am Coll Cardiol*. 2021;78:1266-1274.
4. Chetty K, Lavoie A, Deghani P. A Literature Review of Cannabis and Myocardial Infarction-What Clinicians May Not Be Aware Of. *CJC Open*. 2021;3:12-21.

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Role of drug-coated balloon in the management of very late stent thrombosis

Papel del balón fármacoactivo en el tratamiento de la trombosis muy tardía de stent

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To the Editor,

Very late stent thrombosis—the one occurring, at least, 1 year after stenting—is a rare complication of tremendous clinical relevance. The mechanisms underlying its physiopathology have been widely studied thanks to the use of intracoronary imaging modalities, especially optical coherence tomography. The 2 main mechanisms of action found are, in the first place, neoatherosclerosis, and secondly, no strut endothelization.[1] Despite of this, its approach is still under discussion and focused on resolution or minimization of the factors leading to its appearance.

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Table 1. Clinical and procedural characteristics

	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #6
Sex	Woman	Man	Man	Man	Man	Man
Age (years)	71	81	83	52	63	75
Hypertension	Yes	Yes	Yes	Yes	Yes	No
Diabetes	No	Yes	No	No	No	No
Dyslipidemia	Yes	Yes	Yes	Yes	Yes	Yes
Smoking	Yes	Former smoker	Former smoker	Yes	Former smoker	Former smoker
Kidney disease	No (Cr, 0.79)	No (Cr, 0.78)	No (Cr, 1.02)	No (Cr, 1.02)	No (Cr, 1.13)	No (Cr, 0.98)
Years since stenting	19	3	4	6	15	10
Previous treatment	ASA	NOA	ASA	ASA	Clopidogrel	NOA + clopidogrel
Location of culprit lesion	Mid-right coronary artery	Mid-left anterior descending coronary artery	Saphenous vein graft	Distal left circumflex artery	Diagonal branch	Mid-right coronary artery
Early TIMI grade flow	0	0	3	0	3	0
Predilatation device	Scoring	NC	Cutting + NC	Scoring + cutting	NC	NC
Final TIMI grade flow	3	3	3	3	3	3
Intracoronary images	No	No	No	Yes	No	No
Size of DCB used	3.5	2.5 + 3	4	3	2.5	3
Treatment at discharge	ASA + prasugrel	NOA + ASA + clopidogrel	ASA + ticagrelor	ASA + ticagrelor	ASA + ticagrelor	NOA + ASA + clopidogrel
Follow-up (months)	10	9	6	6	3	2
Adverse events at follow-up	No	No	No	No	No	No

ASA, acetylsalicylic acid; Cr, plasma creatinine concentration (mg/dL); DCB, drug-coated balloon; NC, noncompliant balloon; NOA, new oral anticoagulant; TIMI, Thrombolysis in Myocardial Infarction.

On the other hand, drug-coated balloon (DCB) has been part of the therapeutic armamentarium of interventional cardiologists for quite some time. Currently, its main indications are to treat in-stent restenosis, and small vessel de novo coronary artery lesions. New indications are emerging like bifurcations (especially of the side branch) and large vessel de novo lesions. However, there is a clinical setting where its use has instilled quite a few serious doubts: ST-segment elevation acute coronary syndrome (STEACS). Since plaque rupture followed by thrombosis is its main pathogenic mechanism and it's different from the therapeutic target of DCB—the inhibition of neointimal proliferation—the use of DCB to treat STEACS is ill-advised. Former studies on this matter have proven so.[2] However, isolated, and well-designed studies have obtained good results like the REVELATION.[3]

However, in very late stent thrombosis—the one associated with the thrombotic phenomenon *per se*—other pathogenic processes are involved like restenotic lesions and neoatherosclerosis, which could respond to DCB therapy even with a lower risk of complications compared to new stenting since this approach is less aggressive and avoids stenting multiple overlapping stents in the culprit vessel.

This is the first series ever reported of patients with very late stent thrombosis treated with DCB. All of them signed the informed consent form, and received the approval of our hospital ethics committee.

Table 1 shows the clinical, anatomical, and procedural characteristics of the 6 patients included. We should mention the very late onset of stent thrombosis that occurs in 1 of the cases occurred 19 years after the index procedure. A total of 4 patients had complete vessel thrombosis. In all of them percutaneous thrombectomy was performed unlike in the other 2 who had partial thrombosis with baseline TIMI (Thrombolysis in Myocardial Infarction) grade-3 flow. We should mention that in 2 out of the 6 patients significant changes were reportes regarding measurements taken on the days that preceded the onset of STEACS. In the first patient, single antiplatelet therapy was withdrawn due to a scheduled dental procedure while in the second patient, dual antiplatelet therapy was changed for single antiplatelet therapy plus oral antiacoagulation due to the presence of deep venous thrombosis. In the only patient treated with optical coherence tomography, neoatherosclerosis was identified as the pathogenic mechanism of thrombosis (figure 1 and figure 2). All the lesions received proper preparation with different predilatation and plaque modification devices before using the DCB, the SeQuent Please Neo with paclitaxel coating technology (BBraun, Germany) in all cases. No adverse events were ever reported at a median follow-up of 6 months.

Scientific evidence on the utility of DCB to treat STEACS due to very late stent thrombosis is scarce, only just a few isolated case reports.[4] Since, conceptually, the DCB looks like an excellent therapeutic tool in this clinical setting, we believe trials with big enough samples and clinical and angiographic follow-up should be conducted to confirm or refute such hypothesis. We should mention

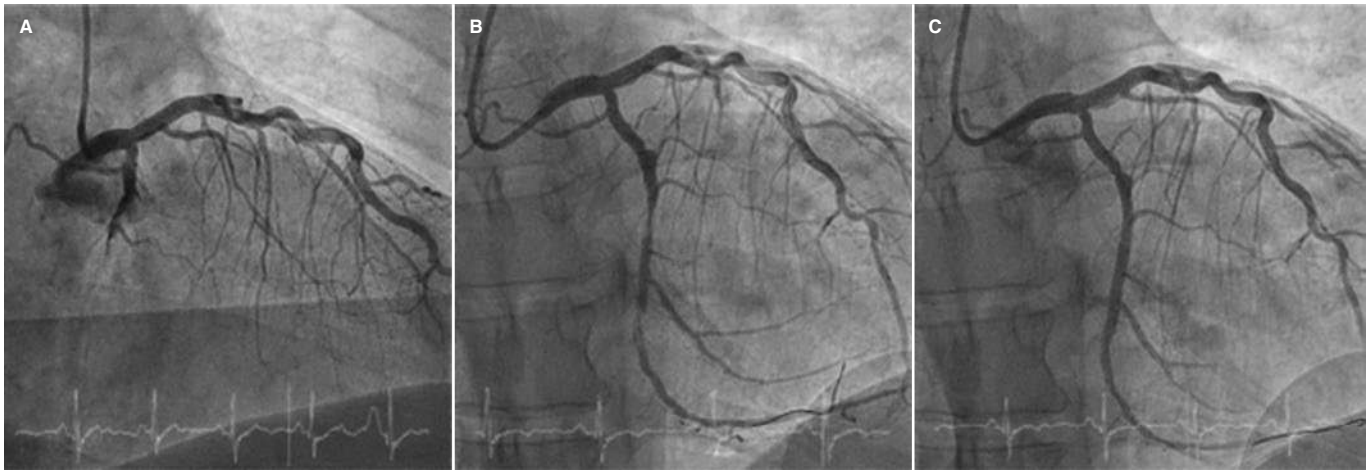

Figure 1. Angiography of the patient treated with optical coherence tomography. Baseline coronary angiography imaging showing a thrombotic occlusion at left circumflex artery level **(A)** after predilatation with plaque modification balloons (**B**), and final clinical outcomes after drug-coated balloon implantation (**C**).

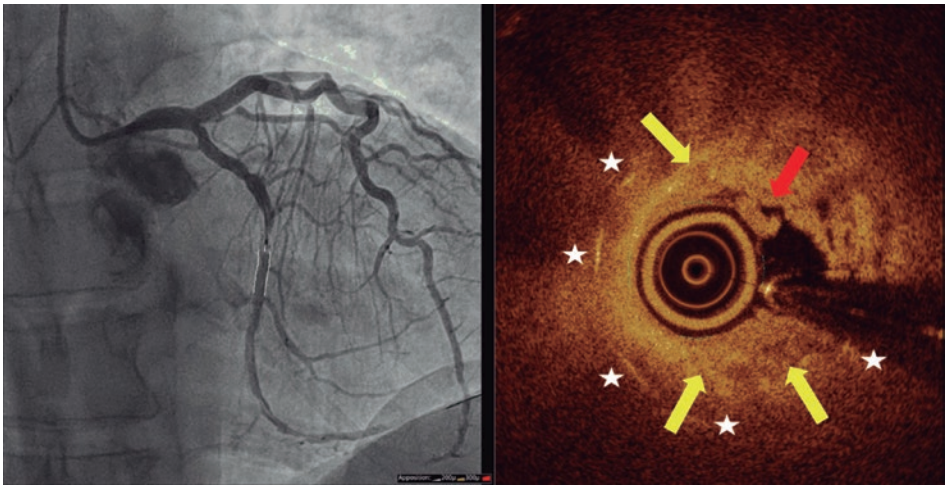

Figure 2. Optical coherence tomography imaging with angiographic co-registration after achieving flow. Yellow arrows are indicative of the process of neoatherosclerosis (restenotic heterogeneous plaque), the red arrow points at a red thrombus, and white stars are indicative of the stent struts.

the need for proper lesion preparation before using DCBs, and how important—actually mandatory—should be to use intracoronary imaging modalities (especially optical coherence tomography for its greater resolution capabilities) to clearly identify the pathogenic mechanisms involved. Therefore, the scarce use of such techniques in our series was our study main limitation.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors were involved in the process of patient recruitment and manuscript revision. J. Valencia drafted the manuscript, conducted the clinical follow-up, and prepared the images.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Adriaenssens T, Joner M, Godschalck TC, et al. Optical Coherence Tomography Findings in Patients With Coronary Stent Thrombosis. A Report of the PRESTIGE Consortium (Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort). *Circulation.* 2017;136:1027-1031.
2. 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.
3. 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.
4. Alfonso F, Bastante T, Cuesta J, Benedicto A, Rivero F. Drug-Coated Balloon Treatment of Very Late Stent Thrombosis Due to Complicated Neoatherosclerosis. *Arq Bras Cardiol.* 2016;106:541-543.

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Clinical case

Intracoronary fibrinolysis as a bailout strategy for massive thrombotic catastrophe

La fibrinolisis intracoronaria como estrategia de rescate ante una catástrofe trombótica masiva

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CASE PRESENTATION

This is the case of a 57-year-old man—Canadian immigrant—who presented to the emergency department due to chest pain. His past medical history showed hypertension, previous smoking, rheumatoid arthritis, and ischemic heart disease. He had previously undergone percutaneous angioplasty in 2006 in Canada. He had no past family history of heart condition or sudden cardiac death. His usual medication included aspirin, clopidogrel, ramipril, metoprolol, leflunomide, and prednisolone. He complained of constrictive chest pain of 2-hour evolution associated with dizziness. He denied syncope. He was admitted while clinically stable, and pain-free. Physical examination was normal. We performed serial electrocardiograms that appeared normal. Blood work showed elevated troponin I levels (5.23 ng/mL, normal range < 0.05 ng/mL). The remaining blood study was normal. Transthoracic echocardiogram showed good biventricular systolic function with inferior wall hypokinesis. The most likely diagnosis was acute coronary syndrome without ST-segment elevation (typical chest pain accompanied by elevated troponin I levels, and segmental hypokinesis). Other diagnoses like Takotsubo syndrome and myocarditis were less likely.

Due to suspected acute coronary syndrome, he started anticoagulation with weight-adjusted enoxaparin (1 mg/Kg) and loading doses of ticagrelor (180 mg). About 24 hours later, the coronary angiography performed revealed the presence of right dominance (figure 1 and videos 1 and 2 of the supplementary data). A stent was seen at left anterior descending coronary artery level with an acceptable angiographic result up to the distal segment, a location in which a 90% in-stent lesion was found. The right coronary artery had an 80% stenosis in the middle segment, an intermediate in-tent restenosis in the distal segment, and a 90% stenosis proximal to the crux. Additionally, the posterior descending coronary artery had an ostial lesion of 90%. It was decided to proceed with angioplasty (Figure 1, videos 1-4 of the supplementary data) of right coronary artery due to the high thrombotic load reported at this location and de novo segmental wall motion abnormalities. Two protection guidewires were advanced towards the distal portion of the vessels. We subsequently predilated the lesion in the right coronary artery distal segment. Almost immediately after deflating the balloon, we observed an interruption of distal flow. The patient developed chest pain and the electrocardiogram revealed the presence of ST-segment elevation. A stent was quickly implanted into the distal segment without flow improvement. Proximal thrombus propagation continued, and 2 additional stents were implanted. Despite these efforts, the artery remained occluded. Intensive intracoronary aspiration was attempted with 2 different EXPORT systems (Medtronic, Portugal) with removal of large amounts of thrombus. Despite the extraction, the scenario remained the same. Additionally, an attempt was made to dilate various segments of the artery throughout its length. Again, recanalization was unsuccessful. The patient's written informed consent was obtained.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

R. Flores analyzed data, and designed the manuscript. J. Costa, C. Braga, C. Vieira, and C. Quina-Rodrigues reviewed the manuscript.

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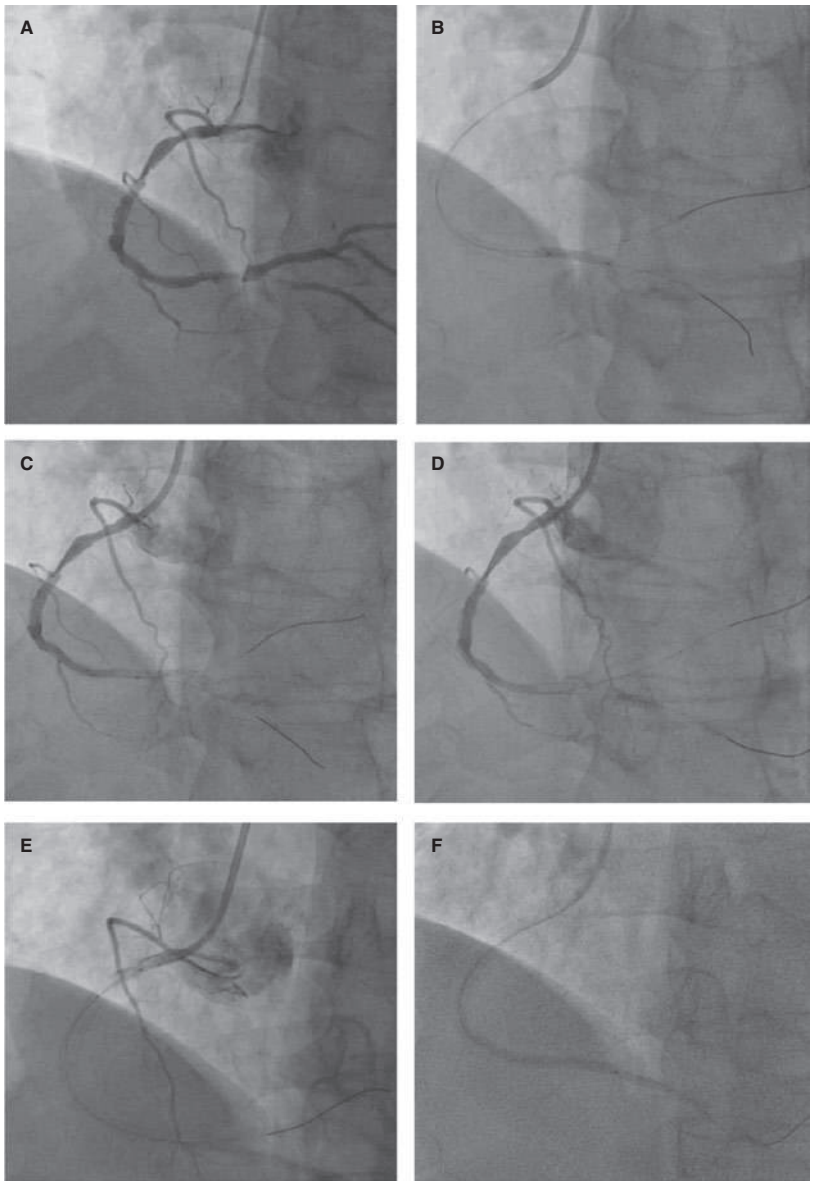

Figure 1. Coronary angiography images. **A:** dominant right coronary artery showing an 80% stenosis in the middle segment and a 90% stenosis in the segment distal to the crux. Additionally, the posterior left descending coronary artery has an ostial lesion of 90%. **B:** lesion predilatation on the right coronary artery distal segment. **C:** no-reflow phenomenon after balloon deflation. **D:** implantation of a Synergy stent [Everolimus, 2.75 mm x 32 mm] without flow improvement. **E:** proximal thrombus propagation after implantation of 2 additional Synergy stents [Everolimus, 3.5 mm x 18 mm; 3.5 mm x 12 mm]. **F:** intracoronary aspiration with 2 different EXPORT systems facilitated the removal of large amounts of thrombus.

CONFLICTS OF INTEREST

None reported.

SUPPLEMENTARY DATA

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Intracoronary fibrinolysis as a bailout strategy for massive thrombotic catastrophe. How would I approach it?

La fibrinolisis intracoronaria como estrategia de rescate ante una catástrofe trombótica masiva. ¿Cómo lo haría?

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HOW WOULD I APPROACH IT?

This is the case of a 57-year-old man with a past medical history of ischemic heart disease treated percutaneously years ago who was admitted with signs of non-ST-elevation acute coronary syndrome and inferior wall hypokinesis on the echocardiogram. The coronary angiography performed 24 hours after admission revealed the presence of restenosis in a stent implanted into the mid left anterior descending coronary artery and severe stenosis of distal right coronary artery. The angiographic imaging suggested the presence of 1 intraluminal thrombus spreading towards the ostium of the posterior descending coronary artery. The right coronary artery underwent immediate percutaneous treatment with balloon predilatation, which immediately triggered the appearance of the no-reflow phenomenon (NRP).

NRP is defined as a reduced coronary flow after the angioplasty for the lack of a mechanical obstruction of the epicardial coronary artery. Although its incidence rate has somehow dropped over the last few years with the use of more powerful antiplatelet drugs and early approach of coronary syndromes, the therapeutic management of this entity is still challenging for the lack of standard therapies. From the pathophysiological point of view, the NRP has been associated with an occlusion of coronary microcirculation of multifactorial origin including microembolization, microcirculation vasospasm, and edema or myocardial bleeding in the necrosis setting. These mechanisms would activate the inflammatory cascade and promote the release of free radicals and eventually platelet therapy.

Former clinical trials have assessed different strategies to prevent this phenomenon from happening using thrombus aspiration prior to angioplasty (TASTE and TOTAL clinical trials) or through the intracoronary administration of abciximab (INFUSE-AMI). However, none of them has been able to prove definitive clinical benefits. Similarly, there are contradictory data on the use of vasodilators like adenosine, verapamil or intracoronary nitroprusside to prevent and treat NRP. Regarding established NRP, only 1 clinical trial recently published (the COAR) has proven the superiority of intracoronary adrenaline compared to adenosine in patients with loss of distal flow after coronary stenting.[1]

Going back to our case , initially, it would be good to complete the study using an intracoronary imaging modality to discard other possible causes of loss of distal flow like dissection or coronary spasm. Once the presence of thrombus has been confirmed, flow recovery is essential before considering stenting. In this context, my initial strategy would be to repeat aspirations using manual thrombectomy devices towards the posterior descending coronary artery and eventually the posterolateral one even accessing the femoral artery differently if needed to advance higher profile extractors (7-Fr) with greater aspiration capabilities. In the presence of persistent NRP the local administration of vasodilators could be considered (table 1 shows drugs validated in former studies and their corresponding doses). In the presence of hypotension and bradycardia the intracoronary infusion of adrenaline may be advised through coaxial microcatheters advanced into the occlusion region or through dedicated catheters with distal infusion holes to keep advancing the guidewire through the vessel during drug infusion (figure 1). In the presence of an aspiration-resistant thrombus, I would choose the intracoronary administration of anti-IIb/IIIa agents or fibrinolytic drugs (by administering a third of the systemic dose) using dedicated catheters.[2] Eventually, I would use the marinade technique[3] with vessel distal occlusion and inflate a balloon at posterior descending coronary artery level while administering the fibrinolytic drug through the guide catheter extension system advanced through the middle-distal right coronary artery (figure 2). Finally, if the above measures don't work, I would treat the restenosis of the mid left anterior descending coronary artery in the same surgical act to reduce myocardial ischemia in other territories.

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Table 1. Drugs used to treat no-reflow phenomenon (dose of intracoronary bolus, and maximum dose described)

Drug	Dose of intracoronary bolus	Maximum dose
Vasodilators		
Adenosine	100 µg	2000 µg
Nitroprusside	50 µg	300 µg
Nicardipine	50µg	400 µg
Verapamil	0.5 µg	1 mg
Nicorandil	0.5 µg	4 mg
Nicardipine	100 µg	2200 µg
Dipyridamole	0.56 mg/kg	200 mg
Anti-IIb/IIIa		
Abciximab	0.25 mg/kg	IV infusion of 0.125 µg/kg/min
Eptifibatide	180 µg	IV infusion of 2 µg/kg/min
Other drugs		
Adrenaline	100 µg	400 µg
Cyclosporine A	IV 2.5 mg/kg	–

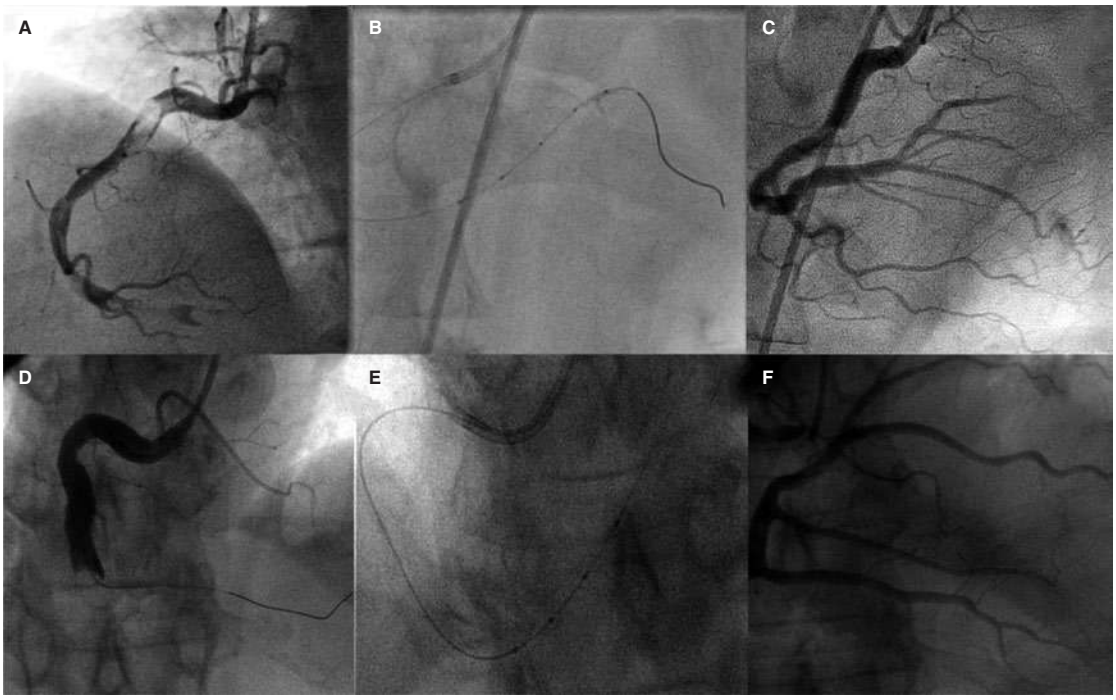

Figure 1. Use of catheter with distal infusion holes for direct administration of intracoronary thrombolytic drug in 2 patients with high thrombotic burden and lack of distal flow after repeated thrombus aspiration. **A** and **D**: early right coronary angiography. **B** and **E:** image of the catheter into the distal right coronary artery. **C** and **F:** final angiographic outcomes.

After finishing the procedure and in the presence of persistent NRP, I would consider using percutaneous circulatory assist devices to improve myocardial diastolic flow.

Some authors have described the use of non-pharmacological therapies to treat NRP like induced hypothermia or the intracoronary high-pressure injection of autologous blood. However, the effectiveness of these strategies is still to be determined. Similarly, multiple studies have been published on the use of different agents both vasodilators (papaverine) and anti-free radical drugs (anisodamine), and growth factors in this context. However, their availability is limited, and their efficacy has not been demonstrated in randomized clinical trials.

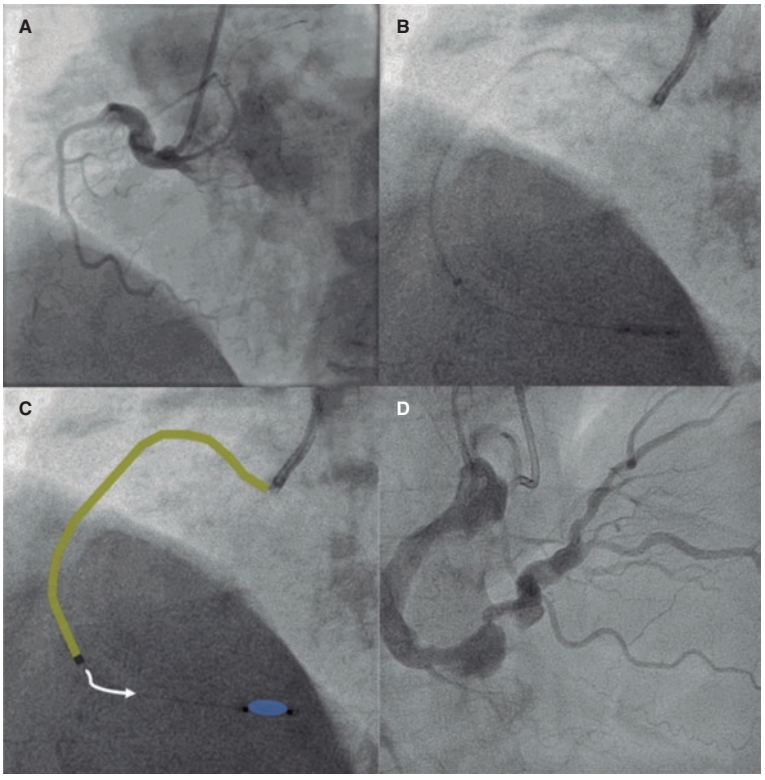

Figure 2. Administration of intracoronary fibrinolytic therapy with distal occlusion (the "marinade" technique). **A:** early angiographic imaging with right coronary occlusion at first curve level. **B** and **C:** infusion of 2000 IU of alteplase through a guide catheter extension system (in yellow) while keeping distal balloon inflation for 5 minutes. **D:** final angiographic outcomes.

Given the multifactorial nature of NRP, the combination of different strategies can be advised considering techniques to eliminate the thrombotic burden (repeat aspiration or local administration of antithrombotic drugs) in cases with predominant distal embolization. Also, the local administration of vasodilators is advised to treat patients with suspected microcirculation disorders.

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Khan KA, Qamar N, Saghir T, et al. Comparison of Intracoronary Epinephrine and Adenosine for No-Reflow in Normotensive Patients With Acute Coronary Syndrome (COAR Trial). *Circ Cardiovasc Interv.* 2022;15:e011408.
2. Unzue L, Garcia E, Teijeiro R, et al. Local intracoronary fibrinolysis in acute mycardial infarction of ectatic coronary arteries in the post-abiximab era. *Cardiovasc Revasc Med.* 2021;32:69-74.
3. Unzue L, García E, Teijeiro-Mestre R. Local fibrinolysis with distal occlusion: "marinade" technique. *Rev Esp Cardiol.* 2022;75:86.

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Intracoronary fibrinolysis as a bailout strategy for massive thrombotic catastrophe. Case resolution

La fibrinolisis intracoronaria como estrategia de rescate ante una catástrofe trombótica masiva. Resolución

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CASE RESOLUTION

Intensive intracoronary vasodilators, including intracoronary nitrates and adenosine also proved ineffective. A total of 0.3 mg/Kg of enoxaparin were given during the procedure. Finally, intracoronary fibrinolysis was attempted with the administration of tenecteplase (8000 IU). About 10 minutes after instillation, recanalization was not possible, and the procedure was terminated. A type 4a myocardial infarction was diagnosed and an additional 48-hour course of eptifibatide was administered (bolus of 180 µg/Kg followed by the perfusion of 2 µg/Kg/min) (figure 1).

After the procedure, the patient complained of chest pain and an ST-segment elevation was seen. Pain was successfully controlled within the first 12 hours. The troponin peak levels were 113 ng/mL. A triple antithrombotic strategy with aspirin, ticagrelor, and full-dose enoxaparin was maintained during hospitalization (1 week). Serial echocardiographic evaluation revealed the presence of mild left ventricular dysfunction with severe inferior wall hypokinesis. Right ventricular systolic function was depressed (a 12 mm tricuspid annular plane systolic excursion [TAPSE]). The patient was discharged on dual antiplatelet therapy. The patient remained asymptomatic at 5-month follow-up. Cardiac magnetic resonance imaging (figure 2) showed a normal-sized right ventricle with preserved function, but mild hypokinesis of the right ventricle free wall. Middle and basal segments showed late gadolinium enhancement. Left ventricular systolic function remained slightly depressed with akinesia of the inferior-lateral and inferior walls. Test for residual ischemia was negative.

This case report illustrates a rare complication of a frequent procedure. Our patient developed an acute coronary occlusion after an attempted elective angioplasty. Furthermore, we rushed and tried revascularization through aspiration and intracoronary fibrinolysis. The no-reflow phenomenon was most likely associated with local thrombosis; nonetheless, mechanisms like iatrogenic coronary dissection are plausible. Intracoronary imaging was considered dangerous in this setting due to the possibility of progression into a hypothetic dissection. Despite the fact that these techniques failed, the case illustrates the numerous possibilities for revascularization. The underlying autoimmune disease and chronic corticosteroid therapy may have contributed to this thrombotic catastrophe.

In the modern era of potent antiplatelet agents, the risk of myocardial infarctions associated with percutaneous coronary revascularization is rare. In many cases, there is an underlying condition that appears to increase the risk of thrombotic events. Moreover, the treatment of type 4a infarcts is difficult, and the emergence of new bailout techniques is essential. Intracoronary fibrinolysis has been suggested as a rescue therapy for patients with high thrombotic burden, but it may become deleterious in certain scenarios due to increasing bleeding complications.[1,2]

Our case shows that not all type 4a infarctions have a favorable outcome, but also highlights the variety of percutaneous approaches that remain at our disposal for the management of these rare complications. The recovery of right ventricular systolic function highlights the adaptability of the coronary tree and right circulation.[3] A written informed consent was obtained from the patient.

FUNDING

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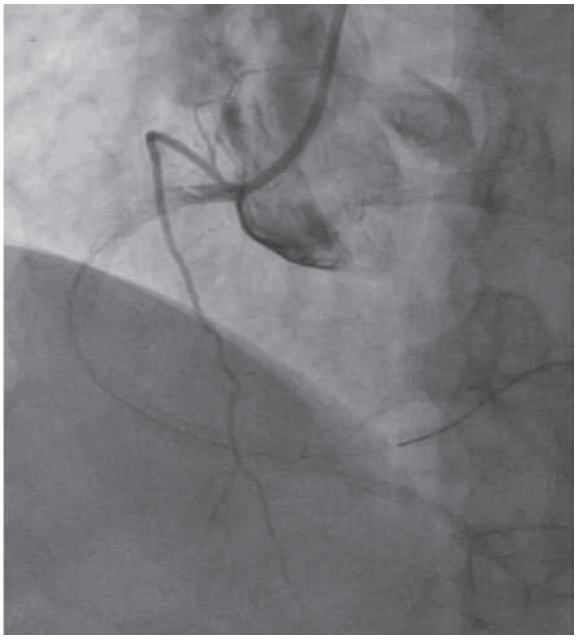

Figure 1. Angiography after instilling 8000 IU of tenecteplase with no reperfusion; then, the procedure was terminated.

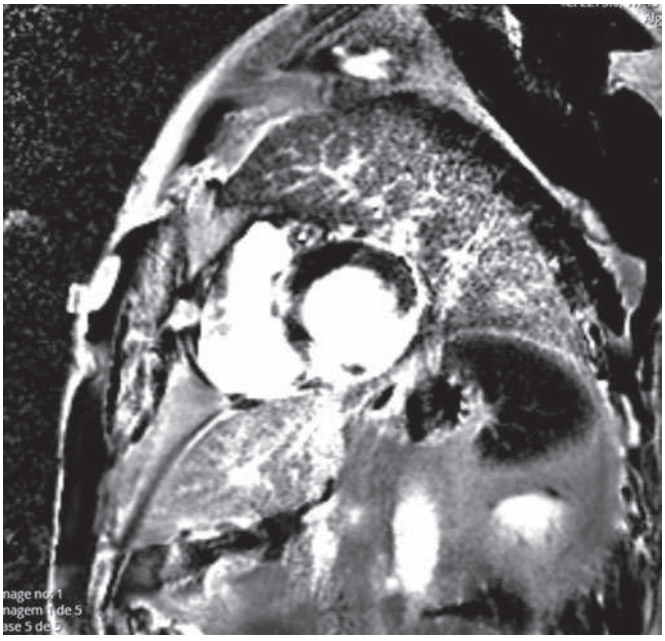

Figure 2. Short-axis cardiac magnetic resonance imaging.

AUTHORS' CONTRIBUTIONS

R. Flores analyzed data and designed the manuscript. J. Costa, C. Braga, C. Vieira, and C. Quina-Rodrigues revised the manuscript.

CONFLICTS OF INTEREST

None reported.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000306.

REFERENCES

1. Unzue L, Garcia E, Teijeiro R, et al. Local Intracoronary Fibrinolysis in Acute Myocardial Infarction of Ectatic Coronary Arteries in the Post-Abciximab Era. *Cardiovasc Revasc Med.* 2021;32:69-74.
2. Kelly RV, Crouch E, Krumnacher H, et al. Safety of adjunctive intracoronary thrombolytic therapy during complex percutaneous coronary intervention: initial experience with intracoronary tenecteplase. *Catheter Cardiovasc Interv.* 2005;66:327–332.
3. Addetia K, Patel AR. Beyond right ventricular size and function: the importance of evaluating the right ventricle's capacity for recovery. *Expert Rev Cardiovasc Ther.* 2014;12:1269-1273.

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The forgotten stent

El stent olvidado

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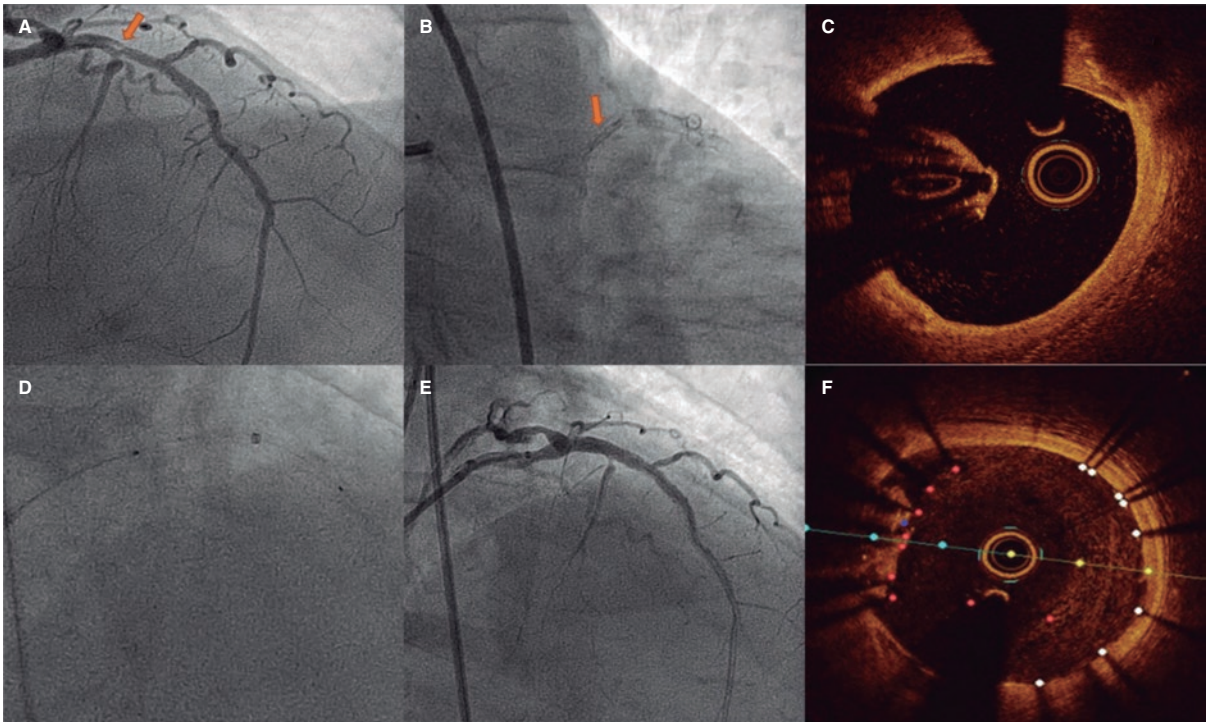

Figure 1.

This is the case of a 78-year-old man with revascularized coronary artery disease 10 years ago (left anterior descending coronary artery and left circumflex artery) who was admitted to the hospital with signs of ST-segment elevation acute coronary syndrome. The angiography shows an unusual image on the proximal left anterior descending coronary artery that seems to be causing an angiographically significant stenosis (figure 1A,B). To confirm diagnosis, a catheter is unsuccessfully advanced with optical coherence tomography (OCT) guidance through a polymeric guidewire while trying to cross the most stenotic region. Two attempts are made after predilatation (with balloons of 1.5 mm and 2.5 mm in diameter) that prove unsuccessful. Afterwards, a guide catheter extension system is advanced (figure 1D) that successfully crosses the lesion facilitating the OCT that reveals the presence of an underexpanded coronary stent with complete endothelization, and a possible thrombus attached to it (figure 1C). Upon suspicion that this is the culprit lesion, decision is made to treat it. To crush the underexpanded stent against the lumen of the vessel, it is first effortlessly predilated using a 3.5 mm x 12 mm balloon. Afterwards, a 3.5 mm x 15 mm drug-eluting stent is implanted with good angiographic results (figure 1E). A new OCT confirms the excellent expansion of the new stent including the entire forgotten stent that is crushed between the new stent and the vessel endothelium (figure 1F).

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Stent loss inside the coronary tree is a rare complication that can, however, be solved if removed during the procedure. However, when forgotten for years, the stent endothelizes and its extraction becomes complicated and is no stranger to complications. In these cases, the most efficient option is to exclude it by implanting a new drug-eluting stent.

The patient's written informed consent was requested before publishing this article.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors were involved in the procedure. They also reviewed the images and drafted the manuscript.

CONFLICTS OF INTEREST

R. Moreno in an associate editor of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure impartial handling of the manuscript has been followed.

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Atrial mass as a complication following complex percutaneous coronary intervention

Masa auricular como complicación después de intervención coronaria percutánea compleja

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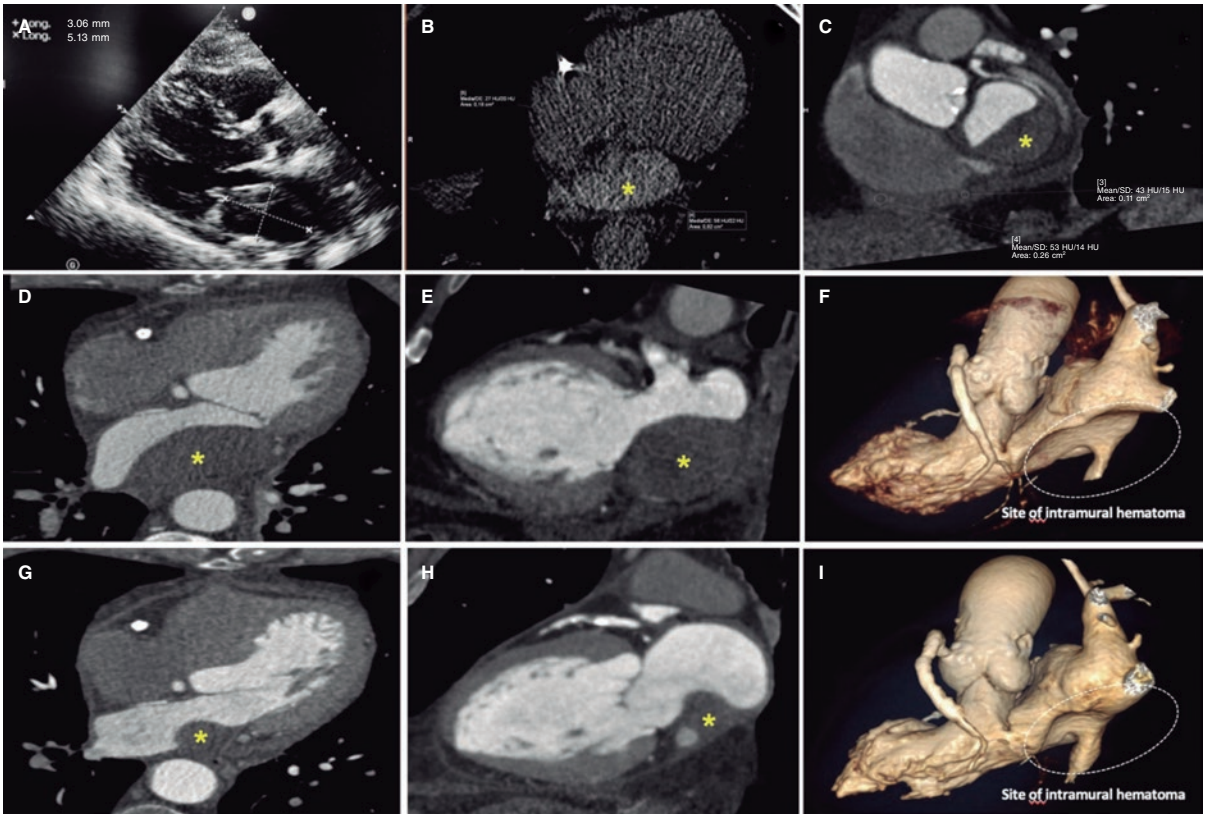

Figure 1.

This is the case of a 75-year-old man who underwent coronary angiography due to new-onset dyspnea and left bundle branch block with a long, diffuse, and heavily calcified lesion with a maximum stenosis of 90% in his dominant right coronary artery. Patient was treated with complex percutaneous coronary intervention (PCI) (double-guidewire technique—both hydrophilic wires—guide catheter extension system, and compliant and non- compliant balloon dilatations), which eventually led to the successful distal-to-proximal implantation of 3 drug-eluting stents. A few hours later, he complained of pleuritic chest pain while remaining hemodynamically stable, and with a normal physical examination. Lab tests showed troponin I levels of 8 ng/mL (reference < 0.012 ng/mL). The echocardiogram showed no regional motion abnormalities, but revealed the presence of a 55.3 mm x 29 mm left atrial mass emerging from the posterior atrial wall almost occluding the complete atrial cavity without conditioning significant mitral valve dysfunction or an impaired transmitral flow. Pericardial

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effusion suggestive of hemopericardium was also described (figure 1A; video 1 of the supplementary data). Left atrial intramural hematoma (LAIH) was suspected and CCTA confirmed the lesion high attenuation (56 Hounsfield Units), which was suggestive of hematic component (*, figure 1B-F). The patient remained hospitalized until the stability of the lesion was confirmed (discharge size, 48 mm x 28 mm) while on dual antiplatelet therapy. After monthly clinical follow-ups, the control CCTA performed at 3 months confirmed significant reduction (30 mm x 20 mm) (*, figure 1G-I). LAIH is a rare complication associated with complex PCI procedures (probably caused while positioning the guidewires, penetrating distal vasculature, and causing the bleeding) being a potential cause for conduction disorders and hemodynamic instability. The patient's verbal consent was obtained.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

L. Nieto-Roca, M. Tomás-Mallebrera, and R. Carda Barrio: contributed substantially to the drafting of this case, obtained the patient's informed consent, and compiled all the images. They gave their approval to the manuscript final version. They take full responsibility for all aspects related to the article and commit themselves to investigating and solving all questions regarding the accuracy and truthfulness of any part of the work. J.A. Esteban-Chapel, and M.L. Martín-Mariscal contributed to the interpretation of the case, and the corresponding images. They gave their approval to the manuscript final version. They take full responsibility for all aspects related to the article and commit themselves to investigating and solving all questions regarding the accuracy and truthfulness of any part of the work.

CONFLICTS OF INTEREST

None reported.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000329.

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Transcatheter aortic valve implantation using FEops HEARTguide co-registration

Implante percutáneo de válvula aórtica mediante corregistro FEops HEARTguide

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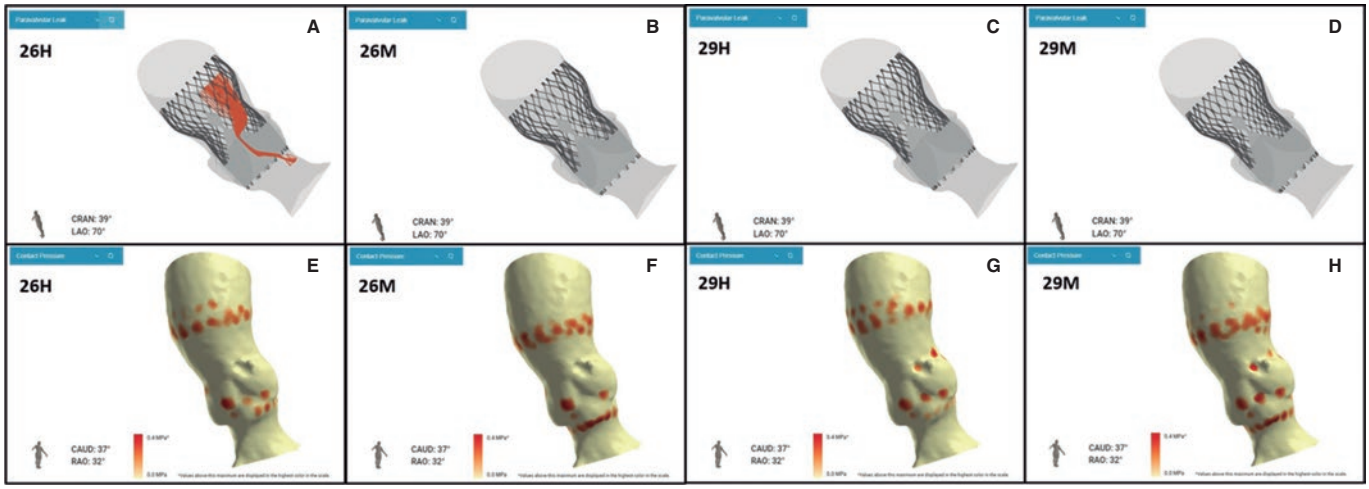

Figure 1.

Transcatheter aortic valve implantation (TAVI) success rate is very high and has a low rate of complications. Therefore, the number of TAVIs has been increasing worldwide. However, complications such as paravalvular leak (PVL) or permanent pacemaker implantation (PPMI) need still to be resolved, particularly in younger patients.

At this point, new technologies may help solve these problems. The FEops HEARTguide is a software that simulates the interaction between the device and patient's anatomy (figure 1A,B). FEops provides the operator with different options and device sizes in a higher or deeper position (EVOLUT no. 26 and no. 29, Medtronic, United States), predicts the theoretical membranous septum, and the device contact pressure by analyzing the tissue characteristics of patient´s anatomy in the computed tomography (CT) images or risk of residual PVL or PPMI (figure 1C-H). Therefore, preoperative planning with FEops can be used to choose the most suitable size and device position for each patient.

On the other hand, synchronized co-registration CT-fluoro has proven useful during TAVI. This is the first case ever performed worldwide using FEops image co-registration with live fluoroscopy in a TAVI procedure (figure 2, video 1 of the supplementary data; red circle: marks the membranous septum). However, no live correlation with heart and lung movements is its main limitation.

In conclusion, FEops is potentially useful in TAVI not only for preoperative planning but also co-registration with fluoroscopy imaging during the procedure may reduce the complications associated with TAVI, especially in complex anatomies. Also, it can reduce the contrast used and the learning curve regarding difficult anatomies.

Written and oral informed consent were obtained before performing the procedure and for publication purposes.

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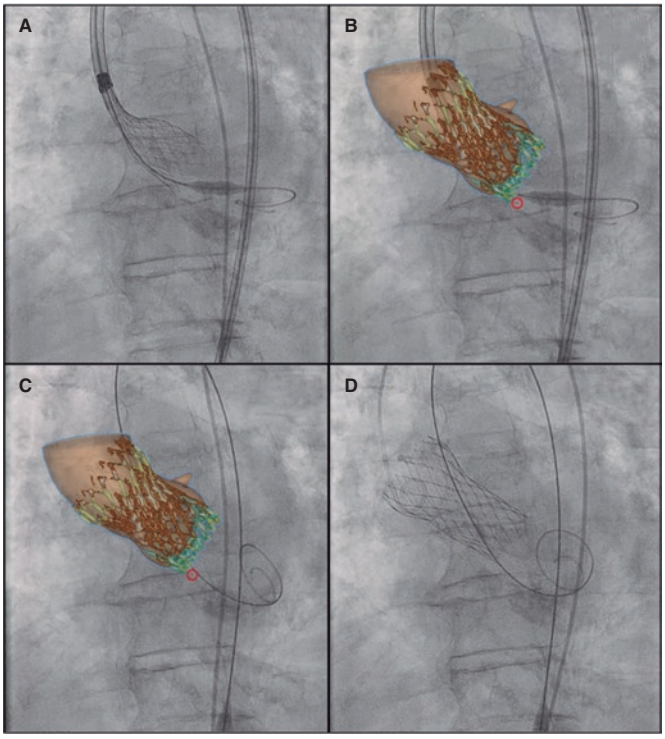

Figure 2.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors participated in this manuscript, reviewed, and fully agreed on its content.

CONFLICTS OF INTEREST

I. Cruz Gonzalez is a proctor and consultor for Medtronic.

SUPPLEMENTARY DATA

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