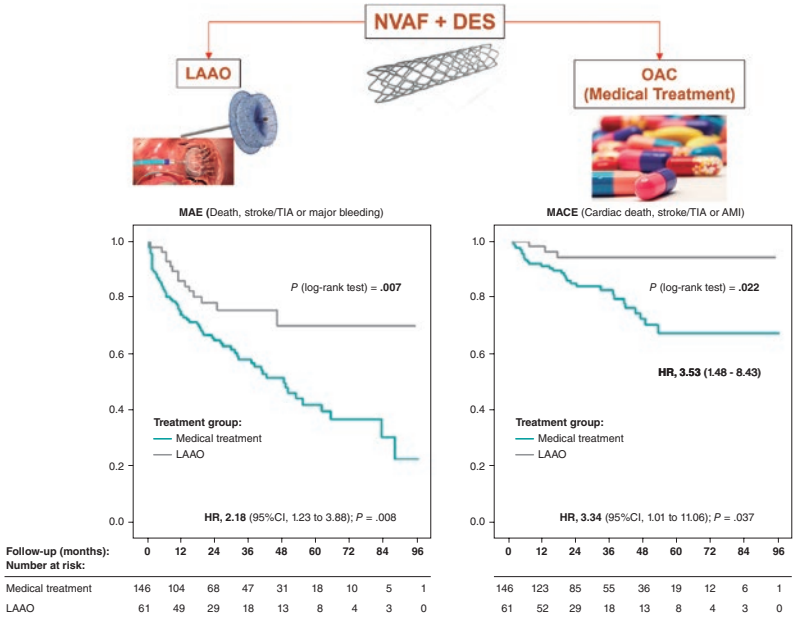
REVISTA ESPAÑOLA DE CARDIOLOGÍA

REC: INTERVENTIONAL CARDIOLOGY

Included in: WoS Core Collection/ESCI, Scopus, Embase, Latindex, Scielo, DOAJ, Dialnet, and Medes

Volume 5, Issue 4 | October-December 2023

ISSN: 2604-7314; e-ISSN:2604-7322



Editor's page

Marking a milestone. *REC: Interventional Cardiology* assigned its first impact factor

Editorials

Optimizing radiation exposure in interventional cardiology: are current doses appropriate?

Forty years of Cardialysis: a leading European cardiovascular research organization

Original articles

Dosimetric parameters in congenital cardiac catheterizations in Spain: the GTH-SECPCC Radcong-21 multicenter registry

Initial experience with the new percutaneous pulmonary self-expandable Venus P-valve

Thermodilution assessment of vasoreactivity and microvascular function in the absence of obstructive coronary artery disease

Design of the ROLLERCOASTR trial: rotational atherectomy, lithotripsy or laser for the management of calcified coronary stenosis

Left atrial appendage occlusion vs oral anticoagulants in AF and coronary stenting. The DESAFIO registry

Debate

Percutaneous revascularization in dilated cardiomyopathy

Scientific letters

Drug-eluting balloon angioplasty for bifurcated chronic total coronary occlusion

Atrial flow regulator and atrial septostomy in pediatric pulmonary hypertension: when procedure and device match

Coronary malperfusion in acute type A aortic dissection

Co-registration assisted 3-vessel orbital atherectomy in de novo calcified multivessel coronary artery disease

Clinical cases

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula

Images in cardiology

New TAVI technique for difficult valve crossing

Unsuspected residual coronary guidewire fragment

The mystery of the Dragon's tail solved by 3D reconstruction

Letters to the Editor

Doctor, I want a TAVI! Should patients choose the type of aortic valve procedure they want?

SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA

Asociación de Cardiología Intervencionista

www.recintervcardiol.org

REC publications

REVISTA ESPAÑOLA DE CARDIOLOGÍA

REC: INTERVENTIONAL CARDIOLOGY

CONTENTS

VOLUME 5, ISSUE 4, OCTOBER-DECEMBER 2023

EDITOR'S PAGE

Marking a milestone. *REC: Interventional Cardiology* assigned its first impact factor
José M. de la Torre-Hernández, Fernando Alfonso, Raúl Moreno, Soledad Ojeda, Armando Pérez de Prado, and Rafael Romaguera 239

EDITORIALS

Optimizing radiation exposure in interventional cardiology: are current doses appropriate?
Eliseo Vañó Carruana, José Miguel Fernández Soto, and Roberto Mariano Sánchez Casanueva 247

Forty years of Cardialysis: a leading European cardiovascular research organization
Ernest Spitzer 250

ORIGINAL ARTICLES

Pediatric cardiology

Dosimetric parameters in congenital cardiac catheterizations in Spain: the GTH-SECPCC Radcong-21 multicenter registry
Fernando Rueda Núñez, César Abelleira Pardeiro, Beatriz Insa Albert, María Álvarez-Fuente, Vanesa Balboa Barreiro, Fernando Ballesteros Tejerizo, Pedro Betrián-Blasco, Félix Coserría Sánchez, Juana María Espín López, Luis Fernández González, Dolores Herrera Linde, Miguel Romero Moreno, Fernando Sarnago Cebada, Ricardo Sanz-Ruiz, and Juan Ignacio Zabala Argüelles 254

Congenital heart disease in adults

Initial experience with the new percutaneous pulmonary self-expandable Venus P-valve
María Álvarez-Fuente, María Toledano, Ignacio Hernández, Elvira Garrido-Lestache, Natalia Rivero, Inmaculada Sánchez, Isabel Molina, Itziar García Ormazábal, and María Jesús del Cerro 263

Ischemic heart disease

Thermodilution assessment of vasoreactivity and microvascular function in the absence of obstructive coronary artery disease
Pau Federico Zaragoza, Teresa Castelló Viguer, Luis Martínez Ortiz de Urbina, Ana Planas del Viejo, Enrique Peris Domingo, and Francisco Pomar Domingo 270

Design of the ROLLERCOASTR trial: rotational atherectomy, lithotripsy or laser for the management of calcified coronary stenosis
Alfonso Jurado-Román, Antonio Gómez-Menchero, Ignacio J. Amat-Santos, Juan Caballero-Borrego, Soledad Ojeda, Raymundo Ocaranza-Sánchez, Santiago Jiménez-Valero, Guillermo Galeote, and Raúl Moreno 279

Structural intervention

Left atrial appendage occlusion vs oral anticoagulants in AF and coronary stenting. The DESAFIO registry
José Ramón López-Mínguez, Estrella Suárez-Corchuelo, Sergio López-Tejero, Luis Nombela-Franco, Xavier Freixa-Rofastes, Guillermo Bastos-Fernández, Xavier Millán-Álvarez, Raúl Moreno-Gómez, José Antonio Fernández-Díaz, Ignacio Amat-Santos, Tomás Benito-González, Fernando Alfonso-Manterola, Pablo Salinas-Sanguino, Pedro Cepas-Guillén, Dabit Arzamendi, Ignacio Cruz-González, and Juan Manuel Nogales-Asensio 287

DEBATE

Debate. Percutaneous revascularization in dilated cardiomyopathy. Apropos of the REVIVED BCIS2 trial: the interventional cardiologist's view
José F. Díaz Fernández 297

Debate. Percutaneous revascularization in dilated cardiomyopathy. Apropos of the REVIVED BCIS2 trial: the clinician's view
Ángel Manuel Iniesta Manjavacas 299

SCIENTIFIC LETTERS

Drug-eluting balloon angioplasty for bifurcated chronic total coronary occlusion
Marcel Almendárez, Rut Álvarez-Velasco, Alberto Alperi García, Pablo Avanzas, Cesar Morís de la Tassa, and Isaac Pascual 302

Atrial flow regulator and atrial septostomy in pediatric pulmonary hypertension: when procedure and device match
Lisa Bianco, Anna Sabaté-Rotés, Alba Torrent-Vernetta, and Pedro Betrián-Blasco 304

Coronary malperfusion in acute type A aortic dissection
Cristina Morante Perea, Tomás Cantón Rubio, Luis Manuel Hernando Romero, José Alfonso Buendía Miñano, José Moreu Burgos, and Luis Rodríguez Padial 306

Co-registration assisted 3-vessel orbital atherectomy in de novo calcified multivessel coronary artery disease
Asad Shabbir, David Chipayo, Adrián Jerónimo, Alejandro Travieso, Nieves Gonzalo, and Javier Escaned 307

CLINICAL CASES

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation
Clara Ugueto-Rodrigo, Alfonso Jurado-Román, Lucía Fernández-Gassó, Guillermo Galeote-García, and Raúl Moreno 311

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation. How would I approach it?
Isaac Pascual 313

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation. Case resolution
Clara Ugueto-Rodrigo, Alfonso Jurado-Román, Lucía Fernández-Gassó, Guillermo Galeote-García, and Raúl Moreno 315

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula
Federico Liberman, Nicolás Zaderenko, Guillermo Pacheco, Juan Pablo Casas, and José Lugones 317

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula. How would I approach it?
Javier Portales Fernández 319

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula. Case resolution
Federico Liberman, Nicolás Zaderenko, Guillermo Pacheco, Juan Pablo Casas, and José Lugones 321

IMAGES IN CARDIOLOGY

New TAVI technique for difficult valve crossing
José M. de la Torre-Hernández, Gabriela Veiga Fernández, Sergio Barrera, Fermín Sainz Laso, Dae-Hyun Lee, and Tamara García Camarero 323

Unsuspected residual coronary guidewire fragment
Felipe Hernández Hernández 325

The mystery of the Dragon's tail solved by 3D reconstruction
Sandra Santos-Martínez, Miguel Leiva-Gordillo, Ricardo García-Belenguer, Paula Tejedor-Viñuela, and Pedro Morillas-Blasco 327

LETTERS TO THE EDITOR

Doctor, I want a TAVI! Should patients choose the type of aortic valve procedure they want?
Manuel Martínez-Sellés 329

REC Interv Cardiol. 2023;5(4):239-246
https://doi.org/10.24875/RECICE.M23000405

Marking a milestone. *REC: Interventional Cardiology* assigned its first impact factor

El año del primer «impacto» para REC: Interventional Cardiology

José M. de la Torre-Hernández,[a,*] Fernando Alfonso,[b] Raúl Moreno,[b] Soledad Ojeda,[b] Armando Pérez de Prado,[b] and Rafael Romaguera[b]

[a] *Editor-in-chief, REC: Interventional Cardiology*
[b] *Associate editor, REC: Interventional Cardiology*

At the time of drafting this Editor's page, we were thrilled to learn that *REC: Interventional Cardiology* has received its very first impact factor (IF) of 1.4 in the latest edition of the Journal Citation Reports.[1] This is outstanding news and the assigned IF greatly exceeds our expectations.

Like many other editors before us, we have previously mentioned on past Editor's pages the excessive and almost obsessive reliance of the current medical publication world on IF.[2-6] Everything seems to revolve around this highly coveted metric, which is made public by all medical journals without exception, especially when it increases.

The manuscripts published in the different sections of *REC: Interventional Cardiology* have significantly impacted the interventional cardiology community in Spain and abroad. Indeed, some of our articles have received numerous citations in top international journals. Likewise, consensus documents drafted by the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC) have achieved significant dissemination and impact.

However, despite the obvious negative aspects of IF, the truth is that it has become the most widely recognized and accepted metric to estimate the value, visibility, and impact of scientific publications. Therefore, if there is anything we would like to highlight in this Editor's page, it is precisely the achievement of the journal's very first IF. This recognition serves to show that our more than 5 years of hard but very satisfying work and has finally paid off and adds to the multiple indexations already achieved to enhance the journal's dissemination and visibility.

The credit for achieving this milestone goes to the entire interventional cardiology community, the boards of directors of the ACI-SEC, authors, reviewers, and everyone on the editorial team and in the journal's editorial office.

As we have worked to position our journal more prominently in terms of visibility, we have made changes to how its contents are structured over the past year, as will be discussed below.

EDITORIAL ACTIVITY

The key issue for a scientific publication is to receive a sufficient number of manuscripts across multiple categories to allow selection of content of the highest possible quality.

Our quarterly issues include original and review articles, scientific letters, case reports, images, debates, and editorial comments on topics of special interest. Periodically, we also feature consensus documents and the abstracts of communications presented at the ACI-SEC congress.

Figure 1 illustrates how the number of research articles published increased within the first 3 years and has remained steady ever since. Figure 2 shows the number of unsolicited manuscripts received.

Original articles

Figure 3 illustrates a notable surge in the submission of original articles in the past year. Given our newly-assigned IF, we anticipate that this upward trend will persist, allowing us to continue to select the best possible manuscripts for publication.

It is striking that the number of articles received in English has been growing steadily (figure 4). In fact, a significant number of the submitted manuscripts (including all types of articles) come from other countries, notably Portugal, Mexico, the United States, Italy, and Argentina.

An essential factor for a scientific journal is how quickly editorial decisions are reached. In this regard, we are highly satisfied with our journal's turnaround times (figure 5), which compare favorably with those of other high-prestige publications.

As emphasized in recent years, our main objective is to consolidate *REC: Interventional Cardiology* as a leading publication in our field. Because our goal is to increase the number of original articles received, we extend an invitation to members of the interventional cardiology community to submit their research articles to our journal.

*** Corresponding author.**
E-mail address: recpublications@secardiologia.es (J.M. de la Torre-Hernández).
𝕏 @RevEspCardiol #recintervcardiol

Online 3 October 2023.

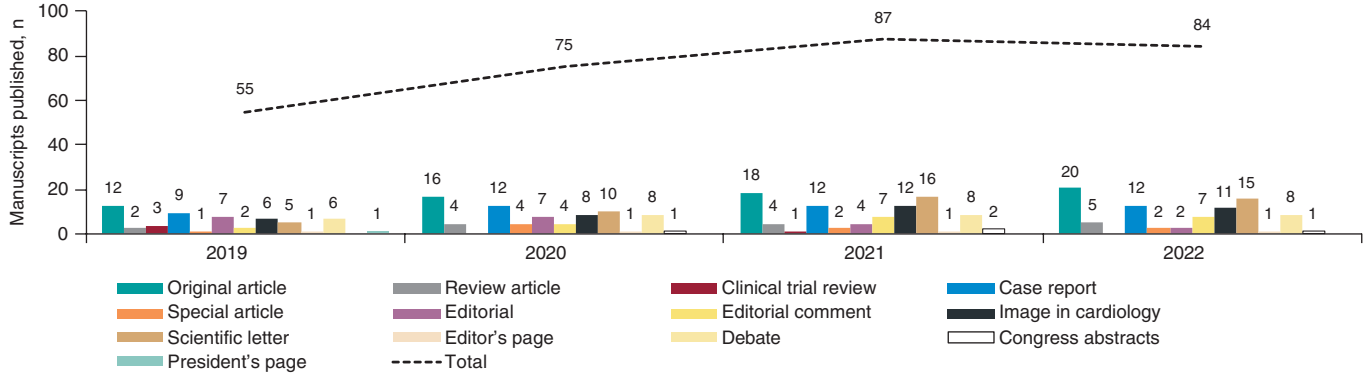


Figure 1. Total contents published, years 2019-2022. Abstracts from congresses are counted as 1 unit. Each case report is counted as 3 units, because it consists of 3 independent articles: *Presentation, How would I approach it?* and *Resolution*.

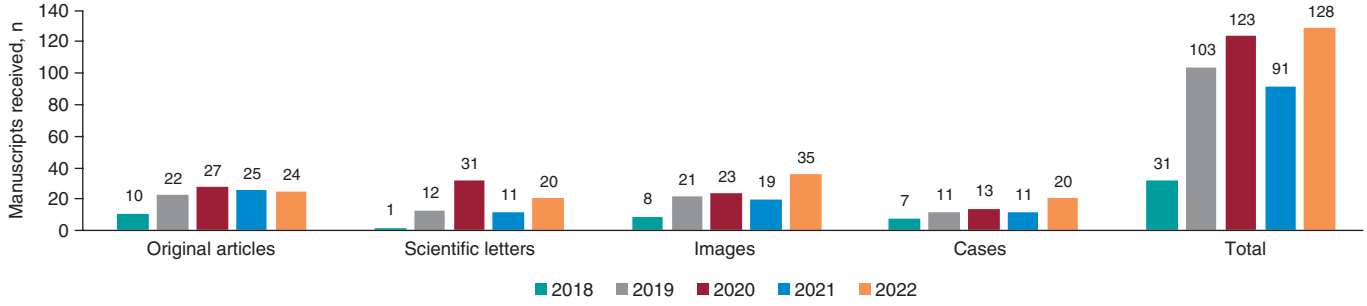


Figure 2. Submission of unsolicited manuscripts, 2018 to 2022.

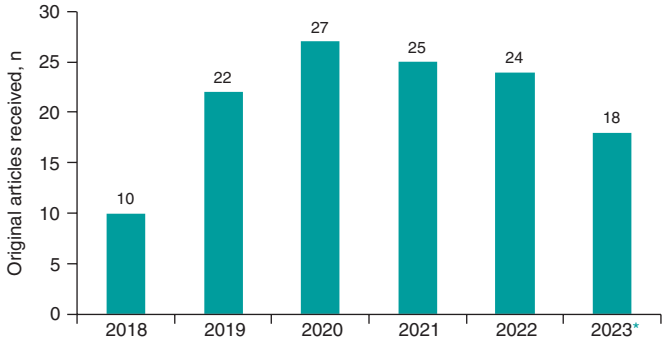


Figure 3. Submission of original articles. *Data until June 30, 2023.

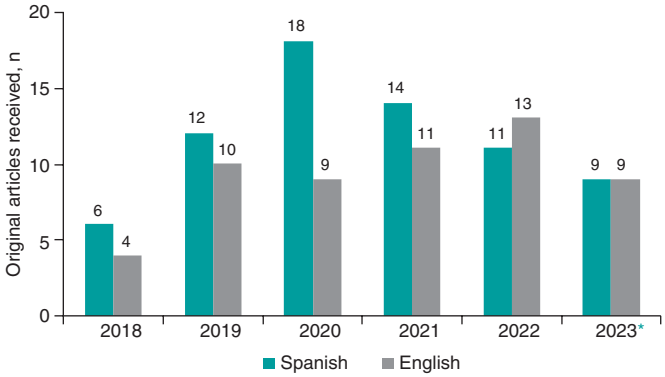


Figure 4. Submission of original articles based on the language of publication. *Data until June 30, 2023.

Scientific letters

This type of article is gaining popularity and is being received more frequently. Figure 6 illustrates the notably high peak in manuscript submissions during the first wave of the COVID-19 pandemic. Because of this increase, the number of letters published per issue varies, depending on demand.

Sometimes, at the suggestion of reviewers and the editorial team, authors have adapted manuscripts initially submitted as original articles into scientific letters. The editorial process of these manuscripts is usually efficient, particularly if they incorporate the scientific recommendations provided by the editorial team in the original version.

Case reports

The number of case reports received increased substantially in 2022 (figure 7). However, only 1 case report is published per issue although each case report consists of 3 parts: *Presentation, How would I approach it?* and *Resolution*, resulting in just 4 cases being published in a single year. Because of the backlog of case reports in the publishing queue, we have to be highly selective in our choices, and our acceptance rate for manuscripts submitted to this section is very low, at < 35%.

Images in cardiology

The field of interventional cardiology creates a huge amount of excellent visuals, making images a limitless source of manuscripts. Although all are interesting, only a few can be published due to space constraints. In the past year, submission of these image-based manuscripts has increased (figure 8), leading to a higher rejection rate, which in 2022 stood at 64%.

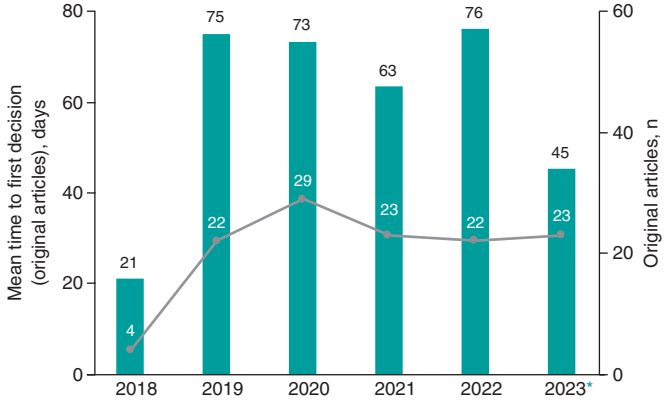


Figure 5. Average days to make the final decision (data above each column) and number of original articles reviewed (in white inside each column). *Data until June 30, 2023.

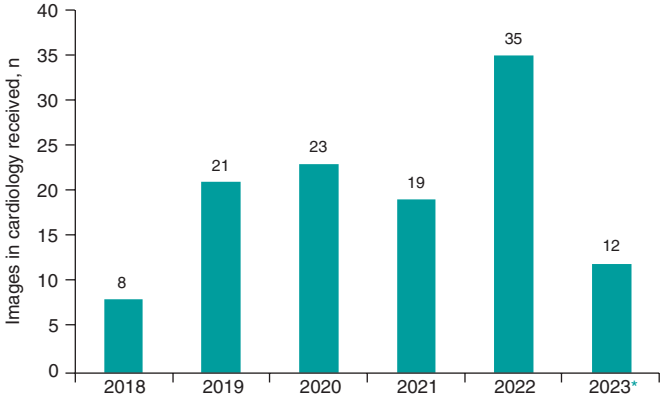


Figure 8. Submission of images in cardiology. *Data until June 30, 2023.

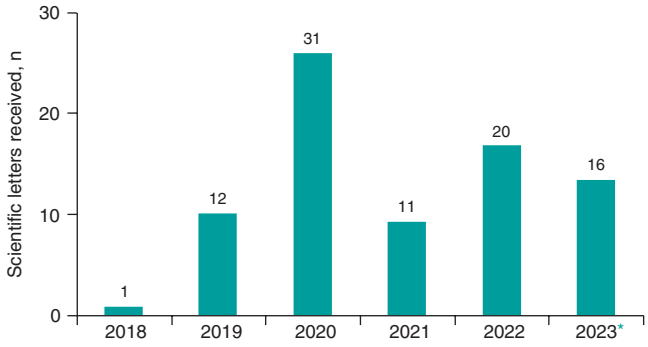


Figure 6. Submission of scientific letters. *Data until June 30, 2023.

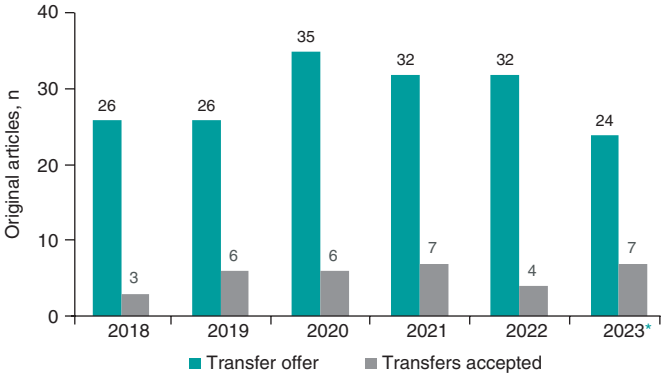


Figure 9. Offers to transfer original articles from *Revista Española de Cardiología* and number of acceptances within the same period. *Data until June 30, 2023.

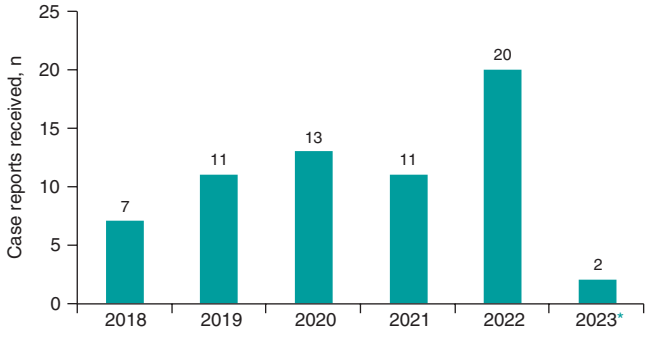


Figure 7. Submission of case reports. *Data until June 30, 2023.

Contents transferred from *Revista Española de Cardiología*

One of the sources of manuscripts for journals within the same editorial family is the transfer of manuscripts from main journal to the sister publications. *Revista Española de Cardiología* attracts an extremely large number of submissions, far exceeding its capacity for acceptance, resulting in a notably high rejection rate, even for articles of undeniable interest. Obviously, there is a risk that the option to transfer manuscripts from a higher- to a lower-impact journal will not be taken up by authors.

Although the offer to transfer remained stable for several years, it has increased during the first half of 2023, coinciding with authors' decisions to transfer their manuscripts to *REC: Interventional Cardiology* (figure 9). This is excellent news, and we are confident that our recently acquired IF will further enhance the appeal of this option to authors.

LATEST EDITORIAL CHANGES

At REC Publications, we are committed to an ongoing process of evaluation and improvement. Changes are often made to enhance the quality of our journal, streamline the editorial process, and improve the overall experience for our authors. While some of these changes are internal and may not be noticeable to our readers, others may be more visible to our regular visitors.

One of the most significant changes made last year was the elimination of the Clinical cases section. Although appealing to many authors, this section has been phased out of most high-ranking journals. In addition, the section created a significant backlog of manuscripts, leading to publication delays of more than 1 year, and an extremely high rejection rate. Nonetheless, clinical cases featuring highly illustrative images may still be submitted, although these should be submitted as "Images in cardiology".

As for the Scientific letters section, only articles containing original data and describing the authors' experience are now considered for this section. Since June 2023, letters describing clinical cases are no longer accepted for evaluation under this section. We no longer accept letters describing case reports for evaluation.

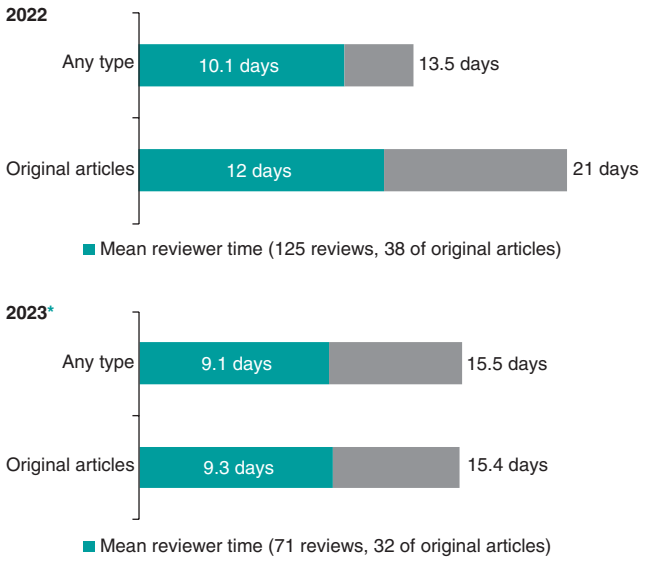


Figure 10. Mean times from receipt to the first editorial decision. *Data until June 30, 2023.

REVIEWERS

Reviewers are key to ensuring the quality of scientific publications through the best method devised for this purpose to date: the peer review process. This commendable work is carried out voluntarily, with reviewers dedicating their valuable time to review and try to improve the quality of the manuscripts assigned to them.

Testament to our reviewers' outstanding work are the excellent review times, which have remained optimal throughout our journal's existence (figure 10).

Table 1 shows the names of all reviewers who reviewed manuscripts for *REC: Interventional Cardiology* from July 1, 2022 through June 30, 2023. Table 2 shows those considered elite reviewers in 2022 due to the volume, speed, and quality of their work.

Once again, we wish to express our gratitude to all those who have made this achievement possible.

DISSEMINATION

The 34th ACI-SEC Congress was held in Santander from June 7 to 9, 2023. The abstracts were published in our journal by the end of May, and *REC: Interventional Cardiology* was present as usual, at the stands of the meeting.[7] At this congress, the prizes for best articles published in *REC: Interventional Cardiology* were awarded: €1500 for the winner and €1000 for the runner-up.[8,9] (figure 11).

Traffic to our website has increased by more than 14% in terms of page views and by 9.4% in terms of users over the past year (from June 2022 through June 2023) compared with the previous period.[10]

Most of our web traffic comes from search engines, 46% from direct searches for the journal, and 31% from keyword searches. Access to the journal from social media has doubled over the past year from 6% to 12%. Our readers come predominantly from Spain, followed by the United States and Mexico, and 60% of them access our contents from their computers, although the journal has been

Table 1. Reviewers of *REC Interventional Cardiology* who conducted evaluations from July 1, 2022 through June 30, 2023

César Abelleira	Felipe Hernández
Juan H. Alonso-Briales	Borja Ibáñez
María Álvarez-Fuente	Andrés Íñiguez
Ignacio Amat	Santiago Jiménez-Valero
Dabit Arzamendi	María López-Benito
Pablo Avanzas	José R. López-Mínguez
Fernando Ballesteros	Ramón López-Palop
Teresa Bastante	Fernando Lozano
José A. Baz	Íñigo Lozano
Pedro Betrián	Gerard Martí
Salvatore Brugaletta	Javier Martín-Moreiras
Ramón Calviño	Guillem Muntané
Santiago Camacho	Luis Nombela
Xavier Carrillo	Imanol Otaegui
Fernando Cebada	Manuel Pan
Ángel Cequier	Isaac Pascual
Belén Cid	Eduardo Pinar
Juan G. Córdoba	Javier Portales
Félix Coserria	Sergio Raposeiras-Roubín
Ignacio Cruz	Fernando Rebollal
Javier Cuesta	Fernando Rivero
María Del Trigo	Oriol Rodríguez
David Del Val	Sergio Rodríguez de Leiras
José F. Díaz	Alejandro Rodríguez-Ogando
Alejandro Diego-Nieto	Fernando Rueda
Felipe Díez-Delhoyo	Rafael Ruiz de Araujo
Jaime Elízaga	Juan M. Ruiz-Nodar
Ignacio Ferreira	Rafael Ruiz-Salmerón
José L. Ferreiro	José Rumoroso
Xavier Freixa	Manel Sabaté
Guillermo Galeote	Pablo Salinas
Sergio García-Blas	Ángel Sánchez-Recalde
Tamara García-Camarero	Juan Sanchis
Bruno García del Blanco	Ricardo Sanz-Ruiz
Arturo García-Touchard	Fernando Sarnago
Javier Goicolea	Ana Serrador
Joan A. Gómez-Hospital	Javier Suárez de Lezo
Josep Gómez-Lara	Luis Teruel
Antonio E. Gómez-Menchero	Ramiro Trillo
Nieves Gonzalo	Leire Unzué
Enrique Gutiérrez-Ibañes	Beatriz Vaquerizo
Federico Gutiérrez-Larraya	

Table 2. Elite reviewers in 2022*

Teresa Bastante
Salvatore Brugaletta
Felipe Hernández
Manuel Pan
Pablo Salinas

* Based on the reviews conducted from September 1, 2021 through August 31, 2022.

increasingly accessed from mobile devices in the last few months. The social network most widely used by cardiologists to read our articles is Twitter, where we have 21 000 followers.[11]

We wish to express our gratitude to REC Publications IT consultant, Juan Quiles, for his excellent work and the changes he has implemented to highlight the authors and revitalize the content through the creation of threads and more multimedia content.

In terms of the most viewed manuscripts, review articles have garnered particular attention over the past year. For instance "Vascular access approach for structural heart procedures" received 3000 views, and "Calcified coronary artery disease: pathophysiology, intracoronary imaging assessment, and plaque modification techniques," received 4258 views. Special articles, such as "Plaque modification techniques to treat calcified coronary lesions. Position paper from the ACI-SEC" marked the introduction of the new Editor's videos format[15] in the first issue published in 2023.

Finally, we have replaced the interviews we used to conduct with a brief 2-minute presentation delivered by one of the authors. This change was made to enhance accessibility on social media and mobile devices. Contents have been added to SEC *CardioTV* structure, resulting in increased visibility. Our audience appears to appreciate this change, with the first videos exceeding 7000 views on multiple platforms compared with the average 800 views with the previous format.

We are on the right path and would like to thank you all for helping to make it possible.

IMPACT FACTOR

As mentioned earlier, the latest edition of Journal Citation Reports, published on June 28, 2023, revealed the new IF data for academic journals.[1] The most significant development for REC Publications is the award of the very first IF for *REC: Interventional Cardiology*, as a journal indexed in the Web of Science Core Collection Emerging Sources Citation Index. The journal has made its debut in this index with a commendable IF of 1.4. Meanwhile, *Revista Española de Cardiología* has retained its position in the first quartile of cardiovascular-themed journals with an IF of 5.9.

This IF of 1.4 not only reflects the quality of the research published but also the impact and dissemination of the journal's content, which is published at no cost to authors and is available in Spanish and English through an open-access model. As the official publication of the ACI-SEC, the journal also publishes consensus documents on current topics[12,14,16,17] (figure 12), whose influence has extended beyond our borders. This was the case of the fast-track publication of documents on COVID-19, which had a tremendous impact on interventional activity in the early stages of the pandemic, as well as other manuscripts whose content has resonated in international conferences. The recently awarded IF adds to all these achievements, which include other indexations already obtained during the 5-year history of our journal: Scopus, Latindex, DOAJ, Dialnet, and Medes. At the time of writing this editorial, we have received news that *REC: Interventional Cardiology* has just been accepted into another prestigious repository: Scielo. All of these achievements contribute to increasing the bibliometric value of all the articles published in our journal (figure 13).

We have now set our sights on Medline, and we are currently undergoing a thorough review of our contents and formats in the hope of obtaining a favorable evaluation.

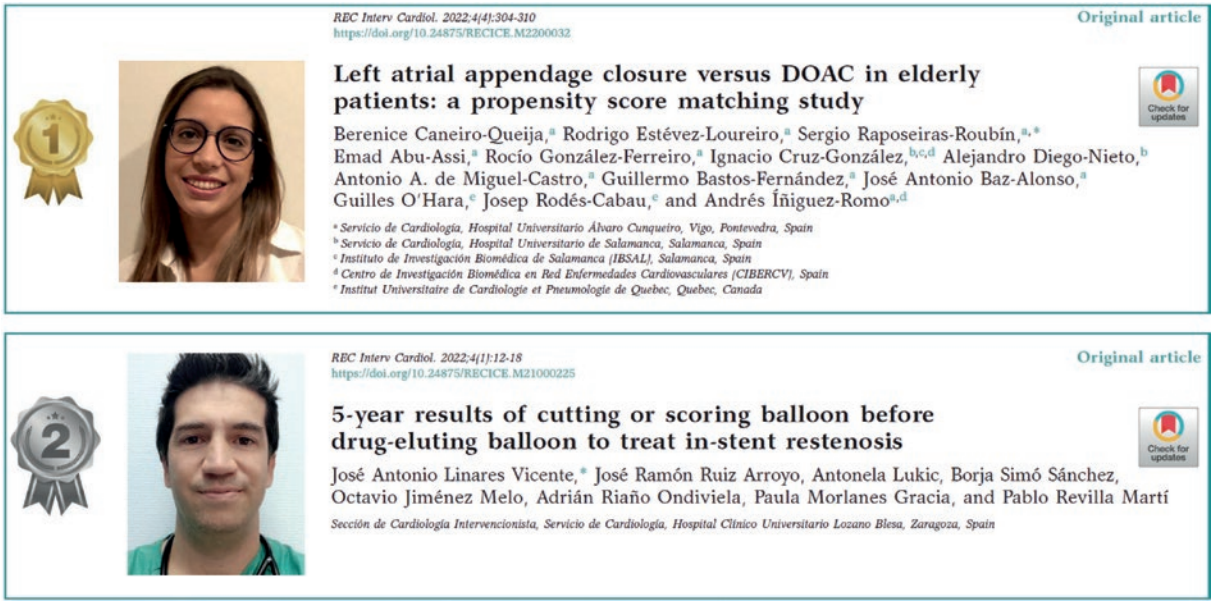


Figure 11. *REC Interv Cardiol* original articles awarded in 2023.

Figure 12. Recent documents drafted by ACI-SEC for the journal.

In the coming years, the bibliometric growth of *REC: Interventional Cardiology* will depend largely on the continued support of the scientific community. Therefore, our team encourages authors to submit their research work. For our part, we are committed to maintaining our swift decision-making times and quality throughout the entire editorial process.

ACKNOWLEDGMENTS

As the editor-in-chief, I wish, once again to express my heartfelt gratitude to the associate editors: Fernando Alfonso, Raúl Moreno, Soledad Ojeda, Armando Pérez de Prado, and Rafael Romaguera (figure 14). The best dream team ever assembled.

REC: Interventional Cardiology is the official publication of ACI-SEC, and very few select journals have the endorsement of a professional association like ours, which truly sets us apart. The unwavering support of the ACI-SEC boards has been instrumental in bringing this project to fruition since its inception. The ACI-SEC fully funds the journal, ensuring its high production quality, and provides free access to readers, which would not be feasible without the selfless support from the interventional cardiology devices market.

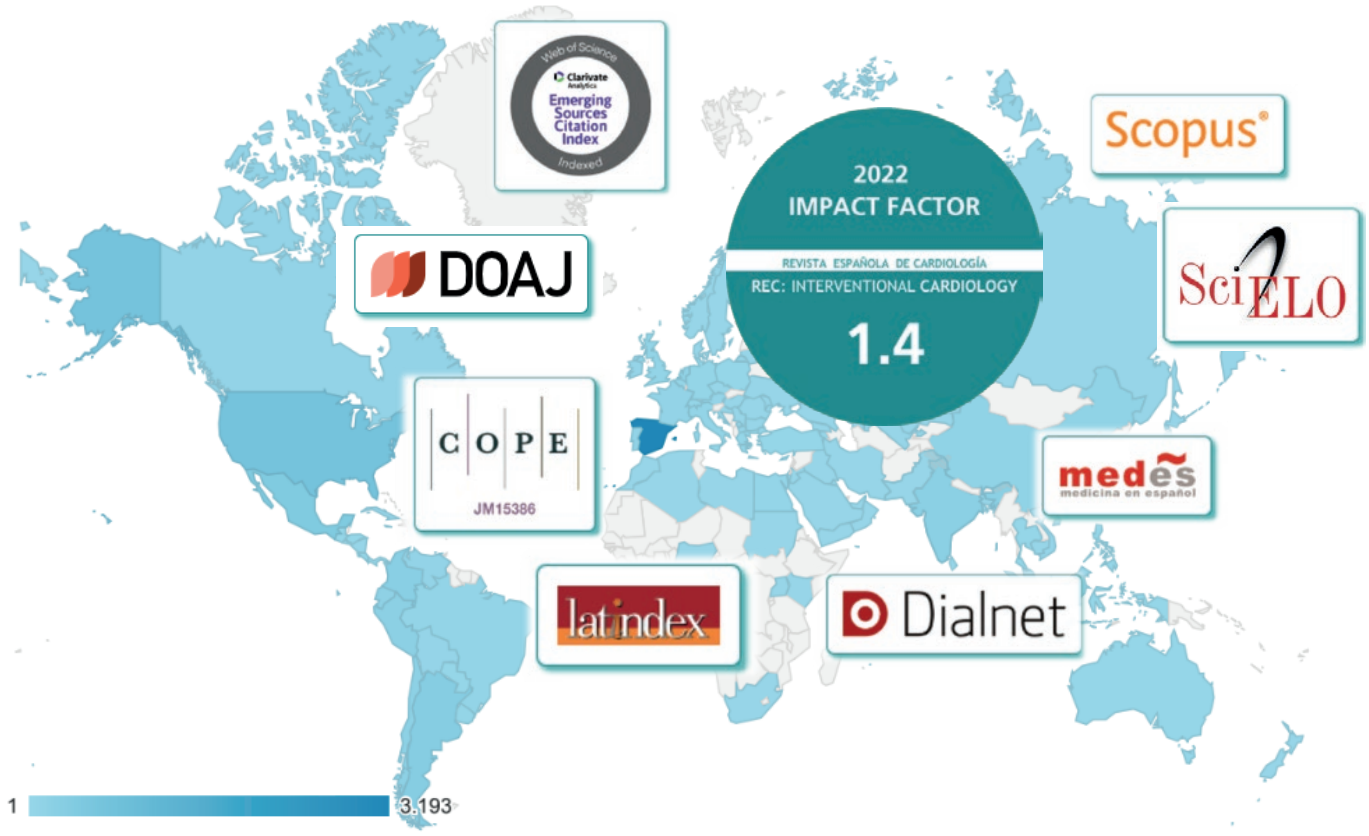


Figure 13. Impact factor and current indexations of *REC Interventional Cardiology*.

Figure 14. *REC Interventional Cardiology* editorial team.

As always, we wish to express our appreciation for the excellent work and dedication shown by the members of REC Publications editorial team, including Iria del Río, Eva M. Cardenal, Belén Juan, María González Nogal, Helena Gómez Lobo, and our latest addition, Javier Esquinas. We also extend our thanks to our IT consultant, Juan Quiles, SEC IT team, and the entire team at Permanyer Group.

What truly matters is not the goals we set in life but the path followed in the meantime. Setting goals is good, but moving step by step and seizing the moment is the true secret of success.

FUNDING

None declared.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Clarivate Analytics. Journal Citation Reports 2023 Edition. Available at: https://clarivate.com/training/journal-citation-reports-2023-edition/. Accessed 28 Jun 2023.
2. De la Torre-Hernández JM, Alfonso F, Moreno R, Ojeda S, Pérez de Prado A, Romaguera R. *REC: Interventional Cardiology*: on the right track. *REC Interv Cardiol*. 2022;4:261-266.
3. De la Torre-Hernández JM, Alfonso F, Sanchis J, Moreno R. *REC: Interventional Cardiology* in the COVID-19 year. *REC Interv Cardiol*. 2021;3:239-244.
4. De la Torre-Hernández JM, Alfonso F, Sanchis J, Moreno R. The first two years of *REC: Interventional Cardiology*. *REC Interv Cardiol*. 2020;2:233-238.
5. De la Torre-Hernández JM, Alfonso F, Sanchis J, Moreno R. *REC: Interventional Cardiology*: A new journal, but not just one more journal. *REC Interv Cardiol*. 2019;1:2-3.
6. Alfonso F, Bermejo J, Segovia J. Impactology, impactitis, impactotherapy. *Rev Esp Cardiol*. 2005;58:1239-1245.

7. Resúmenes presentados al 34 Congreso de la Asociación de Cardiología Intervencionista de la Sociedad Española de Cardiología. *REC Interv Cardiol*. 2023;C1-C7.
8. Caneiro-Queija B, Estévez-Loureiro R, Raposeiras-Roubín S, et al. Left atrial appendage closure versus DOAC in elderly patients: a propensity score matching study. *REC Interv Cardiol*. 2022;4:304-310.
9. Linares Vicente JA, Ruiz Arroyo JR, Lukic A, et al. 5-year results of cutting or scoring balloon before drug-eluting balloon to treat in-stent restenosis. *REC Interv Cardiol*. 2022;4:12-18.
10. REC Interventional Cardiology. Available at: https://recintervcardiol.org/es. Accessed 30 Jun 2023.
11. Twitter. @RevEspCardiol. Available at: https://twitter.com/revespcardiol. Accessed 27 Jun 2023.
12. Freixa X, Romaguera R, Botas J, Trillo R, Martín-Moreiras J, Jurado-Román A. Vascular access approach for structural heart procedures. *REC Interv Cardiol*. 2022;4:311-318.
13. McInerney A, Escaned J, Gonzalo N. Calcified coronary artery disease: pathophysiology, intracoronary imaging assessment, and plaque modification techniques. *REC Interv Cardiol*. 2022;4:216-227.
14. Jurado-Román A, Gómez-Menchero A, Nieves Gonzalo N, et al. Plaque modification techniques to treat calcified coronary lesions. Position paper from the ACI-SEC. *REC Interv Cardiol*. 2023;5:46-61.
15. REC: Interventional Cardiology. Vídeos del Editor. Available at: https://recintervcardiol.org/es/videos-del-editor/. Accessed 30 Jun 2023.
16. Rodríguez-Leor O, Cid-Álvarez AB, Moreno R, et al.; on behalf of the investigators from the Infarction Code Working Group of the ACI-SEC. Regional differences in STEMI care in Spain. Data from the ACI-SEC Infarction Code Registry. *REC Interv Cardiol*. 2023;5:118-128.
17. Ballesteros Tejerizo F, Coserría Sánchez F, Freixa X, et al. Spanish cardiac catheterization in congenital heart diseases registry. Second official report from the ACI-SEC and the GTH-SECPCC (2021). *REC Interv Cardiol*. 2023; 5:185-192.

REC Interv Cardiol. 2023;5(4):247-249
https://doi.org/10.24875/RECICE.M23000399

Editorial

Optimizing radiation exposure in interventional cardiology: are current doses appropriate?

¿Son adecuadas las dosis de radiación que utilizamos en los procedimientos intervencionistas?

Eliseo Vañó Carruana,[a,b,*] José Miguel Fernández Soto,[a,b] and Roberto Mariano Sánchez Casanueva[a,b]

[a] *Servicio de Física Médica, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Madrid, Spain*
[b] *Departamento de Radiología, Universidad Complutense, Madrid, Spain*

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M23000372

Are the radiation doses we use in interventional procedures appropriate? Cardiologists should be able to answer this question, which is particularly important in pediatric patients. However, the answer matters not only to patients but also to the health professionals involved in these procedures. The occupational radiation doses received by health staff are associated with the doses received by patients, and "optimization" (keeping radiation doses to the minimum needed to achieve the clinical objective of the procedures involved) should be managed comprehensively for patients and professionals alike.[1]

The International Commission on Radiological Protection (ICRP) recommends using "diagnostic reference levels" (DRLs) to help in the optimization of imaging modalities with ionizing radiation (including interventional procedures).[2]

DRLs are indicative of "good clinical practice". It is recommended that they be established for specific clinical indications and can be estimated for the local, national, or regional level by using the third quartile of the distribution of the median values of the dose indicators for patients from various centers representative of these clinical practices.[2]

The term "achievable dose value" has been proposed in the United States for the 50th percentile instead of the third quartile. Although the ICRP has stated that the median could be used as an additional step in optimization, the recommendation of using the third quartile recommendation to estimate DRLs still stands.[2]

For interventional procedures, the most widely used radiological measure is the kerma-area product (KAP), which is numerically equivalent to the dose-area product (DAP), and serves as one of the main indicators of the radiation doses received by patients. Secondary indicators that can also be used are the kerma at the patient entrance reference point (15 cm below the isocenter), fluoroscopy time, and the number of cine images acquired. These latter 2 indicators are becoming less relevant because doses depend on different image acquisition modes.

The ICRP recommends taking into consideration the complexity of interventional procedures, since it can increase DRLs significantly. Because complexity can vary widely for a single procedure, carried out for the same or similar clinical indications, it is important to assess its impact on the doses delivered to patients.[3,4]

The ICRP recommendations have been included in the European regulations (Directive 59/2013 EURATOM)[5] and the corresponding practical guidelines of the European Union.[6,7] For pediatric procedures, it is suggested that DRLs be estimated based on patient age and weight categories.[2]

The radiation doses received by pediatric patients vary widely depending on their size and weight. Although variations are inevitable, we should try to avoid those stemming from inappropriate use of imaging modalities (different fluoroscopy or cine modes) or protocols. DRLs help optimize radiation protection.

Different fluoroscopy and cine modes with varying dose rates (and image quality) can be used, substantially impacting the radiation doses received by patients. Factors that play a key role in delivered radiation doses are collimation, C-arm x-ray machine angles, fluoroscopy sequence recording to save cine sequences, and rotational acquisitions.

Ways to significantly reduce the radiation doses received by patients and health professionals are knowing the quality control results of x-ray machines (to understand dose differences between cine and fluoroscopy acquisitions) and fostering collaboration between hospital radiologists and cardiologists, along with continuous medical education programs on radiation safety.

All these variables associated with different operating modes can substantially change the doses delivered to patients and the quality of diagnostic information. Therefore, cardiologists' knowledge and experience of their imaging equipment are crucial. In general, state-of-the-art machines reduce radiation doses while maintaining similar or improved diagnostic information. Quantifying all these

*** Corresponding author.**
E-mail address: eliseov@med.ucm.es (E. Vañó Carruana).

Online 3 October 2023.

factors and deciding whether corrective actions are needed involves comparing radiation doses for specific procedures with the DRLs.

The Royal Decree that transposes part of the European Directive to the Spanish legislation[8] demonstrates the implementation and regular review of DRLs. If these DRLs are consistently and significantly exceeded, or if image quality deteriorates repeatedly, the corresponding local reviews should be undertaken and appropriate corrective measures should be implemented without delay.

Some automated dose management systems allow real-time reception and processing of the radiation doses received by patients and operators. These systems can create alerts for safer interventional practices.[9,10]

Several studies have been published on DRLs in interventional cardiology for adult patients (DOCCACI program) in Spain[11,12] with collaboration from the Spanish Society of Cardiology.

No nationwide results have been published on the doses received by pediatric patients in interventional cardiology until now. However, Rueda Núñez et al.[13] recently presented the results of the Radcong-21 Registry conducted by the Cardiac Catheterization Working Group of the Spanish Society of Pediatric Cardiology and Congenital Heart Disease (GTH-SECPCC) on the overall values from a sample of 1090 procedures across 10 different hospitals. This registry represents a significant initiative that could encourage other centers to compare their values with dose indicators obtained from a representative sample of multiple Spanish hospitals in patients with congenital heart disease treated with cardiac catheterization and categorized by type of procedure and estimated radiation risk (ERR).

The study authors used medians, although DRL values refer to the third quartile of the distribution of the median values in the different centers involved. Specific DAP/kg values are provided for certain specific procedures to treat prevalent conditions such as aortic coarctations, atrial septal defects, ductus arteriosus occlusions, aortic and pulmonary valvuloplasties and pulmonary valve implantations following the methodology proposed by Quinn et al.[14] in the United States.

DAP/kg/fluoroscopy is a parameter that can be confusing when comparing radiation doses. This is because the total DAP includes contributions from fluoroscopic imaging—corresponding to different fluoroscopy modes with very different dose values—and cine acquisitions.

To facilitate comparisons and potential optimization efforts, the authors could provide dose indicator values (DAP/kg) tailored to a wider range of procedure types in future updates of the results. They could also use the third quartiles of the distribution of the median values for each center for the weight categories recommended by the ICRP and European guidelines.[2,6,7]

We could speculate whether it would be better to perform a global analysis across groups of different procedures or an analysis specifically designed for procedures with specific clinical indications. Quinn et al.[14] choose the former, while managing the DAP/kg values as the primary dose parameter. However, a global approach does not allow analysis of specific procedures requiring corrective measures when the doses delivered to some patients may be very high. These doses exceeding the "good clinical practice" threshold can be used in certain procedures, but not in others, within the 3 REC (Radiation Exposure Category) groups proposed by Quinn et al.[14] in their methodology. The advantage of using DRLs per weight group is that these DLRs are estimated for specific clinical indications, thus enabling easy comparisons with the dose indicators used in different hospitals for these procedures.

The global KAP/kg values for groups of different procedures may be balanced if there are procedures using higher radiation doses than necessary (due to excessive cine acquisitions, high-dose fluoroscopy modes, lack of collimation, etc) and other procedures requiring standard doses. This could indicate overall improvement (fewer doses in procedural groups), but does not necessarily indicate improvement in all types of procedures.

The effort made by the GTH-SECPCC to obtain and process PDA/kg values represents a significant advancement that could be further expanded in the future. This could involve establishing initial DRLs (KAP values) in Spain, based on weight and age groups, following the recommendations of the European guidelines and ICRP.

FUNDING

None.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. ICRP. Occupational radiological protection in interventional procedures. ICRP Publication 139. Ann. ICRP 2018 47. Available at: https://www.icrp.org/publication.asp?id=ICRP%20Publication%20139. Accessed 17 Jun 2023.
2. ICRP. Diagnostic reference levels in medical imaging. ICRP Publication 135. Ann. ICRP 2017. Available at: https://www.icrp.org/publication.asp?id=ICRP%20Publication%20135. Accessed 17 Jun 2023.
3. Bernardi G, Padovani R, Morocutti G, et al. Clinical and technical determinants of the complexity of percutaneous transluminal coronary angioplasty procedures: analysis in relation to radiation exposure parameters. *Catheter Cardiovasc Interv.* 2000;51:1-9; discussion 10.
4. Balter S, Miller DL, Vano E, et al. A pilot study exploring the possibility of establishing guidance levels in x-ray directed interventional procedures. *Med Phys.* 2008;35:673-680.
5. EUR-LEX. Council directive 2013/59/Euratom of 5 December 2013 laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation and repealing Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122/Euratom. Official Journal of the European Union. Available at: https://eur-lex.europa.eu/eli/dir/2013/59/oj. Accessed 3 Jul 2023.
6. Radiation Protection No 185 - European Guidelines on Diagnostic Reference Levels for Paediatric Imaging. Directorate-General for Energy Directorate D. Radiation Protection and Nuclear Safety. 2018. Available at: https://energy.ec.europa.eu/system/files/2018-09/rp_185_0.pdf. Accessed 17 Jun 2023.
7. Radiation Protection 195. European study on clinical diagnostic reference levels for X-ray medical imaging EUCLID. Luxembourg: Publications Office of the European Union, 2021. Available at: European study on clinical diagnostic reference levels for X-ray medical imaging - Publications Office of the EU (europa.eu). Accessed 3 Jul 2023.
8. Real Decreto 601/2019, de 18 de octubre, sobre justificación y optimización del uso de las radiaciones ionizantes para la protección radiológica de las personas con ocasión de exposiciones médicas. Boletín Oficial del Estado núm. 262, de 31 de octubre de 2019. Available at: https://www.boe.es/eli/es/rd/2019/10/18/601. Accessed 19 Jun 2023.
9. Vano E, Sanchez RM, Fernandez JM. Strategies to optimise occupational radiation protection in interventional cardiology using simultaneous registration of patient and staff doses. *J Radiol Prot.* 2018;38:1077-1088.
10. Vano E, Fernandez-Soto JM, Ten JI, Sanchez Casanueva RM. Occupational and patient doses for interventional radiology integrated into a dose management system. *Br J Radiol.* 2023;96:20220607.
11. Sánchez RM, Vano E, Fernández JM, Escaned J, Goicolea J, Pifarré X;

DOCCACI Group. Initial results from a national follow-up program to monitor radiation doses for patients in interventional cardiology. *Rev Esp Cardiol.* 2014;67:63-65.
12. Sánchez R, Vañó E, Fernández Soto JM, et al. Updating national diagnostic reference levels for interventional cardiology and methodological aspects. *Phys Med.* 2020;70:169-175.
13. Rueda Núñez F, Abelleira Pardeiro C, Insa Albert B, et al. Dosimetric parameters in congenital cardiac catheterizations in Spain: the GTH-SECPCC Radcong-21 multicenter registry. *REC Interv Cardiol.* 2023. https://doi.org/10.24875/RECICE.M23000372.
14. Quinn BP, Cevallos P, Armstrong A, et al. Longitudinal Improvements in Radiation Exposure in Cardiac Catheterization for Congenital Heart Disease: A Prospective Multicenter C3PO-QI Study. *Circ Cardiovasc Interv.* 2020;13:e008172.

REC Interv Cardiol. 2023;5(4):250-253
https://doi.org/10.24875/RECICE.M23000400

Editorial

Forty years of Cardialysis: a leading European cardiovascular research organization

Cuarenta años de Cardialysis: una organización europea líder en investigación cardiovascular

Ernest Spitzer,[a,b,c,*]

[a] *Cardialysis, Rotterdam, The Netherlands*
[b] *European Cardiovascular Research Institute, Rotterdam, The Netherlands*
[c] *Cardiology Department, Thoraxcenter, Erasmus University Medical Center, Rotterdam, The Netherlands*

Cardialysis was founded in 1983 by visionary professionals from the Thoraxcenter at Erasmus University Medical Center (EMC) in Rotterdam, The Netherlands. This initiative emerged to address the need for a specialized research organization able to plan, execute, and report European cooperative clinical investigations in the field of cardiovascular research.[1] The mission of Cardialysis is "*to be at the heart of cardiovascular research*" in the fullest sense of the phrase. To achieve this mission, the organization strives to collaborate with clinicians, trialists, research professionals, regulators, industry partners, and research organizations that share the same passion. Throughout the first 40 years, its well-established reputation has been based on dedication, diligence, and industry-leading standards. This has been made possible by attracting and retaining talented employees, as well as by cultivating long-standing relationships with investigators, clients, and partners.

Organizations similar to Cardialysis are typically classified as either academic research organizations (AROs) or contract research organizations (CROs). AROs, such as clinical trial units and epidemiology departments, are typically affiliated with universities or university hospitals, and usually design and manage investigator-initiated single-center or multicenter national clinical trials. These organizations are academically-driven and their traditional objectives are to facilitate research and education, publish innovative research in peer-reviewed journals, and support PhD programs. In contrast, CROs are private entities performing sponsor-driven clinical trials across all phases of clinical development. These organizations are business-driven, and expected to remain self-sustaining by establishing research contracts with the medical industry in a strict regulatory environment.

Similar to other world-leaders in cardiovascular research, Cardialysis has successfully adopted a hybrid ARO/CRO model, combining the best of the 2 models. First, the organization participates in innovative research that has played a pivotal role in the development and improvement of therapies in cardiology. This involvement has resulted in numerous high-impact publications and the completion of more than 100 theses through its support of in-house academic research. Figure 1 lists notable trials in which Cardialysis participated, including research in coronary artery disease, structural heart disease, heart failure, hypertension, and peripheral artery disease. Second, the organization proudly maintains a global network of renowned investigators who play key roles in the academic leadership of trials (eg, within steering committees), independent clinical events committees (CECs),[2] independent data and safety monitoring boards,[3] and imaging core lab supervision. Third, Cardialysis operates as a private, independent entity that serves both university hospitals worldwide, as well as leading pharmaceutical and medical device industry partners. Fourth, the organization maintains state-of-the-art infrastructure and follows standardized procedures, ensuring efficiency and quality. Finally, Cardialysis consistently adheres to applicable regulatory requirements for trial execution in all active regions, including Europe, the United States of America, and China.

THE CARDIALYSIS CORE LAB

Over the past half century, clinical research has had an enormous impact on clinical outcomes, which was eloquently summarized by Nabel and Braunwald.[4] These advancements are inextricably linked to the development of therapeutic and diagnostic devices, especially in interventional cardiology. The development of coronary angioplasty involved progressive iterations in coronary stent technologies and continuous innovation in intracoronary imaging.[5] Similarly, advancements in transcatheter therapies for aortic, mitral, and tricuspid conditions have paralleled the progress in imaging modalities and techniques.[6] Independent and consistent assessments of imaging outcomes are an important component of dossier evaluations when commercialization approvals are sought for new devices.[7]

Cardialysis started as a central reading facility for electrocardiography-Holter monitoring. However, over time it has validated and implemented rigorous analysis methodologies for various imaging techniques within the coronary core lab. These include quantitative coronary angiography (n = 67 000+), intravascular ultrasound (n = 16 000+), near-infrared spectroscopy (n = 1500+), and optical coherence tomography (n = 5000+). Notably, Cardialysis also launched and maintains the globally used SYNTAX score (n = 10 000+) website.[8] Due to a shift toward structural heart research, its echocardiography core lab has become its largest

*** Corresponding author.**
E-mail address: espitzer@cardialysis.nl (E. Spitzer).
@spitzertweets

Online 31 July 2023.

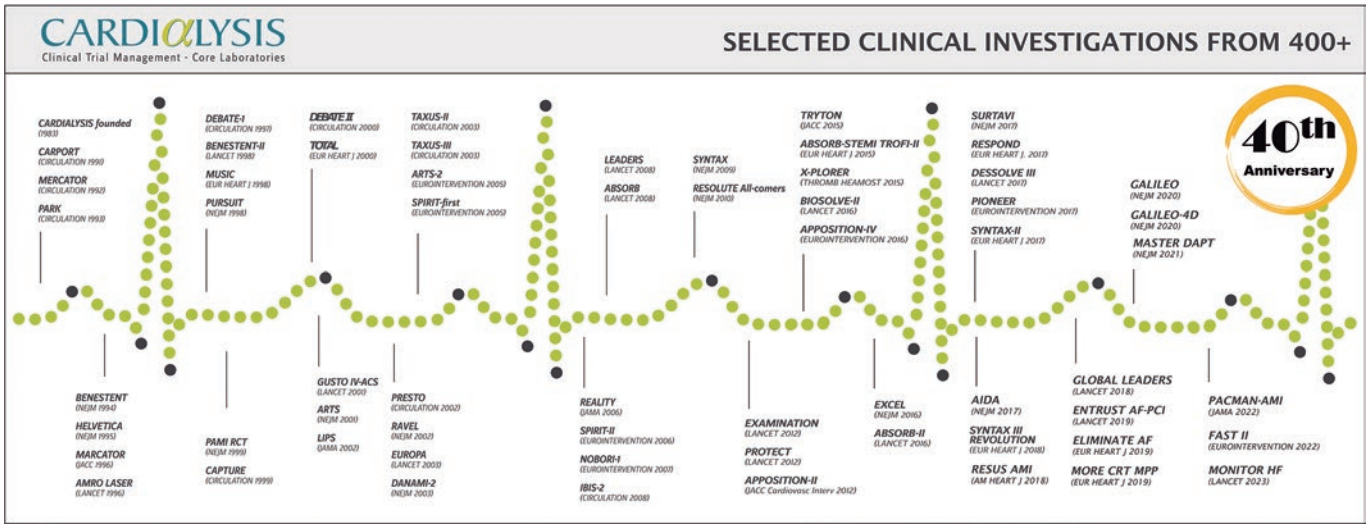


Figure 1. Timeline of landmark trials conducted with Cardialysis.

laboratory and serves large European and global investigations (n = 39 000+). Additionally, the organization operates magnetic resonance imaging (n = 1000+), cardiac computed tomography (n = 1000+), and electrocardiography-Holter core laboratories (n = 270 000+).

CARDIALYSIS CLINICAL TRIAL ACTIVITIES

The workload involved in a clinical investigation should not be underestimated. For example, the ongoing IVUS CHIP randomized clinical trial (NCT04854070) involves 40 sites in Europe and more than 200 professionals in the execution of the study, excluding the members of the Ethics Committees. Managing and coordinating more than 200 professionals across 7 countries for a minimum of 5 years requires high levels of availability, dedication, consistency, and well-established standardized procedures. Having an all-inclusive research organization performing ambitious trials increases efficiencies. Table 1 lists the activities performed at Cardialysis, which are those expected of any all-round professional research organization. Further information is available on the Cardialysis website.[8]

THE ACADEMIC RESEARCH CONSORTIUM

In 2006, with the increasing need for consistent endpoint definitions in coronary artery disease research, and specifically due to the challenges posed by the classification of stent thrombosis, leading AROs in the United States and Europe, including Cardialysis, collaborated to found the Academic Research Consortium (ARC).[8] The primary mission of the ARC is to promote informed and collaborative dialogue among stakeholders, with the goal of developing consensus definitions and nomenclature for targeted areas of new medical device development, and to disseminate such definitions in the public domain.[8] The first initiative focused on endpoint definitions and classifications for coronary intervention trials and was published in 2007.[9] This consensus document was developed in consultation with regulatory agencies in both the United States and Europe, and became one of the most cited articles in interventional cardiology. To date, the ARC has successfully launched and completed 20 programs and is currently running 15 new initiatives based on an unprecedented level of global scientific collaboration.[8]

Table 1. List of activities performed at a cardiovascular research organization

Trial design and protocol development
Steering committee set-up and coordination
Site feasibility and selection
Site start-up and regulatory submissions
Site contracting
Project management
Monitoring management
Site management and site monitoring
Safety reporting
Medical monitoring
Electronic case report forms development and hosting
Data management
Clinical events committee set-up and coordination
Data and safety monitoring board set-up and coordination
Publication committee set-up and coordination
Biostatistics: sample sizing, statistical analysis plan, and statistical reporting
Medical writing including patient narratives
Publication strategy
Quality assurance and regulatory compliance

EUROPEAN CARDIOVASCULAR RESEARCH INSTITUTE

Europe is known for its stringent regulations on academic research. Importantly, the sponsor of a clinical investigation is the legal entity (or individual) that ensures that regulations are met and that monitors patient safety either directly or through a data and safety monitoring board. The sponsor holds full rights to the study data (ie, has sole ownership) and is responsible for verifying data integrity, ensuring that published results are consistent with the locked

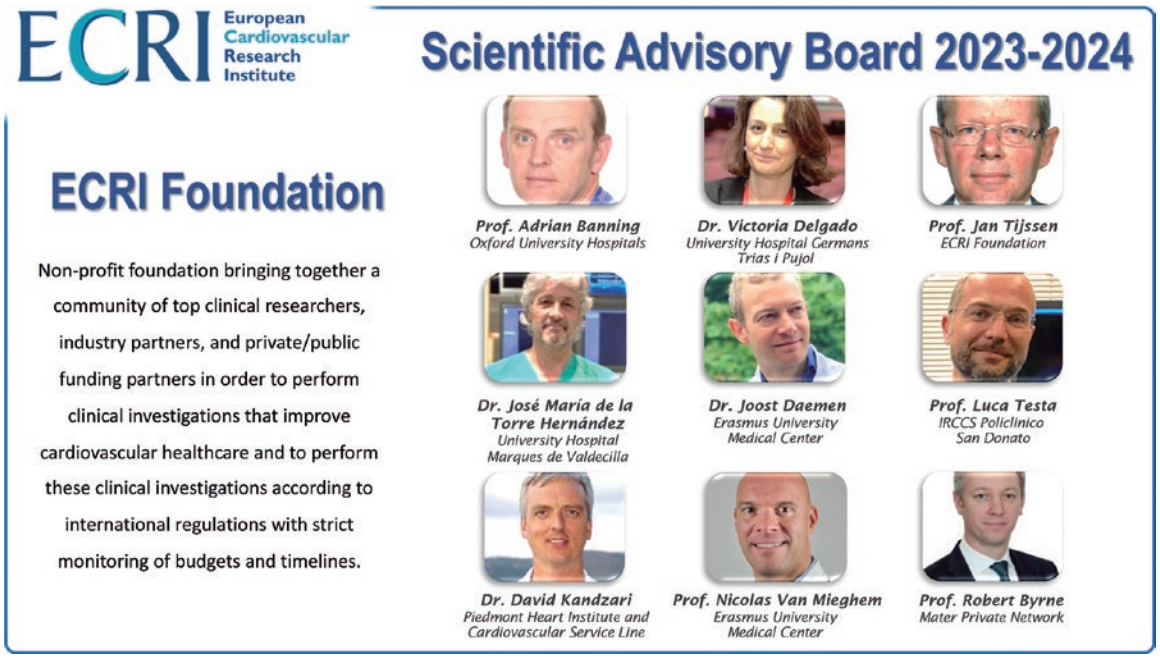


Figure 2. European Cardiovascular Research Institute foundation and its scientific advisory board. ECRI, European Cardiovascular Research Institute.

final analysis database. Although prominent academic centers possess the expertise to sponsor clinical trials, the size of certain studies requires external support for manageability.

In response to this need, the European Cardiovascular Research Institute (ECRI) was founded in 2012 by the Cardialysis group as an academic research platform capable of overseeing the execution of large, multicenter clinical trials and of fulfilling sponsor responsibilities. Since April 2023, the ECRI has become an independent foundation (*Stichting*) under Dutch law. This institute combines 3 elements of success: its outstanding academic leadership represented by its *pro bono* scientific advisory board (figure 2), a well-established network of investigators and research professionals, and the possibility to conduct clinical research activities in partnership with Cardialysis. Through this collaborative model, the ECRI-Cardialysis joint venture has successfully conducted some of the largest interventional cardiology trials, with the GLOBAL LEADERS trial being the most representative.[10] This trial enrolled 15 968 patients at 130 sites across 18 countries. Another example is the MASTER DAPT trial,[11] which enrolled 4579 high-bleeding risk patients at 140 sites in 30 countries.

The ECRI-Cardialysis partnership is currently conducting 3 landmark investigations on the use of coronary imaging and coronary physiology to guide percutaneous coronary interventions. Up-to-date details are available on the Cardialysis website.[8]

A LANDMARK FIGURE

Numerous clinicians and clinical research professionals have passed through the door of Cardialysis, with some staying for a lifetime and others for a short period. Undoubtedly, the most salient contributor to the organization's innovations and successes has been Prof. Patrick W. Serruys. His mentor, Prof. Paul Hugenholtz, acknowledged as the father of the European Society of Cardiology, and one of the founding members of Cardialysis, recognized Prof. Serruys as a natural talent and luminary in clinical research. Prof. Serruys joined Cardialysis during its early days and since then played a decisive role in the organization. His innovations and contributions included the development of coronary imaging techniques (eg, he was coinventor of quantitative coronary angiography); the establishment of best practices in interventional clinical trials, including the design and execution of the BENESTENT study,[12] which was the first of its kind and remains one of the most cited publications in interventional cardiology; research in bioresorbable scaffolds; and an illustrious career that garnered multiple distinctions and awards.[13] Although Prof. Serruys left the organization in 2019, his scientific legacy remains highly esteemed.

Currently, a new generation is shaping the present and future of the organization with unwavering commitment to innovation, collaborative research, and, above all, commitment to improved patient outcomes. The 40-year timeline of Cardialysis (figure 1) starts with the CARPORT trial led by Prof. Serruys from the Thoraxcenter, and concludes with the FAST II study led by Dr Joost Daemen[14] and the MONITOR HF trial led by Dr Jasper Brugts,[15] both also from the Thoraxcenter. While Cardialysis envisions expanding its European and global collaborations in the coming decades, its scientific partnership with EMC has remained strong and will continue to flourish.

THE FUTURE

Cardialysis pledges to continue contributing to the design, execution and reporting of clinical trials as an independent and scientifically-driven cardiovascular research organization and core laboratory. Its priorities are patient safety, data integrity, and the production of high-quality data, which have been achieved by committed employees, passionate investigators, and long-standing collaboration with its valued partners.

Additionally, Cardialysis remains committed to further advancing continued standardization of clinical trial definitions, design principles, and core laboratory methods, given that standardization has proven to be a catalyst in clinical research. Current innovations at Cardialysis focus on implementing artificial intelligence, streamlining clinical trial processes, harnessing the potential of real-world data, and mastering applicable regulatory science.

FUNDING

None.

CONFLICTS OF INTEREST

E. Spitzer is a board member and shareholder of Cardialysis and a board member of the ECRI.

ACKNOWLEDGMENTS

Our 40th anniversary is dedicated to our beloved colleague Eline Montauban van Swijndregt†.

REFERENCES

1. Organization, review, and administration of cooperative studies (Greenberg Report): a report from the Heart Special Project Committee to the National Advisory Heart Council, May 1967. *Control Clin Trials*. 1988;9:137-148.
2. Spitzer E, Fanaroff AC, Gibson CM, et al. Independence of clinical events committees: A consensus statement from clinical research organizations. *Am Heart J*. 2022;248:120-129.
3. United States Food and Drug Administration. Guidance for Clinical Trial Sponsors. Establishment and Operation of Clinical Trial Data Monitoring Committees. March 2006. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/establishment-and-operation-clinical-trial-data-monitoring-committees. Accessed 30 June 2023.
4. Nabel EG, Braunwald E. A tale of coronary artery disease and myocardial infarction. *N Engl J Med*. 2012;366:54-63.
5. van Zandvoort LJC, Ali Z, Kern M, van Mieghem NM, Mintz GS, Daemen J. Improving PCI Outcomes Using Postprocedural Physiology and Intravascular Imaging. *JACC Cardiovasc Interv*. 2021;14:2415-2430.
6. Casenghi M, Popolo Rubbio A, Menicanti L, Bedogni F, Testa L. Durability of Surgical and Transcatheter Aortic Bioprostheses: A Review of the Literature. *Cardiovasc Revasc Med*. 2022;42:161-170.
7. United States Food and Drug Administration. Clinical Trial Imaging Endpoint Process Standards. Guidance for Industry. April 2018. Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-imaging-endpoint-process-standards-guidance-industry. Accessed 30 June 2023.
8. Cardialysis. Available at: www.cardialysis.nl/library/links. Accessed 2 July 2023.
9. Cutlip DE, Windecker S, Mehran R, et al; and Academic Research C. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344-2351.
10. Vranckx P, Valgimigli M, Juni P, et al; and Investigators GL. Ticagrelor plus aspirin for 1 month, followed by ticagrelor monotherapy for 23 months vs aspirin plus clopidogrel or ticagrelor for 12 months, followed by aspirin monotherapy for 12 months after implantation of a drug-eluting stent: a multicentre, open-label, randomised superiority trial. *Lancet*. 2018;392:940-949.
11. Valgimigli M, Frigoli E, Heg D, et al; and Investigators MD. Dual Antiplatelet Therapy after PCI in Patients at High Bleeding Risk. *N Engl J Med*. 2021;385:1643-1655.
12. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Study Group. *N Engl J Med*. 1994;331:489-495.
13. Serruys DP. Featuring: Dr Patrick Serruys. *Eur Cardiol*. 2018;13:80-82.
14. 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.
15. Brugts JJ, Radhoe SP, Clephas PRD, et al; investigators M-H. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. *Lancet*. 2023;401:2113-2123.

REC Interv Cardiol. 2023;5(4):254-262
https://doi.org/10.24875/RECICE.M23000372

Original article

Dosimetric parameters in congenital cardiac catheterizations in Spain: the GTH-SECPCC Radcong-21 multicenter registry

Fernando Rueda Núñez,[a,*] César Abelleira Pardeiro,[b] Beatriz Insa Albert,[c] María Álvarez-Fuente,[d] Vanesa Balboa Barreiro,[e] Fernando Ballesteros Tejerizo,[f] Pedro Betrián-Blasco,[g] Félix Coserría Sánchez,[h] Juana María Espín López,[i] Luis Fernández González,[j] Dolores Herrera Linde,[k] Miguel Romero Moreno,[l] Fernando Sarnago Cebada,[m] Ricardo Sanz-Ruiz,[n,o] and Juan Ignacio Zabala Argüelles[p]

[a] *Unidad de Cardiología Infantil, Servicio de Pediatría, Complexo Hospitalario Universitario de A Coruña, Servicio Gallego de Salud, A Coruña, Spain*
[b] *Unidad de Hemodinámica, Servicio de Cardiología Infantil, Hospital Universitario La Paz, Madrid, Spain*
[c] *Sección de Cardiología Infantil, Hospital Universitario y Politécnico La Fe, Valencia, Spain*
[d] *Unidad de Hemodinámica, Servicio de Cardiología Infantil, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[e] *Unidad de Apoyo a la Investigación, Instituto de Investigación Biomédica de A Coruña, Complexo Hospitalario Universitario A Coruña, Servicio Gallego de Salud, Universidade da Coruña, A Coruña, Spain*
[f] *Unidad de Hemodinámica, Servicio de Cardiología Infantil, Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[g] *Unidad de Hemodinámica Pediátrica, Servicio de Cardiología Pediátrica, Hospital Universitari Vall d'Hebron, Barcelona, Spain*
[h] *Servicio de Cardiología Pediátrica, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[i] *Sección de Cardiología Pediátrica, Hospital Universitario Virgen de la Arrixaca, El Palmar, Murcia, Spain*
[j] *Sección de Hemodinámica-Cardiología, Hospital Universitario de Cruces, Barakaldo, Bilbao, Spain*
[k] *Instituto Pediátrico del Corazón, Hospital Universitario 12 de Octubre, Instituto de Investigación Sanitaria 12 de Octubre, Madrid, Spain*
[l] *Servicio de Cardiología, Hospital Universitario Reina Sofía, Universidad de Córdoba, Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba, Spain*
[m] *Unidad de Cardiopatías Congénitas del Adulto, Servicio de Cardiología, Hospital Universitario 12 de Octubre, Madrid, Spain*
[n] *Servicio de Cardiología, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, Universidad Complutense de Madrid, Madrid, Spain*
[o] *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[p] *Sección de Cardiología Pediátrica, Hospital Regional Universitario de Málaga, Málaga, Spain*

ABSTRACT

Introduction and objectives: The results of the Radcong-21 Registry of the Spanish Society of Pediatric Cardiology and Congenital Heart Disease Working Group on Hemodynamics are described to analyze data, establish updated reference parameters, and compare them to other registries.
Methods: Retrospective, cross-sectional, observational, multicenter registry of patients with congenital heart disease undergoing cardiac catheterization in 2021. Each cath lab sent the last 100 cases performed prior to January 2022. A descriptive analysis was conducted of anthropomorphic variables, procedural (grouped by type and radiation exposure categories [REC]) and technical characteristics, and dosimetric parameters with additional review of all values outside the 95%CI of the median.
Results: A total of 1090 procedures performed in 11 cath lab of 10 hospital centers were analyzed. Age distribution: 22.8% < 1 year, 60.7% between 1-18 years, and 16.4% > 18 years. In dose area product (DAP)/Kg and DAP/Kg/fluoroscopy, the distribution was very similar regardless of the type of cath lab as is the case with most pediatric patients in terms of age, weight, and REC group. The DAP/Kg was higher in the REC I and III groups compared to other countries with registries and improvement programs in this area (78% and 8,3%, respectively).
Conclusions: Representative data of dosimetric parameters by age and procedures in congenital cardiac catheterizations were obtained in Spain back in 2021. DAP/Kg is the parameter with the lowest dispersion in the sample. There is room for improvement compared to other countries with optimization programs in this area.

Keywords: Congenital heart disease. Angiography. Pediatric cardiac cath lab. Radiation dose. Radiation protection.

*** Corresponding author.**
E-mail address: Fernando.Rueda.Nunez@sergas.es (F. Rueda Núñez).

Received 10 January 2023. Accepted 15 February 2023. Online 3 May 2023.

Parámetros dosimétricos en cateterismos para cardiopatías congénitas en España: registro multicéntrico Radcong-21 del GTH-SECPCC

RESUMEN

Introducción y objetivos: Se describen los resultados del Registro Radcong-21 del Grupo de Trabajo de Hemodinámica de la Sociedad Española de Cardiología Pediátrica y Cardiopatías Congénitas con el objetivo de analizar los datos, establecer parámetros de referencia actualizados y compararlos con otros registros.
Métodos: Registro multicéntrico, observacional, transversal y retrospectivo de pacientes con cardiopatías congénitas tratados con cateterismo cardiaco en 2021. Cada sala de hemodinámica remite los últimos 100 casos realizados hasta enero de 2022. Análisis descriptivo de variables antropomórficas, procedimientos (agrupados por tipo y riesgo estimado de radiación [RER]), características técnicas y parámetros dosimétricos. Revisión adicional de todos los valores fuera del intervalo de confianza del 95% de la mediana.
Resultados: Se analizaron 1.090 procedimientos en 11 salas de hemodinámica de 10 centros hospitalarios. De los pacientes, el 22,8% fueron < 1 año, el 60,7% entre 1 y 18 años, y el 16,4% > 18 años. Los valores del producto dosis-área (PDA)/kg y del PDA/kg/fluoroscopia fueron muy similares independientemente del tipo de sala, al igual que ocurre con la edad, el peso y el grupo RER en la mayor parte de las salas pediátricas. El PDA/kg fue superior en los grupos RER I y III comparado con otros países con registros y programas de mejora activos en este campo (un 78 y un 8,3%, respectivamente).
Conclusiones: Se obtienen datos representativos de los parámetros dosimétricos por edad y procedimientos en los cateterismos cardiacos congénitos en España en el año 2021. El PDA/kg es el que tiene menor dispersión en la muestra total. Existen áreas de mejora en comparación con otros países con programas de optimización.

Palabras clave: Cardiopatía congénita. Angiografía. Sala de hemodinámica pediátrica. Dosis de radiación. Protección radiológica.

Abbreviations

ASD: atrial septal defect. **CL:** cath lab. **DAP:** dose-area product. **REC:** radiation exposure category. **SECPCC:** Spanish Society of Pediatric Cardiology and Congenital Heart Disease. **VSD:** ventricular septal defect.

INTRODUCTION

Over the past few years, interventional procedures to treat congenital heart diseases have become an inescapable reality across all age ranges. The use of ionizing radiation is no stranger to health risks for the patients and health professionals involved, which is why the Spanish legislation and the International Commission on Radiological Protection recommend registering the dose of radiation received and establishing and applying reference values for the different fluoroscopy-guided procedures. Doses that should be reviewed on a regular basis.[1-3] In this context, it is necessary to register local data to facilitate comparisons and good clinical practice analysis across different centers.

The Spanish Society of Cardiology Working Group on Pediatric Cardiology and Congenital Heart Disease (GTH-SECPCC) presented a communication in its National Meeting held back in 2017 to establish the very first approach to this problem. Previous attempts had been made regarding coronary procedures like the one published by the Interventional Cardiology Association of the Spanish Society of Cardiology Working Group on Dosimetry and Quality Criteria in Interventional Cardiology.[4] However, to this date, no similar reports on the pediatric age or patients with congenital heart diseases have been published in our country.

The main objective of this study was to show and analyze current data of representative dosimetric parameters from cardiac catheterizations performed in patients with congenital heart disease in Spain. Also, an attempt was made to establish the reference values for such parameters in our country by age group and type of intervention and compare them with other registries already established in different countries.

METHODS

This was a multicenter, observational, cross-sectional, and retrospective study. It describes the dosimetric parameters of procedures performed in Spain in a large number of patients with congenital heart diseases in 2021. The rules and regulations settled by the different centers involved have been observed at all times to access clinical data. Patients and hospitals have been anonymized and coded with consecutive numerical tags. The study protocol was approved by the reference research unit Ethics Committee (code 2018/491). Informed consent was not deemed necessary due to the retrospective and observational nature of the study with the sole purpose of improving healthcare.

The study population included the last 100 cardiac catheterizations performed in patients with congenital heart diseases in each cath lab (CL) until January 2022. GTH-SECPCC affiliated centers were asked to participate. Case mining was performed consecutively and regardless of the type of procedure performed and the patient's characteristics. No external auditing was possible. However, to have maximum quality control according to the principle established in the STROBE (Strengthening the reporting of observational studies in epidemiology) checklist[5] it was decided that all data received outside the 95% confidence interval (95%CI) values of the median should be submitted to researchers for additional outcome review, confirmation, and justification. Therefore, the exclusion criteria were an n < 50 cases per CL, cardiac catheterizations performed prior to 2021, those performed in patients without congenital heart disease, failure to fill in the registry form with all the variables (except for air kerma), and negative responses (or no response at all) to the review and additional confirmation, if necessary. The foramen ovale was not considered a congenital heart disease, and CLs with > 75% of cases rejected were excluded from the analysis.

The following variables were collected:

- Anthropomorphic parameters: age, weight (kg), height (cm), and body surface area (m^2).
- Types of procedure grouped into 16 different categories: pulmonary branch angioplasty, right ventricular outflow tract angioplasty, stenting in ductus arteriosus or fistula, coarctation of aorta, other angioplasties, pulmonary valve implantation, closure of atrial septal defect (ASD), closure of ventricular septal defect, closure of ductus arteriosus, closure of collaterals, aortic valvuloplasty, pulmonary valvuloplasty, combined procedure, pulmonary vasodilator test, diagnostic catheterization, and other. Also, to compare them with other series published, the procedures were grouped into radiation exposure categories (REC) based on the criterion used by Quinn et al.[6] in 3 different groups of diseases with similar doses of radiation anticipated and arranged in descending order.
- Technical characteristics: use of biplane or 3D rotational angiography (3DRA), and type of CL.
- Dosimetric parameters: dose-area product (DAP, μGym^2), air kerma (AK, mGy), and fluoroscopy time (min).

Statistical analysis

The descriptive analysis of the variables included in the study was conducted using the statistical software packages SPSS, version 28.0, and R version 4.1.2. Bilateral comparisons were used, and *P* values < .05 were considered statistically significant. Qualitative variables were expressed as absolute and relative frequencies. The quantitative ones were expressed as median and its 95%IC following the criterion used in former reference studies to facilitate comparison with our results, and read and interpret the tables much easier. Median comparisons were also drawn. The supplementary data includes the mean and interquartile range for each variable in the description of the overall sample (table 1 of the supplementary data), the REC groups (tables 2 to 4 of the supplementary data), and type of CL (tables 5 to 7 of the supplementary data).

A description of the entire sample based on the REC group and type of CL was made. Radiation parameters were described both in general and by participant CL, per type of CL, age group and type of procedure.

The comparison of radiation parameters based on the type of CL was made through median comparison by applying Bonferroni correction. Scatter plots were used among the different exposure parameters DAP/Kg, and DAP/Kg/fluoroscopy (Y axis), and weight (X axis) both in general and by REC gruop.

RESULTS

Sample population

In Spain, interventional activity to treat patients with congenital heart diseases is performed in 3 different types of CLs based on the profile of each patient: preferential dedication to patients < 18 years (pediatric type), preferential dedication to patients > 18 years (adult type), and no age discrimination (hybrid type). A total of 12 hospitals responded to the registry request. In 2 of them, interventional activity takes place in different CLs and with different heart teams depending on whether patients are children or adults. Therefore, the total number of participant CLs was 14: 8 pediatric, 4 hybrid, and 2 adult CLs. After applying the exclusion criteria, data from 3 CLs were excluded: 1 for having an n < 50, and 2 because > 75% of the cases met the exclusion criteria (most of them for not responding to the review petition and additional confirmation request). The total number of procedures submitted by the remaining 11 CLs was 1100, 10 of which were excluded due to negative responses to the additional review. Finally, in this study, data of 1090 procedures from 10 hospitals for a total of 11 CLs (7 pediatric, 3 hybrid, and 1 adult) were analyzed. Flowchart is shown on figure 1. The medians of age and weight were 6 years old (95%CI, 6-7), and 20 Kg (95%CI, 19-22.1). Distribution by age group was 22.8% < 1 year, 60.7% between 1 and 18 years, and 16.4%

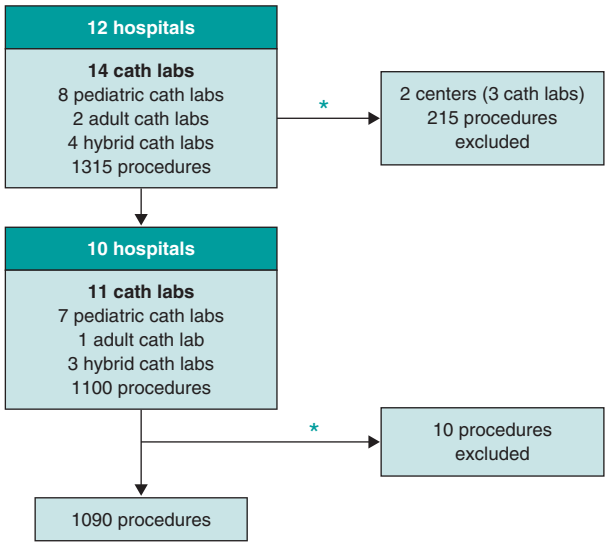


Figure 1. Flowchart of the selection of the procedures analyzed. * Exclusion criteria: n < 50 cases per cath lab, catheterizations performed before 2021, in patients without congenital heart disease, failure to fill in the registry form with all the variables (except for air kerma), and negative responses (or no reponse at all) to review or additional confirmation, if necessary. All cath labs with > 75% of cases rejected were excluded from the analysis.

Table 1. Demographic characteristics and dosimetric parameters of the overall sample

	N	Mean	Median	95%CI (median)
Age	1090	11.03	6	6-7
Weight (kg)	1090	29.69	20	19-22.1
Height (cm)	1090	113.46	114	109-119
BSA (m^2)	1090	0.93	0.8	0.77-0.87
Air kerma (mGy)	889	286.26	83.02	76.47-92.8
DAP (μGym^2)	1090	3783.27	1128.9	975.62-1275
Fluoroscopy (min)	1090	21.29	15.12	14.13-16.2
DAP/fluoroscopy ($\mu Gy.m^2/kg/min$)	1090	216.18	77.62	70.11-88.89
DAP/kg ($\mu Gy.m^2/kg$)	1090	132.38	62.3	56.75-69.03
DAP/BSA	1090	3500.87	1633.57	1480-1811.09
DAP/Kg/fluoroscopy	1090	8.28	3.81	3.54-4.06
DAP/BSA/fluoroscopy	1090	213.84	99.73	91.99-107.09

95%CI, 95% confidence interval; BSA, body surface area; DAP: dose-area product.

Table 2. Procedures per REC group and type of cath lab

	Total	REC	Type of cath lab		
			Pediatric	Adult	Hybrid
	N (%)	N (%)[a]	N (%)	N (%)	N (%)
Total general	1090 (100)	910 (100)	691 (63.4)	100 (9.2)	299 (27.4)
Total REC I	743 (68.2)	743 (81.7)	453 (65.6)	78 (78)	212 (70.9)
Stenting of the ductus arteriosus or fistula	9 (0.8)	9 (1)	5 (0.7)	0 (0)	4 (1.3)
Coarctation of aorta	66 (6.1)	66 (7.3)	45 (6.5)	1 (1)	20 (6.7)
Occlusion of ASD	128 (11.7)	128 (14.1)	79 (11.4)	8 (8)	41 (13.7)
Occlusion of ductus arteriosus	155 (14.2)	155 (17)	98 (14.2)	1 (1)	56 (18.7)
Aortic valvuloplasty	29 (2.7)	29 (3.2)	19 (2.8)	1 (1)	9 (3)
Pulmonary valvuloplasty	67 (6.2)	67 (7.4)	48 (7)	2 (2)	17 (5.7)
Pulmonary vasodilator test	12 (1.1)	12 (1.3)	6 (0.9)	0 (0)	6 (2)
Diagnostic catheterization	277 (25.4)	277 (30.4)	153 (22.1)	65 (65)	59 (19.7)
Total REC II	145 (13.3)	145 (15.9)	103 (15)	10 (10)	32 (10.7)
Pulmonary branch angioplasty	81 (7.4)	81 (8.9)	57 (8.3)	5 (5)	19 (6.4)
RVOT angioplasty	21 (1.9)	21 (2.3)	14 (2)	4 (4)	3 (1)
Occlusion of VSD	24 (2.2)	24 (2.6)	19 (2.8)	0 (0)	5 (1.7)
Collateral closure	19 (1.7)	19 (2.1)	13 (1.9)	1 (1)	5 (1.7)
Total REC III	22 (2)	22 (2.4)	8 (1.2)	4 (4)	10 (3.3)
Pulmonary valve implantation	22 (2)	22 (2.4)	8 (1.2)	4 (4)	10 (3.3)
Total no REC	180 (16.5)	0	127 (18.3)	8 (8)	45 (15.1)
Other angioplasties	32 (2.9)	0	14 (2)	7 (7)	11 (3.7)
Combined	90 (8.3)	0	72 (10.4)	1 (1)	17 (5.7)
Other	58 (5.3)	0	41 (5.9)	0 (0)	17 (5.7)

ASD, atrial septal defect; REC, radiation exposure category; RVOT, right ventricular outflow tract; VSD, ventricular septal defect.
[a] Percentage on the total number of patients included in REC groups; in the remaining columns, percentage is on the overall number.

> 18 years. In the overall sample, the median of dosimetric parameters was 1128.9 µGym^2 (95%CI, 975.6-1275) for the DAP (n = 1090), 15.12 min (95%CI, 14.1-16.2) for fluoroscopy time (n = 1090), and 83 mGy (95%CI, 76.5-92.8) for AK (n = 889). We should mention that 2 of the CLs (1 adult and 1 pediatric) just don't register AK on a routine basis (table 1).

Type of procedures

Table 2 shows the distribution of procedures based on the REC group developed by Quinn et al.,[6] and the type of CL. A total of 83.5% of all procedures performed were categorized into some of the REC groups (81.7%, 15.9%, and 2.4% in groups I, II, and III, respectively). A total of 63.4%, 27.4%, and 9.2% of the procedures were performed in pediatric, hybrid, and adult CLs, respectively. The most common procedure in all the CLs is diagnostic catheterization, especially in adult CLs (65% of the total). Closure procedures of ductus arteriosus (14.2%) and ASD (11.7%) followed by pulmonary branch angioplasty (7.4%) or coarctation of aorta (6.1%) are among the most predominant interventional procedures reported.

Comparison among participant cath labs

Result comparison by age and REC group in the overall sample and per participant CL is shown on table 3. Most pediatric CLs show a very similar distribution by age, weight, and REC group. In all CLs, more patients fall into the REC I group. Compared to the pediatric ones, adult, and hybrid CLs (4% vs 1%) show slightly more REC III group procedures. Regarding DAP/Kg and DAP/Kg/fluoroscopy, distribution is very similar in the 3 types of CL except for CL4 that shows higher values compared to the total (261.3 µGym^2/kg vs 62.3 µGym^2/kg, and 37.1 µGym^2/kg/min vs 3.8 µGym^2/kg/min).

Analysis of dosimetric parameters

In scatter plots of weight vs DAP, weight vs DAP/Kg, and weight vs DAP/Kg/fluoroscopy in the overall sample and per REC group, lowest dispersion is seen in the DAP/kg parameter especially in the overall sample and the REC I group (figure 2 and figure 1 of the supplementary data). Regarding distribution based on the type of CL by age, REC group, and dosimetric parameters, significant differences were reported in all the median comparisons for 2

Table 3. Demographic characteristics, DAP/kg, and DAP/Kg/fluoroscopy per cath lab and radiation exposure category group

	Total	CL1	CL2	CL3	CL4	CL5	CL6	CL7	CL8	CL9	CL10	CL11
N	1090	100	99	100	100	99	100	100	100	100	92	100
Type of cath lab		Adult	Hybrid	Hybrid	Hybrid	Pediatric	Pediatric	Pediatric	Pediatric	Pediatric	Pediatric	Pediatric
Median age (95%CI)	6 (6-7)	34 (30-42)	7 (6-10)	8 (7-15)	5.5 (4-8)	3 (2-5)	4 (3-9)	3.7 (2.4-4.9)	2 (1-3)	7.5 (6-10)	4 (4-6)	5.5 (5-8)
< 1 year (%)	249 (22.8%)	0	21	13	23	40	25	32	36	25	15	19
1-18 years (%)	662 (60.8%)	2	59	56	61	59	63	68	64	74	75	81
> 18 years (%)	179 16.4%)	98	19	31	16	0	12	0	0	1	2	0
Weight, median (95%CI)	20 (19-22.1)	66.9 (62.8-71.2)	26 (21.6-34)	36 (25-49)	19.5 (16-26)	12 (9.1-16.3)	15.2 (11.8-18.3)	15 (12-20.3)	11.4 (9.5-13.4)	23.5 (20-32)	16 (14-20)	21 (18-27)
REC	N = 910	92	86	89	79	79	91	76	96	77	82	63
REC I (%)	743 (81.6%)	78 (84.8%)	69 (80.2%)	76 (85.4%)	67 (84.8%)	54 (68.4%)	60 (65.9%)	59 (77.6%)	85 (88.5%)	59 (76.6%)	79 (96.3%)	57 (90.5%)
REC II (%)	145 (16%)	10 (10.9%)	14 (16.3%)	10 (11.2%)	8 (10.1%)	25 (31.6%)	26 (28.6%)	17 (22.4%)	11 (11.5%)	16 (20.8%)	3 (3.7%)	5 (7.9%)
REC III (%)	22 (2.4%)	4 (4.3%)	3 (3.5%)	3 (3.4%)	4 (5.1%)	0 (0%)	5 (5.5%)	0 (0%)	0 (0%)	2 (2.6%)	0 (0%)	1 (1.6%)
DAP/kg (μGy.m²/kg), median (95%CI)	62.3 (56.7-69)	64.0 (52.2-78.7)	50.1 (37.6-65.8)	56.2 (45.3-73.5)	261.3 (213.2-326.9)	52 (44.5-75.9)	44.6 (34.3-61.9)	69.8 (55-93.8)	33.2 (27.2-38.3)	95.9 (74.4-136.5)	37.6 (29.5-44.6)	80.9 (64.4-97.6)
REC I	48.1 (43.6-53.1)	53.4 (38.8-69)	54.4 (37.6-72.9)	49.1 (39.7-59.8)	215.7 (180.5-284.4)	30.3 (23.4-45.2)	21.5 (18.2-34.7)	54.3 (47.7-101.2)	30.5 (25.1-35.7)	71.2 (59.7-92.2)	31.8 (23.5-39.8)	54.3 (38-83.3)
REC II	104.7 (80.7-130)	116.5 (53-195.9)	38.9 (21-80.7)	135.5 (53.1-276.9)	417.1 (262.7-644.4)	81 (52-105.8)	91.7 (57.1-122.4)	91.9 (78.1-216.1)	80 (46.5-131.5)	238.8 (139.8-561.7)	47.6 (37.5-223.7)	175.7 (170.8-223.8)
REC III	213.5 (161.9-291.6)	202.4 (113-351)	178.3 (65.8-291.7)	144.7 (105.4-225.9)	253.4 (145.1-328.6)	0	298.5 (233.8-471.9)	0	0	195.8 (176.8-214.8)	0	161.9
DAP/kg/fluoroscopy (μGy.m²/kg/min)	3.8 (3.5-4.1)	3.22 (2.81-3.62)	2.9 (2.2-3.9)	4.8 (3.7-5.7)	37.1 (31.2-41.2)	2.2 (1.8-2.6)	2.8 (2.4-3.4)	2.6 (2.3-3)	3.9 (3.5-4.4)	6.8 (5.9-7.9)	2.8 (2.5-3.3)	5.4 (4.7-7.2)
REC I	3.61 (3.4-3.9)	2.9 (2.4-3.4)	3.4 (2.5-4.5)	4.4 (3.5-5.6)	39.6 (30.7-46)	1.8 (1.5-2.5)	2.7 (2.3-3.2)	2.5 (2.2-3.2)	3.8 (3.4-4.3)	6.3 (5-7)	2.8 (2.5-3.3)	5.1 (4.6-7.6)
REC II	3.6 (3-4.4)	4.3 (3.1-4.8)	1.7 (1-4.1)	4.8 (2.6-9.9)	29.3 (12.5-43.3)	2.3 (1.8-2.8)	3 (2.4-4.5)	2.3 (2.2-3.4)	4.4 (3.6-7)	8.6 (5.3-10.1)	3.5 (2.8-5.4)	8.1 (7.8-9.1)
REC III	7.03 (5.3-8.9)	5 (3-6.1)	7 (1.5-8.5)	5.3 (4.5-16)	6.3 (4.4-9.9)	0	7.5 (7.4-9.7)	0	0	9.3 (8.9-9.7)	0	11.4

95%CI, 95% confidence interval; DAP, dose-area product; REC: radiation exposure category.

independent samples except in the DAP/kg, and DAP/kg/fluoroscopy parameters between adult and pediatric CLs (figure 3).

DISCUSSION

As far as we know, the current is the first study ever published on the dose of radiation associated with interventional procedures performed in patients with congenital heart diseases in Spain. Radiation in the cardiac catheterizations of these patients should be the main concern since these are particularly long, complex, and intricate procedures. This problem mainly affects the pediatric population with congenital heart diseases who will undergo multiple cardiac catheterizations throughout their lives.[7,8] Also, the dose accumulated by the operator is a relevant issue here, especially with pediatric patients in whom distance to the x-ray tube (which is key in the amount of radiation received[9]) is much shorter compared to the adult population. Therefore, the imaging modality used for image acquisition should follow the principles established in the «ALARA» concept (As Low As Reasonable Achievable) that includes recommendations like rationing the zoom, using collimation, proper table position, the characteristics of the beam (images per second, voltage, amperage), and image storage since fluoroscopy, instead of cine.[10-13] Therefore, using the proper technique can reduce the dose of radiation received without changing the overall fluoroscopy times while observing enough clinical guarantees for the decision-making process and work at the CL.

There is a history of lower doses being received after the implementation of training programs involving machines, and interventional cardiologists,[13,14] the development of specific image acquisition protocols,[15,16] and the creation of registries on the amount of radiation received. Therefore, in the United States, several reports have been published on this topic drafted by the multicenter Congenital Cardiac Catheterization Outcomes Project Working Group founded back in 2006.[17] Using data from this working group, in 2014, Ghelani et al. published the results of a retrospective study conducted from 2009 through 2013 to establish the dosimetric parameters of reference for 6 congenital diseases.[18] Parallel to this, the Congenital Cardiac Catheterization Outcomes Project – Quality Improvement (C3PO-QI) for radiation dose optimization was developed. It included training seminars for health professionals on radiologic protection, information exchange between centers and manufacturers, image acquisition optimization protocols, the development of digital tools for registry purposes, and the identification of areas with room for improvement. Then, in 2017, Cevallos et al. published the results of a prospective registry conducted from 2014

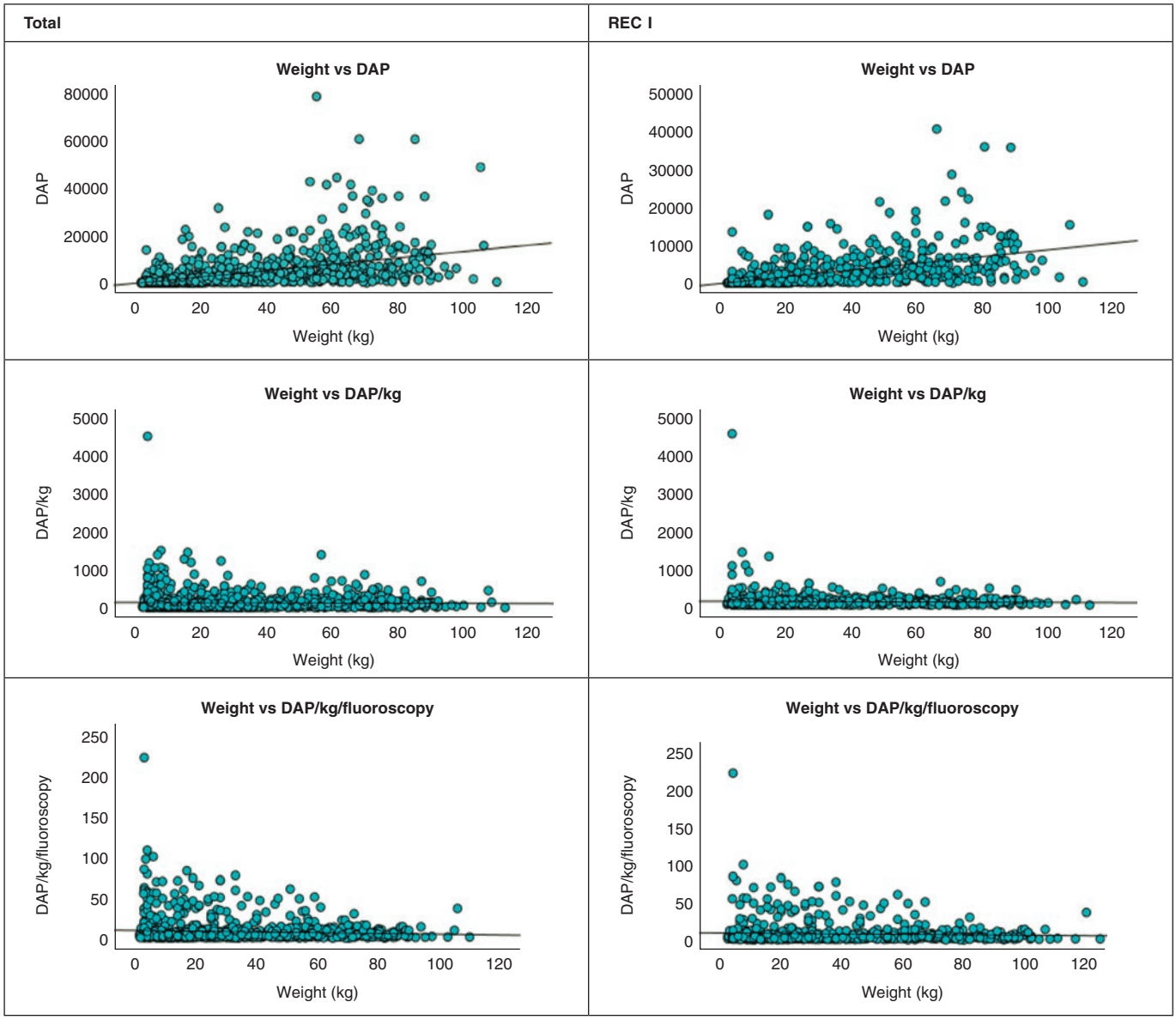
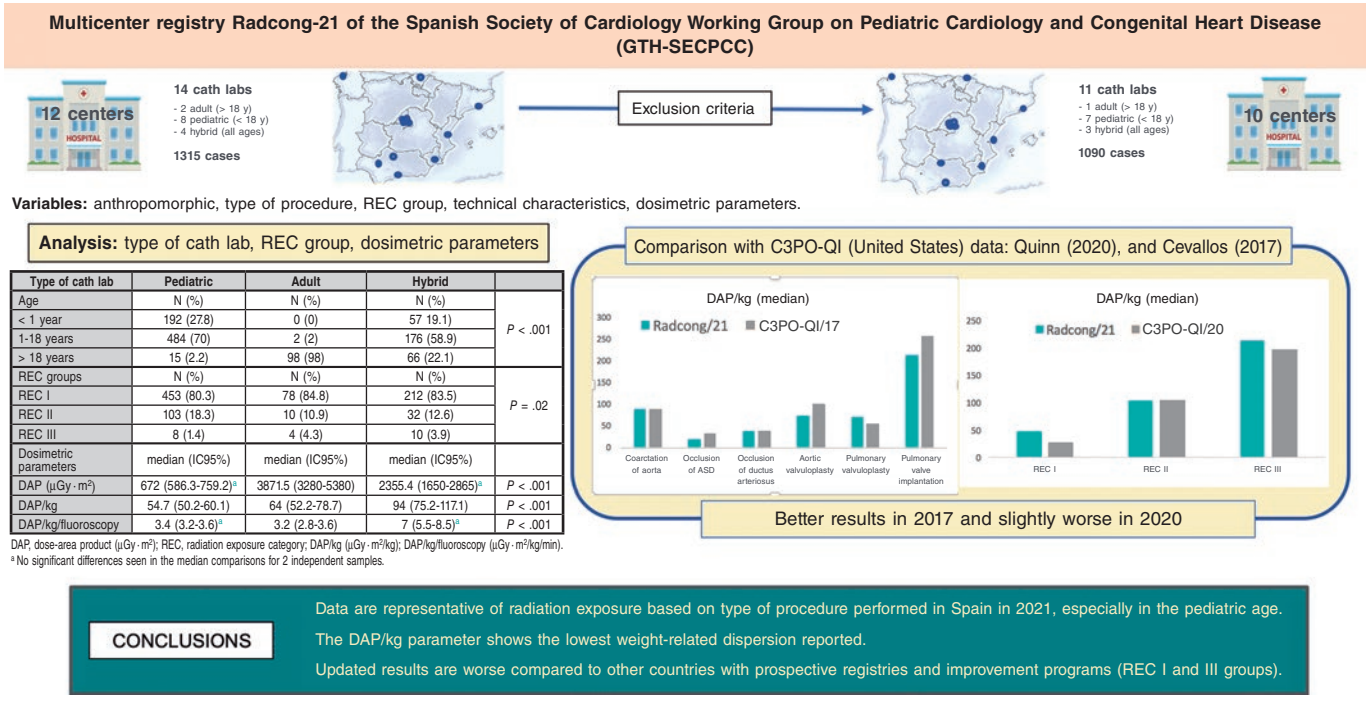


Figure 2. Scatter plots from the overall sample and radiation exposure categories (REC) group for the values of weight (kg) vs dose-area product (DAP) (μGy.m^2), weight vs DAP/kg (μGy.m^2/kg), and weight vs DAP/Kg/fluoroscopy (μGy.m^2/kg/min). All plots from the overall sample and procedures from the REC I group are shown here (the remaining ones from the other groups are shown in the supplementary data). The lowest dispersion is seen in the central column of weight vs DAP/kg, both in the overall sample and in the REC I group.

through 2015.[19] The implementation of such program resulted in lower doses of radiation for all the aforementioned diseases. Finally, in 2020, Quinn et al.[20] presented the data prospectively included in the C3PO-QI from 2015 through 2017 on 40 simple or combined procedures grouped into the 3 REC groups previously proposed[6] demonstrating a significant reduction in the dose of radiation received.

This study conducted by the GTH-SECPCC can lay the foundations for the development of similar programs in our country. The distribution of patients by age, procedure, and REC group is fairly similar to that of former registries with larger numbers of patients.[17,19,20] Although 16.5% of the patients could not be categorized in any REC groups, most correspond to combined procedures or other angioplasties, which would presumably increase the number of patients in REC II or III groups. Maybe the greatest limitation of the Radcong-21 is the scarce participation of centers and CLs with special dedication to the adult population. The 31st Spanish Cardiac Catheterization and Coronary Intervention Registry of the Interventional Cardiology Association of the Spanish Society of Cardiology (ACI-SEC) included 527 interventional procedures performed on congenital heart diseases in adults in 2021.[21] Although our series doesn't cover the entire 2021 (just 100 cases per hospital), a total of 179 procedures are reported in individuals > 18 years, which is far from the numbers mentioned above. Nonetheless, almost all Spanish CLs with special dedication to pediatric congenital heart diseases participated in our registry (12 out of 14 total). Therefore, percentage wise, data from the Radcong-21 are very similar to the distribution per type of procedure in patients < 18 years in the 1st official report from the ACI-SEC and GTH-SECPCC on the 2020[22] Spanish Cardiac Catheterization and Coronary Intervention Registry including, predominantly, closure procedures of ASD and ductus arteriosus, and pulmonary angioplasty or coarctation of aorta.



Type of cath lab	Pediatric	Adult	Hybrid	
Age	N (%)	N (%)	N (%)	
< 1 year	192 (27.8)	0 (0)	57 19.1)	*P* < .001
1-18 years	484 (70)	2 (2)	176 (58.9)	
> 18 years	15 (2.2)	98 (98)	66 (22.1)	
REC groups	N (%)	N (%)	N (%)	
REC I	453 (80.3)	78 (84.8)	212 (83.5)	*P* = .02
REC II	103 (18.3)	10 (10.9)	32 (12.6)	
REC III	8 (1.4)	4 (4.3)	10 (3.9)	
Dosimetric parameters	median (IC95%)	median (IC95%)	median (IC95%)	
DAP (μGy·m^2)	672 (586.3-759.2)[a]	3871.5 (3280-5380)	2355.4 (1650-2865)[a]	*P* < .001
DAP/kg	54.7 (50.2-60.1)	64 (52.2-78.7)	94 (75.2-117.1)	*P* < .001
DAP/kg/fluoroscopy	3.4 (3.2-3.6)[a]	3.2 (2.8-3.6)	7 (5.5-8.5)[a]	*P* < .001

DAP, dose-area product (μGy·m^2); REC, radiation exposure category; DAP/kg (μGy·m^2/kg); DAP/kg/fluoroscopy (μGy·m^2/kg/min).
[a] No significant differences seen in the median comparisons for 2 independent samples.

Figure 3. Central illustration. Summary of the design of case selection, results by type of cath lab, age, REC group, DAP/kg, and DAP/Kg/fluoroscopy compared to other registries and study conclusions. 95%CI, 95% confidence interval; ASD, atrial septal defect; DAP, dose-area product; REC: radiation exposure category.

Quantifying the dose of radiation received by an individual during cardiac catheterization is extremely challenging. The purpose of using coversion factors is overlooking the discrepancy among the different systems of measurement. However, we should mention that, on many occasions, these are based on artificial models and applied differently.[23] To make things harder, there is not such a thing as a homogeneous criterion of units among the different manufacturers, which complicates direct comparisons among hospitals. For several authors, the closest parameter to the dose of radiation received by a patient is the DAP.[19,20] Former studies say that fluoroscopy time is not indicative of the dose of radiation received since very different values like air kerma or DAP are associated with the same fluoroscopy times.[16-20] Some suggest using weight-based air kerma.[17] However, in our setting we, know that this parameter is not collected across centers on a routine basis. Consistent with former studies, our data show that with older age higher doses of radiation received, which can be explained by the patient's increased weight (table 1). Other factors can significantly impact the dose of radiation received like the difficulty of each procedure and the operators' experience. To minimize these limitations, DAP can be indexed based on weight (reduces the bias of increased radiation based on the characteristics of each patient) and fluoroscopy (reduces the bias of increased radiation due to the special complexity of the procedure or the operator's lack of experience). Therefore, some authors suggest that DAP/kg would allow more reliable comparisons between procedures and age ranges.[20] Others claim that it would only allow standardization among patients of the same age group with significant weight differences.[19] According to our information, DAP/kg is the lowest dispersion value of the entire sample, and in type I REC (figure 2 and figure 1 of the supplementary data), which would recommend its use in comparative studies. According to our data, it is surprising to see that in some CLs with DAP/Kg values higher compared to other CLs, such a relation is inverted in the DAP/Kg/fluoroscopy parameter probably due to differences among operators like we mentioned before. Here we should mention the comparison between CL2, CL5, and CL7 with DAP/kg of 50, 52, 69.8, and DAP/Kg/fluoroscopy of 2.9, 2.2, and 2.6, respectively, and CL6 and CL8 with DAP/kg of 44.6 and 33.2, and DAP/Kg/fluoroscopy of 2.8 and 3.9, respectively. It would be interesting to do more in-depth analyses of these data in future studies to see what the variability is among operators across different centers or CLs.

If we compared our data to those published by C3PO-QI (table 4) we'll be able to see that the numbers of DAP/kg from our series are better or similar to the ones published in 2017,[19] yet unfavorable compared to REC I and III groups in 2020[20] (dose increases of 78% and 8.3%, respectively). Differences don't seem to be too significant, especially if we consider the 95%CIs. They don't relate to all the centers from the registry either. However, reflection should be made on the need for training and awareness policies on the amount of radiation received while performing cardiac catheterizations in our country.

Limitations

This study has some limitations due to its retrospective nature. Data mining was voluntary and unaudited. The participant centers had different volumes of patients, which is why the time interval to meet the goal of procedures set was not constant. This criterion was followed to promote the representativity of the reality nationwide that can be considered appropriate in the pediatric, not in the adult age, where participation dropped. Contribution from the operator's own experience or the technical quality of the CL to the dose of radiation can be a confounding factor. Still, it is part of the day-to-day reality of a CL. Patients with repeated procedures could not be considered either or those in whom additional imaging modalities plus the scheduled catheterization were performed, which led to increased doses of radiation.

Table 4. Comparison between Radcong-2021 and data from the C3PO-QI from 2017,[19] and 2020[20]

Prevalent diseases	Radcong-2021			C3PO-QI 2017[19]	
	n (% total)	PDA/kg[a] (IC95%)	PDA/kg[a] (P95)	n (% total)	DAP/kg (95thP)
Coarctation of aorta	66 (6.1%)	90.2 (56.7-121.1)	90.2 (413)	288 (3.3%)	90 (384)
Occlusion of ASD	128 (11.7%)	20.5 (18.1-26.1)	20.5 (358)	295 (3.4%)	34 (199)
Occlusion of ductus arteriosus	155 (14.2%)	37.5 (31.8-44.4)	37.5 (216)	443 (5.1%)	37 (217)
Aortic valvuloplasty	29 (2.7%)	72.1 (52.7-129.5)	72.1 (284)	136 (1.6%)	99 (383)
Pulmonary valvuloplasty	67 /6.2%)	71.2 (48.6-90)	71.2 (450)	258 (3%)	53 (335)
Pulmonary valve implantation	22 (2%)	213.5 (161.9-291.6)	213.5 (327)	199 (2.3%)	257 (671)
REC group	**Radcong-2021**			**C3PO-QI 2020[20]**	
	N (% total)		**DAP/kg[a] (95%CI)**	**N (% total)**	**DAP/kg[a] (95%CI)**
REC I	743 (81.6%)		48.1 (43.6-53.1)	10 649 (70%)	27 (7-66)
REC II	145 (16%)		104.7 (80.7-130)	2771 (18%)	106 (50-216)
REC III	22 (2.4%)		213.5 (161.9-291.6)	1837 (12%)	197 (13-119)

95%CI, 95% confidence interval; 95thP, 95th percentile of the median; ASD, atrial septal defect; DAP, dose-area product; REC, radiation exposure category.
[a] DAP/Kg in μGy.m^2/kg.

CONCLUSIONS

Representative data from age and procedure-based dosimetric parameters in catheterizations performed in patients with congenital heart disease in Spain in 2021 were obtained. The DAP/Kg parameter has the lowest dispersion from the sample. Results are representative of the pediatric reality in our country since they include almost all centers performing interventional procedures. These results could be used as the reference in this age range, but just as a mere guidance among adults. Overall, the results obtained are worse compared to other countries with prospective registries and training and improvement programs in this area. Figure 3 shows the registry design, overall general results, and final conclusions.

Keeping registries helps control quality of care and identify areas with room for improvement. Training and educational programs in this area should be conducted, and prospective registries with more adult CLs. Therefore, this registry is an important step forward to develop future improvement programs or projects in this area at both local and national level.

FUNDING

This study received no specific funding from public, private or non-profit organizations.

AUTHORS' CONTRIBUTIONS

F. Rueda Núñez, B. Insa Albert, C. Abelleira Pardeiro, and M. Álvarez-Fuente drafted the manuscript. V. Balboa Barreiro conducted the statistical analysis. All the authors contributed to the study idea and design, data curation, critical review, and final approval of the manuscript.

CONFLICTS OF INTEREST

None whatsoever.

WHAT IS KNOW ABOUT THIS TOPIC?

- On many occasions, cardiac catheterization is needed to treat patients with congenital heart diseases at an early age and, repeatedly, over time across the patient's lifetime. These are long and complex procedures that increase the risk of radiation exposure for both patients and health professionals.
- Local registries are needed to establish reference values of radiation exposure per type of procedure and patient.
- The implementation of registries and training programs reduces the dose of radiation as seen in prospective studies.

WHAT DOES THIS STUDY ADD?

- This is the first study ever conducted in our country on dosimetric parameters of cardiac catheterizations in patients with congenital heart diseases.
- Representative data on age and procedure-based dosimetric parameters in congenital cardiac catheterizations performed in Spain in 2021 were obtained. Therefore, reference values regarding comparative or prospective studies have been established, especially in the pediatric age.
- Overall, results in our country are worse compared to other countries with prospective registries and training and improvement programs in this area.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M23000372.

REFERENCES

1. International Commission on Radiological Protection. ICRP Publication 103: The 2007 Recommendations of the International Commission on Radiological Protection. *Ann ICRP.* 2007;37:1-332.
2. Real Decreto 1976/1999, de 23 de diciembre, por el que se establecen los criterios de calidad de radiodiagnóstico. Boletín Oficial del Estado núm. 311, de 29 de diciembre de 1999. Available at: https://www.boe.es/eli/es/rd/1999/12/23/1976. Accessed 1 Oct 2022.
3. Real Decreto 601/2019, de 18 de octubre, sobre justificación y optimización del uso de las radiaciones ionizantes para la protección radiológica de las personas con ocasión de exposiciones médicas. Boletín Oficial del Estado núm. 262, de 31 de octubre de 2019, páginas 120840 a 120856. Available at: https://www.boe.es/eli/es/rd/2019/10/18/601. Accessed 1 Oct 2022.
4. Sánchez RM, Vano E, Fernández JM, Escaned J, Goicolea J, Pifarré X; DOCCACI Group. Initial results from a national follow-up program to monitor radiation doses for patients in interventional cardiology. *Rev Esp Cardiol.* 2014;67:63-65.
5. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology.* 2007;18:805-835.
6. Quinn BP, Armstrong AK, Bauser-Heaton HD, et al. Congenital Cardiac Catheterization Project on Outcomes-Quality Improvement (C3PO-QI). Radiation Risk Categories in Cardiac Catheterization for Congenital Heart Disease: A Tool to Aid in the Evaluation of Radiation Outcomes. *Pediatr Cardiol.* 2019;40:445-453.
7. Andreassi MG, Ait-Ali L, Botto N, Manfredi S, Mottola G, Picano E. Cardiac catheterization and long-term chromosomal damage in children with congenital heart disease. *Eur Heart J.* 2006;27:2703-2708.
8. Andreassi MG. Radiation risk from pediatric cardiac catheterization: friendly fire on children with congenital heart disease. *Circulation.* 2009;120:1847-1849.
9. Ingwersen M, Drabik A, Kulka U, et al. Physicians' radiation exposure in the catheterization lab: ¿does the type of procedure matter? *JACC Cardiovasc Interv.* 2013;6:1095-1102.
10. Patel C, Grossman M, Shabanova V, Asnes J. Reducing radiation exposure in cardiac catheterizations for congenital heart disease. *Pediatr Cardiol.* 2019;40:638-649.
11. Justino H. The ALARA concept in pediatric cardiac catheterization: techniques and tactics for managing radiation dose. *Pediatr Radiol.* 2006;36(Suppl 2):146-153.
12. Chida K, Kato M, Saito H, et al. Optimizing patient radiation dose in intervention procedures. *Acta Radiol.* 2010;51:33-39.
13. Hill KD, Frush DP, Han BK, et al. Image Gently Alliance. Radiation Safety in Children with Congenital and Acquired Heart Disease: A Scientific Position Statement on multimodality dose optimization from the Image Gently Alliance. *JACC Cardiovasc Imaging.* 2017;10:797-818.
14. Verghese GR, McElhinney DB, Strauss KJ, Bergersen L. Characterization of radiation exposure and effect of a radiation monitoring policy in a large volume pediatric cardiac catheterization lab. *Catheter Cardiovasc Interv.* 2012;79:294-301.
15. Boudjemline Y. Effects of reducing frame rate from 7.5 to 4 frames per second on radiation exposure in transcatheter atrial septal defect closure. *Cardiol Young.* 2018;28:1323-1328.
16. Glatz AC, Patel A, Zhu X, et al. Patient radiation exposure in a modern, large-volume, pediatric cardiac catheterization laboratory. *Pediatr Cardiol.* 2014;35:870-878.
17. Kobayashi D, Meadows J, Forbes TJ, et al. Standardizing radiation dose reporting in the pediatric cardiac catheterization laboratory. A multicenter study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). *Catheter Cardiovasc Interv.* 2014;84:785-793.
18. Ghelani SJ, Glatz AC, David S, et al. Radiation dose benchmarks during cardiac catheterization for congenital heart disease in the United States. *JACC Cardiovasc Interv.* 2014;7:1060-1069.
19. Cevallos PC, Armstrong AK, Glatz AC, et al. Radiation dose benchmarks in pediatric cardiac catheterization: A prospective multi-center C3PO-QI study. *Catheter Cardiovasc Interv.* 2017;90:269-280.
20. Quinn BP, Cevallos P, Armstrong A, et al. Longitudinal Improvements in Radiation Exposure in Cardiac Catheterization for Congenital Heart Disease: A Prospective Multicenter C3PO-QI Study. *Circ Cardiovasc Interv.* 2020;13:e008172.
21. Freixa X, Jurado-Román A, Cid B, Cruz-González I; en representación de la ACI-SEC. Registro español de hemodinámica y cardiología intervencionista. XXXI Informe Oficial de la Asociación de Cardiología Intervencionista de la Sociedad española de Cardiología (1990-2021). *Rev Esp Cardiol.* 2022;75:1040-1049.
22. Ballesteros F, Coserría F, Romaguera R, et al. Registro español de intervencionismo en cardiopatías congénitas. Primer informe oficial de la ACI-SEC y el GTH-SECPCC (2020). *REC Interv Cardiol.* 2022;4:173-180.
23. Chida K, Kagaya Y, Saito H, Ishibashi T, Takahashi S, Zuguchi M. Evaluation of patient radiation dose during cardiac interventional procedures: what is the most effective method? *Acta Radiol.* 2009;50:474-481.

REC Interv Cardiol. 2023;5(4):263-269
https://doi.org/10.24875/RECICE.M23000373

Original article

Initial experience with the new percutaneous pulmonary self-expandable Venus P-valve

María Álvarez-Fuente,* María Toledano, Ignacio Hernández, Elvira Garrido-Lestache, Natalia Rivero, Inmaculada Sánchez, Isabel Molina, Itziar García Ormazábal, and María Jesús del Cerro*

Servicio de Cardiología Pediátrica y Cardiopatías Congénitas del Adulto, Hospital Universitario Ramón y Cajal, Madrid, Spain

ABSTRACT

Introduction and objectives: Percutaneous pulmonary valve implantation is currently a common procedure in patients with congenital heart disease with a dysfunctional right ventricular outflow tract. Until April 2022, there were only balloon-expandable valves available in Europe, which did not cover the needs of the different anatomies of the right ventricular outflow tract. Since that date we have available the self-expandible Venus P-valve (Venus MedTech, China). We present the initial experience with this new percutaneous pulmonary valve in our center.
Methods: Description of the valve implants with the new self-expandible valve performed between September and November 2022.
Results: Eight valve implants have been performed, all successful and without severe complications during the procedure. All patients had severe pulmonary regurgitation with a dilated right ventricle and severe dilatation of the pulmonary trunk and were not good candidates for percutaneous balloon-expandable valves. Five patients had a tetralogy of Fallot. In 7 patients, the implant was performed through the femoral vein and in one through jugular access. As a safety measure, all valves were implanted through a DrySeal sheath (Gore, W.L. Gore & Associates, Inc., United States). The mean hospital stay was 3-day.
Conclusions: Valve implantation with the new self-expandible Venus P-valve was, in our preliminary experience, a safe and feasible procedure, allowing us to treat very dilated right outflow tracts, not suitable for the current balloon-expandable valves.

Keywords: Percutaneous valve implantation. Venus P-valve. Tetralogy of Fallot. Pulmonary regurgitation. Pulmonary valve. Congenital heart disease.

Experiencia inicial con la nueva válvula pulmonar percutánea autoexpandible Venus P

RESUMEN

Introducción y objetivos: El implante percutáneo de válvula pulmonar es, actualmente, un procedimiento habitual en pacientes con cardiopatías congénitas con un tracto de salida del ventrículo derecho disfuncionante. Hasta abril de 2022, en Europa solo estaban disponibles las válvulas expandibles con balón, que no cubrían las necesidades de las distintas anatomías del tracto de salida derecho. Desde esa fecha está disponible la válvula autoexpandible Venus P (Venus MedTech, China). Presentamos la experiencia inicial en nuestro centro con esta nueva válvula pulmonar para implante percutáneo.
Métodos: Descripción de los implantes valvulares con la nueva válvula autoexpandible realizados entre septiembre y noviembre de 2022.
Resultados: Se han realizado 8 implantes valvulares, todos con éxito y sin complicaciones graves durante el procedimiento. Todos los pacientes presentaban insuficiencia pulmonar grave con repercusión sobre el ventrículo derecho y dilatación del tronco pulmonar, y no eran buenos candidatos para las válvulas expandibles con balón. Cinco pacientes tenían una tetralogía de Fallot de base. En 7 pacientes el implante se llevó a cabo por vía femoral y en 1 por vía yugular. Como medida de seguridad, en todos los pacientes el implante se hizo a través de una vaina DrySeal (Gore, W.L. Gore & Associates, Inc., Estados Unidos). La media de tiempo de ingreso fue de 3 días.
Conclusiones: El implante de la nueva válvula autoexpandible Venus P fue, en nuestra experiencia preliminar, un procedimiento seguro y factible, que permite valvular tractos de salida derechos muy dilatados con contraindicación para las actuales válvulas expandibles con balón.

Palabras clave: Implante percutáneo valvular. Válvula pulmonar Venus P. Tetralogía de Fallot. Insuficiencia pulmonar. Válvula pulmonar. Cardiopatías congénitas.

*** Corresponding authors.**
E-mail addresses: maria.alvarezfuente@gmail.com (M. Álvarez-Fuente); majecerro@yahoo.es (M.J. del Cerro).

Received 3 January 2023. Accepted 15 February 2023. Online 26 April 2023.

Abbreviations

CT: computed tomography. **LMCA:** left main coronary artery. **MRI:** magnetic resonance imaging. **PAT:** pulmonary arterial trunk. **RV:** right ventricle. **RVOT:** right ventricular outflow tract.

INTRODUCTION

Currently, transcatheter pulmonary valve implantation is a common procedure in patients with congenital heart disease and dysfunctional right ventricular outflow tract (RVOT).[1] Transcatheter balloon-expandable pulmonary valves (Melody by Medtronic Inc., United States, and Sapien by Edwards Lifescience, United States, both with CE marking) have an indication for conduit, native tract, and prosthetic valve implantation.[1-3] However, a large number of patients—most with tetralogy of Fallot—who require pulmonary valve implantation are treated with transannular repair or post-commissurotomy pulmonary regurgitation or valvuloplasty for pulmonary valve stenosis. These patients have very pulsatile outflow tracts with larger sizes compared to the ones of current balloon-expandable valves (22 mm and 29 mm for Melody and Edwards, respectively).[4] Not even the 32 mm Myval device (Meril Life Sciences Pvt. Ltd., India) without an indication for pulmonary valve implantation would be adequate for the largest RVOTs out there.

Back in April 2022, the self-expanding Venus P-valve (Venus MedTech, China) achieved the CE marking, and became an actual alternative for the largest native tracts.

This is our initial experience with this new transcatheter pulmonary valve at our center and in our country.

METHODS

Valve description

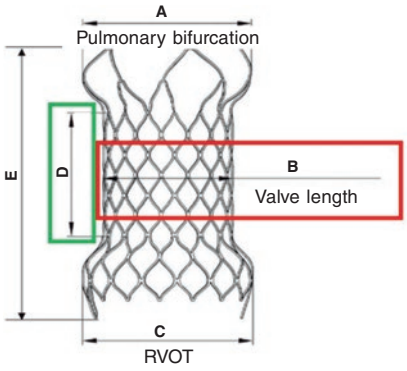
The structure of the Venus-P valve consists of a nitinol stent. Both the leaflets, and the stent coverage are made of porcine pericardium. Nitinol provides the stent with some sort of shape memory so it can adapt to the pulmonary arterial trunk (PAT) without compressing neighboring structures. This valve is available in sizes from 28 mm to 36 mm in diameter with 2 mm increases (figure 1). It can be used with the largest caliber native tracts.[5] The Venus P-valve stent has a diabolo-shaped configuration and adds 10 mm to the borders of the central region (figure 1). It is wider in its borders because it has been designed for tubular PAT implantation without distal or pulmonary artery stenosis. Both the central region and the proximal border are covered with porcine pericardium to prevent paravalvular leak. The distal border remains uncovered to avoid occluding the pulmonary arteries (figure 2).[6] The stent has radiopaque marks in the distal border of its tubular region and in its proximal border both indicative of the degree of the porcine valve implantation. The valve crimping system on its delivery system is performed under ice water. In these conditions, nitinol becomes softer and can be crimped onto the delivery system (figure 3). The valve is then fixed to the delivery system through 2 small hooks (figure 2). Once the valve has been attached and its size reduced, it is covered with the delivery sheath capsule in such a way that the valve enters the patient fully covered (figure 3 and figure 4) [22-Fr sheaths in 28 mm and 30 mm valves, and 24-Fr sheaths in the largest ones (> 30 mm)]. Once in the pulmonary tree and in the desired location, the delivery sheath capsule will be retracted so the valve can regain its diabolo-shaped configuration when entering blood flow at 36 °C to 37 °C temperature.

Procedural description

Cardiac catheterization was performed under general anesthesia while the patient remained intubated and with heparinization at 100 U/kg. Two femoral veins where cannulated, 1 for diagnostic catheterization, cutting, and advance of the valve delivery system, and the other one to perform the follow-up angiography with a pigtail catheter in the RVOT during valve implantation (figure 4). The coronary arteries of all the patients were interrogated through aortograms or selective coronary angiographies with the same 34 mm cutting balloon (Sizing Balloon, AGA Medical Corp., United States) inflated in the RVOT to discard the risk of coronary compression during the procedure (figure 5B). Similarly, the RVOT was cut with the same 34 mm balloon to see if the anatomy was viable and choose the right valve diameter and length. Cutting was considered occlusive when aortic pressure dropped during balloon inflation and the lack of right ventricular (RV) flow to the pulmonary arteries was angiographically confirmed through an intracoronary injection of contrast into the RV during the balloon peak inflation rate (figure 5A).

Although the imaging modalities performed while planning (computed tomography scan [CT] with or without magnetic resonance imaging (MRI)] inform us on the most appropriate valvular size for each patient, size was picked based on angiography measurements (30° lateral and 30°cranial right anterior oblique), and on the diameter and location of the notch seen in the balloon during occlusive cutting. Balloon cutting allows us to assess the compliance of the PAT, something that is merely suggested on the MRI. Therefore, this is an essential step that should be made before selecting the size of the valve. We select a 2 mm-to-4 mm larger valve compared to the waist of the cutting balloon with a length that should leave the distal border at pulmonary bifurcation level, and the diabolo proximal border at RV level.

The Venus P-valve is implanted without the need for previous stenting to create a landing zone. A Lunderquist high-support guidewire is placed (Cook Medical, Denmark) preferably in the left pulmonary artery. In the presence of stenosis, hypoplasia or unfavorable angle, the guidewire is placed in the right pulmonary artery. The delivery system is advanced through a 65 cm 26-Fr or 24-Fr Dryseal sheath (Gore, W.L. Gore & Associates, Inc., United States) for valves > 30 mm or < 30 mm in diameter, respectively. Once the Dryseal sheath is in position into the selected pulmonary artery, the Venus P-valve delivery system is advanced. Afterwards, the Dryseal sheath is retracted and the correct position of the capsule into the pulmonary artery is verified. Then, the valve is slowly uncovered by withdrawing the capsule (with a clockwise twist of the wheel of the delivery system). As it gradually enters the patient's bloodstream, the valve regains its normal diabolo-shaped configuration. When its most distal border has been partially adapted to the pulmonary branch, the whole system is then smoothly removed to the PAT and the valve is slowly uncovered while checking—through pigtail catheter injections into the RVOT—that the valve is in position (figure 4). The valve has 2 lines of radiopaque markers to guide implantation. The distal marks that indicate the distal border of the stent tubular region will remain at bifurcation level. The proximal ones should remain at PAT narrowest region or native annulus level (in the location of the



Model	Specifications	Diameter (mm)			D mm	E mm
		A	B	C		
L28P	P28-25	38.0	28.0	38.0	25.0	53.1
	P28-30				30.0	60.0
L30P	P30-25	40.0	30.0	40.0	25.0	54.3
	P30-30				30.0	59.9
L32P	P32-25	42.0	32.0	42.0	25.0	58.0
	P32-30				30.0	64.5
L34P	P34-25	44.0	34.0	44.0	25.0	61.5
	P34-30				30.0	67.0
L36P	P36-25	46.0	36.0	46.0	25.0	63.0
	P36-30				30.0	67.0

Figure 1. Selection of different valvular sizes with the dimensions of the different parts of the valve. RV, right ventricle.

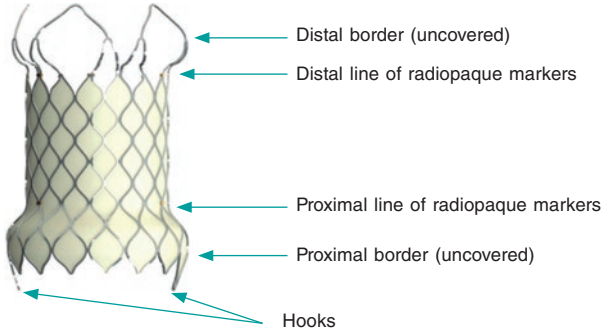


Figure 2. Image of the Venus P-valve with its typical diabolo-shaped configuration, and coverage of the entire valve leaving both the distal border and the radiopaque markers uncovered.

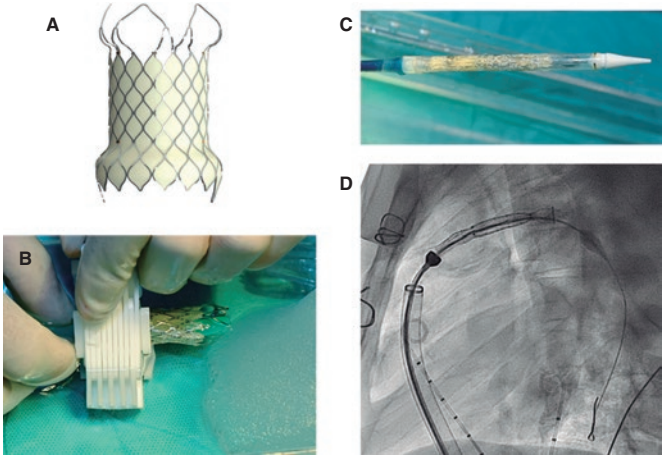


Figure 3. **A:** Venus P-valve prior to crimping. **B:** valve crimping onto the delivery system inside a frozen physiological saline solution with a specific crimping system. **C:** crimped valve inside the delivery system while covered by a capsule. **D:** fluoroscopy showing the valve in the delivery system inside the capsule already inserted into the patient's pulmonary artery.

notch seen during balloon cutting), thus reducing the risk of embolization. The valve proximal region—10 mm larger than the central one—will remain, in most cases, in the infundibulum of the RV.

Procedure should be performed through a Dryseal sheath to facilitate the maneuverability of the valve delivery system and guarantee safe valve recapture should repositioning be required. The valve can be recaptured until half of its structure has been uncovered.

An aortogram was performed at the end of all procedures (preferably 30° caudal and 20° left anterior oblique) to confirm the lack of coronary artery compression (figure 6).

Patient selection

A previous study through diagnostic catheterization or MRI with or without CT scan was conducted to see whether the anatomy of potentially eligible patients with valve implantation criteria according to the clinical practice guidelines published by the ESC[7,8] was ripe for Venus P-valve implantation (figure 7). CT or MRI acquired images were analyzed by Venus Medtech image technicians who video-called our hospital heart team to discuss the convenience of valve implantation and proper valvular size that best suited the patient's RVOT size. However, the final size was not decided until balloon cutting was used during cardiac catheterization.

This first imaging study discarded 5 patients with unsuitable anatomies for this kind of valve: 2 patients with stents and pulmonary artery stenoses, 2 patients with larger RVOTs compared to the sizes recommended for this kind of valve, and 1 patient with pyramid-shaped right ventricular outflow tract.

Study description

This was a prospective study of the first patients treated with Venus P-valve implantation conducted at our center from September 20th through November 4th, 2022. These are the very first implantations of this type of valve ever performed in our country.

Inclusion criteria

This study included patients with dysfunctional native RVOTs and an indication for pulmonary valve implantation in whom diagnostic catheterization and cutting test allowed such procedure.

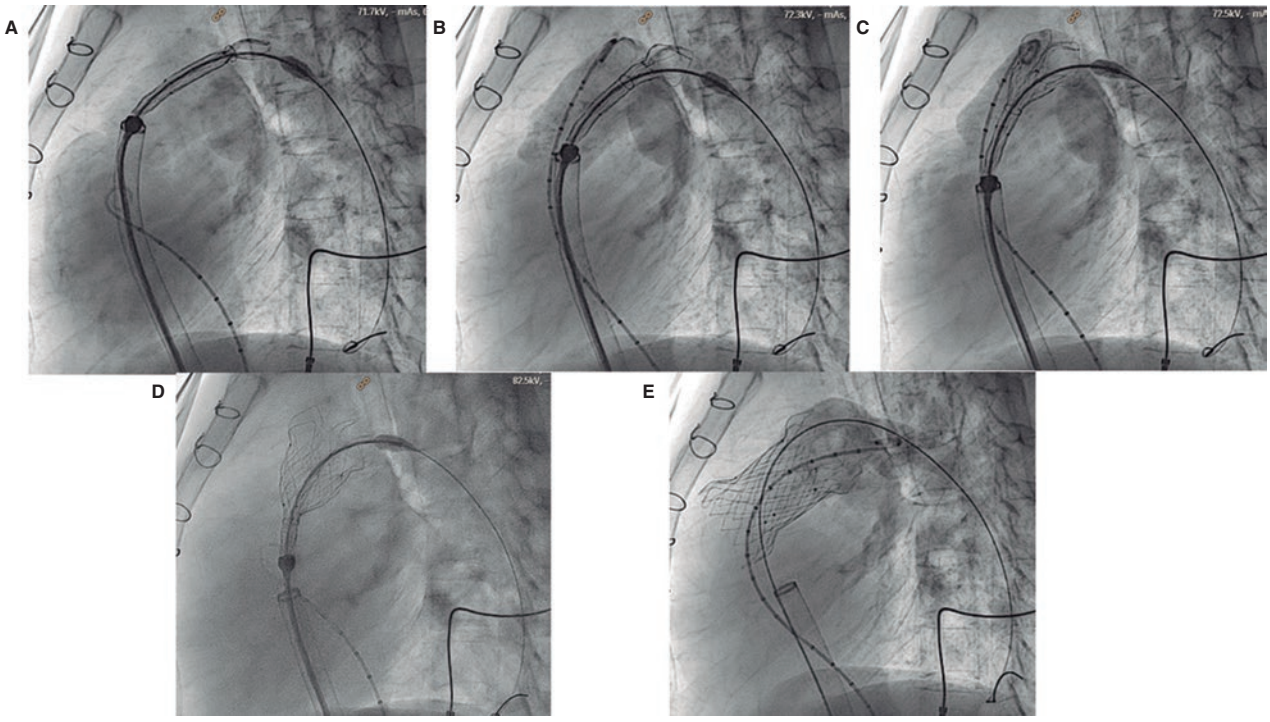


Figure 4. Valve implantation process. **A-D:** slow capsule removal so the valve can adapt to the left ventricular outflow tract (LVOT). Angiography monitorization with the pigtail catheter placed in the LVOT. **E:** final outcomes after valve implantation.

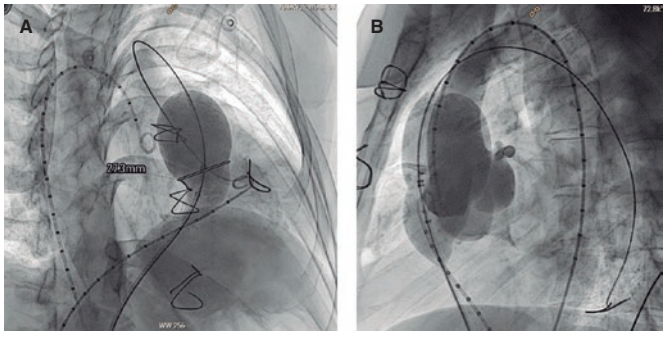


Figure 5. Right ventricular outflow tract cutting with a 34 mm cutting balloon. **A:** simultaneous angiography in the right ventricle showing the complete occlusion of the RVOT by the balloon that shows a 27 mm notch at stenosis level. **B:** coronary artery interrogation during cutting balloon inflation without coronary compromise.

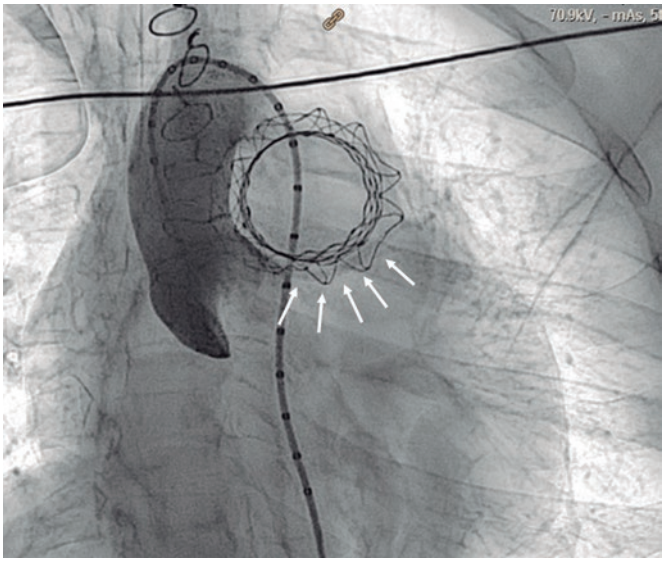


Figure 6. Final aortogram for coronary artery assessment. Arrows are indicative of the trajectory of the left anterior descending coronary artery.

Variables

Demographic and anthropometric data were collected, as well as imaging modality and procedural data to conduct a descriptive analysis of our own experience.

Definitions

Complications were categorized as minor or major. The later were death, potentially life-threatening adverse events, and events requiring surgery (embolization, myocardial perforation, vascular rupture, residual PR, hemolysis, valvular lesion). The former were complications that resolve spontaneously or subside with clinical treatment without potentially fatal outcomes (vascular access

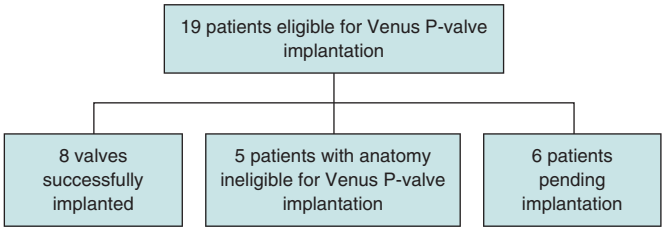


Figure 7. Flowchart of patients included in the study.

Table 1. Overall description of the sample

Patient	Sex	Age (years)	Weight (kg)	RV (mlLm^2)	PAT (mm) MRI	PAT (mm) CT	PAT (mm) angiography	Cutting balloon (mm)	Valvular size
1	W	41	56	122	28	NA	26	26	30-25
2	M	34	62	164	28	27	28	28	32-25
3	W	25	66	NA	NA	NA	28	28	32-25
4	M	33	90	NA	NA	33	31	32	36-25
5	M	34	68	134	31	NA	26	27	34-25
6	M	17	63	173	29	31	31	31	34-25
7	M	45	68	NA	NA	34	26	32	34-30
8	W	43	42	130	25	NA	24	24	28-25

CT, computed tomography scan; M, man; MRI, magnetic resonance imaging; NA, not available; PAT, pulmonary arterial trunk; RV, right ventricle; W, woman.

problems, fever, neuroapraxias, etc.). Implantation was considered successful in the absence of major complications 24 hours after the procedure.

RESULTS

A total of 8 Venus P-valves were implanted in 8 patients at our center from September 20th through November 4th, 2022. The underlying conditions were tetralogy of Fallot (5 patients), pulmonary atresia with ventricular septal defect (1 patient), atrial septal defect with pulmonary stenosis (1 patient), and ventricular septal defect and pulmonary artery banding (1 patient) who required RVOT dilatation in its configuration. All the patients had a transannular patch. Also, all patients had severe pulmonary regurgitation with RV repercussion and PAT dilatation, and were ineligible for transcatheter balloon-expandable valve implantation due to the size of their RVOTs. Table 1 shows a overall description of the patients.

All patients had dilated PATs as seen on the CT scan or MRI—meaning they were suboptimal candidates for balloon-expandable valve implantation—and tubular PATs without stenoses in, at least, 1 pulmonary artery.

The valves were successfully and uneventfully implanted in all the patients with optimal valvular competence immediately after implantation. A total of 7 implantations were performed via femoral access, and 1 via right jugular vein due to bilateral femoral venous thrombosis. High-support guidewires were placed in the left pulmonary artery (6 cases), and right pulmonary artery (2 cases, 1 due to moderate left pulmonary artery stenosis, and the other one because it was a jugular access). In 7 and 1 cases, respectively, 26-Fr and 24-Fr Dryseal sheaths were used through which implantation occurred. The length of the valves implanted was 25 mm (n = 7) and 30 mm (n = 1).

The median fluoroscopy time was 34 min (interquartile range, 32-37), and the mean radiation dose, 307 mGy/m^2 (standard deviation, 64.4). We saw an adequate correlation between the CT and MRI measurements of the PAT and the angiography measurements and the cutting balloon.

No severe complications were reported in any of the cases. In 1 case, while the valve was being deployed, 1 of the proximal hooks got trapped in the delivery system due to incomplete removal of the capsule covering the valve. It, however, resolved uneventfully (figure 8). A total of 3 patients had mild thoracic pain 24 hours after implantation not showing elevated troponin levels or ECG abnormalities. Also, 1 patient complained of right scapula pain. One of the patients had common ventricular extrasystole that started right after valve implantation and subsided spontaneously within the next 48 hours not requiring any therapy at discharge. One patient broke a fever 48 hours after implantation without elevation of acute phase reactants.

The mean length of stay was 3 days (range 2-4). All patients were discharged on acetylsalicylic acid.

DISCUSSION

Transcatheter pulmonary valve implantation is, currently, a procedure widely performed in the cath labs of congenital coronary care units. Up until now, the valves available—with sizes up to 29 mm—left a significant number of patients without transcatheter therapeutic options available. In some cases, off-label techniques were used (several stents implanted in the PAT to reduce its caliber, stent landing in the left pulmonary artery, etc.) or larger sized balloon-expandable valve implantation with an indication for the aorta (32 mm Myval valve), but not approved for the RVOT.[9]

Among the main advantages of the Venus P-valve is the possibility or performing one-stage diagnostic catheterizations and valve implantations since previous stenting is not required to create a landing zone (as it was the case with the Melody and Edwards valves in several native tracts). In the most dilated pulmonary arterial trunks (> 24 mm-to-26 mm) one-stage stenting is the gold standard. Then, wait for, at least, 6 weeks until endothelization occurs to minimize the risk of embolization while the valve is being implanted, which requires a second catheterization to implant the valve. Another advantage of the Venus P-valve is how easy it is to use. It is a short procedure with 34 min fluoroscopy times in our cases (shorter to the times reported in our series of native RVOTs and other valves between 40 min and 50 min).

The flexibility of the valve allows PAT adaptation without exerting radial strength on adjacent structures, which is a plus for cases of coronary RVOT-related anatomies.

The short 25 mm valve was used in 7 cases since these patients' PAT anatomy allowed such length. With longer length, less flexibility for the valve and higher risk of long-term fractures. Up until today, a rate of fractures between 11% and 27% has been reported

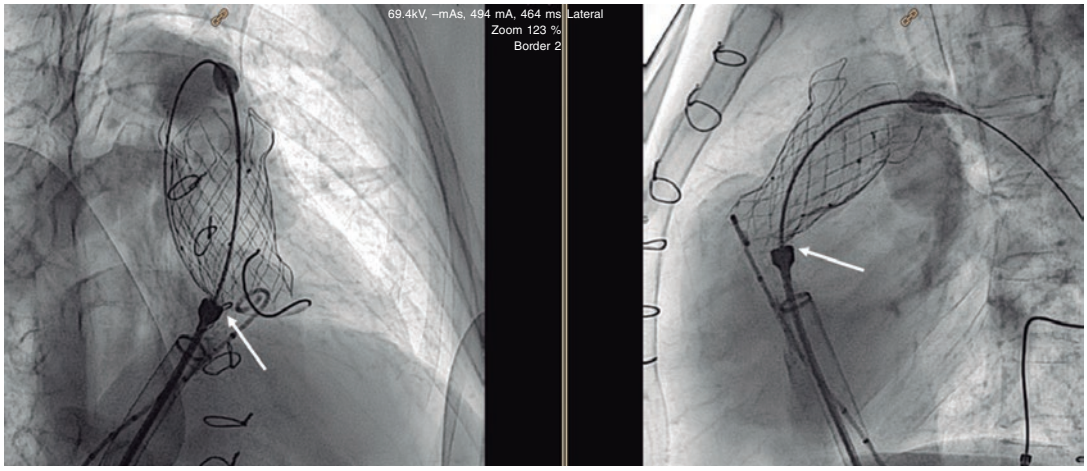


Figure 8. Arrows indicate, in 2 different projections, that 1 of the attachment hooks is still trapped in the delivery system preventing full valve deployment.

without associated complications or loss of valvular competence associated with the fractures.[5,10]

We should pay special attention to the complete removal of the capsule at the end of valve deployment because, if removal is incomplete as it happened with our case (figure 8), hooks can't be released, and the valve does not get deployed with the corresponding risk of RV embolization.[11] To make sure that the system has been released, the hooks should be checked in, at least, 2 different views or projections.[6]

The diabolo-shaped configuration makes this valve unsuitable for all RVOT anatomies. In cases of distal stenosis at PAT level or at the origin of pulmonary arteries this valve is ill-advised because such stenoses would be limiting the opening of the valve distal border. Regarding this shape—wider in its borders—the onset of transient ventricular extrasystole due to contact with the infundibulum proximal border has been reported. However, to this date, no arrhythmias have ever been reported requiring ablation or cardioversion. In our own experience, only 1 patient had frequent extrasystoles, yet no sustained ventricular arrhythmias were ever reported.

The clinical trial (NCT 02846753) conducted to obtain the CE marking revealed the presence of isolated endocarditis (incidence rate of 1.2%). When long-term follow-up results become available, the actual rates of endocarditis, fractures, and valvular dysfunction will be assessed.

Limitations

The short follow-up of patients is this study main limitation. We've been closely monitoring these patients including the use of Holter monitor and imaging modalities (echocardiography, CT scan, and MRI) to properly assess the mid- and long-term evolution of valve implantation. Another limitation is the lack of a control surgical group, which means that comparison can only be made with a historic cohort.

CONCLUSIONS

In conclusion, valve implantation with the new self-expanding Venus P-valve was, in our own preliminary experience, a safe and feasible procedure for valve implantation in very dilated RVOTs with a contraindication for the current balloon-expandable valves with CE marking.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors contributed to the management and follow-up of the patients, data mining, and approved the manuscript final version for publication. M. Álvarez-Fuente, and M.J. del Cerro designed the study, analyzed data, and drafted the manuscript. Hernández, and I. García Ormazábal also drafted the manuscript.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THIS TOPIC?

- Transcatheter pulmonary valve implantation is a common procedure in patients with congenital heart diseases. However, the current valves available are not suitable for all anatomical variants or sizes of the pulmonary arterial trunk.
- New self-expanding valves with larger diameters to solve this problem are currently in the pipeline.

WHAT DOES THIS STUDY ADD?

- The early experience with the new self-expanding pulmonary Venus P-valve has been satisfactory in the first 8 implantations performed at our center.
- It allowed transcatheter studies of patients whose anatomies would have required surgery.
- This new valve allows one-stage implantations and is easy to use.

REFERENCES

1. McElhinney DB, Hellenbrand WE, Zahm EM, et al. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US melody valve trial. *Circulation*. 2010;122:507-516.
2. Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet*. 2000;356:1403-1405.
3. Boone RH, Webb JG, Horlick E, et al. Transcatheter pulmonary valve implantation using the Edwards SAPIEN transcatheter heart valve. *Catheter Cardiovasc Interv*. 2010;75:286-294.
4. Schievano S, Coats L, Migliavacca F, et al. Variations in right ventricular outflow tract morphology following repair of congenital heart disease: implications for percutaneous pulmonary valve implantation. *J Cardiovasc Magn Reson*. 2007;9:687-695.
5. Sivakumar K, Sagar P, Qureshi S, et al. Outcomes of Venus P-valve for dysfunctional right ventricular outflow tracts from Indian Venus P-valve database. *Ann Pediatr Cardiol*. 2021;14:281-292.
6. Garay F, Pan X, Zhang YJ, Wang C, Springmuller D. Early experience with the Venus p-valve for percutaneous pulmonary valve implantation in native outflow tract. *Neth Heart J*. 2017;25:76-81.
7. Alvarez-Fuente M, Garrido-Lestache E, Fernandez-Pineda L, et al. Timing of Pulmonary Valve Replacement: How Much Can the Right Ventricle Dilate Before it Looses Its Remodeling Potential? *Pediatr Cardiol*. 2016;37:601-605.
8. Baumgartner H, De Backer J, Babu-Narayan SV, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J*. 2021;42:563-645.
9. Rodríguez Ogando A, Ballesteros F, Martínez JLZ. Pulmonary percutaneous valve implantation in large native right ventricular outflow tract with 32mm Myval transcatheter heart valve. *Catheter Cardiovasc Interv*. 2022;99:E38-E42.
10. Morgan G, Prachasilchai P, Promphan W, et al. Medium-term results of percutaneous pulmonary valve implantation using the Venus P-valve: international experience. EuroIntervention. 2019;14:1363-1370.
11. Promphan W, Prachasilchai P, Siripornpitak S, Qureshi SA, Layangool T. Percutaneous pulmonary valve implantation with the Venus P-valve: clinical experience and early results. *Cardiol Young*. 2016;26:698-710.

REC Interv Cardiol. 2023;5(4):270-278
https://doi.org/10.24875/RECICE.M23000376

Original article

Thermodilution assessment of vasoreactivity and microvascular function in the absence of obstructive coronary artery disease

Pau Federico Zaragoza,* Teresa Castelló Viguer, Luis Martínez Ortiz de Urbina, Ana Planas del Viejo, Enrique Peris Domingo, and Francisco Pomar Domingo

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

ABSTRACT

Introduction and objectives: Invasive diagnosis of vasoreactivity and microvascular function may be useful to optimize the management of patients with signs and/or symptoms of myocardial ischemia in the absence of significant coronary stenosis (INOCA). We analyzed the prevalence of the different endotypes, as well as the concordance between 2 diagnostic methods based on thermodilution assessment.
Methods: We prospectively included 60 patients with INOCA who underwent a vasoreactivity test with intracoronary acetylcholine, and measurement of absolute coronary blood flow (Q) and minimum microvascular resistance (R) using continuous thermodilution assessment. Finally, calculations of the coronary flow reserve (CFR) and index of microcirculatory resistance index (IMR) were made using the bolus thermodilution method considering CFR < 2 and MRI ≥ 25 as established pathological cut-off values.
Results: The invasive functional diagnostic procedure allowed patients to be categorized into 4 subgroups: microvascular dysfunction (40%), epicardial vasospasm (17%), mixed disorder (20%), and normal study (23%). No correlation was seen between the Q and the CFR. Using ROC curves, an R > 435 UW was estimated as the optimal cut-off value to identify patients with IMR ≥ 25 with an area under the curve of 0.67 (95%CI, 0.51-0.82; $P = .04$).
Conclusions: The invasive study of vasoreactivity and microcirculation was feasible and safe. Prevalence of vasospasm and microvascular dysfunction in patients with INOCA was high. The CFR/MRI/Q combined study allowed us to unmask a subtype of microvascular dysfunction characterized by an abnormally high coronary flow at baseline. The concordance seen between the microvascular resistance obtained by continuous thermodilution measurements and the reference method was low so future studies are justified to determine the usefulness of this technique.

Keywords: Microvascular dysfunction. Vasospasm. Acetylcholine. Continuous thermodilution measurements. Microvascular resistance. INOCA.

Estudio de la vasorreactividad y la función microvascular por termodilución en ausencia de enfermedad coronaria obstructiva

RESUMEN

Introducción y objetivos: El diagnóstico invasivo de la vasorreactividad y la función microvascular puede resultar de utilidad para optimizar el manejo de los pacientes con signos o síntomas de isquemia miocárdica en ausencia de estenosis coronarias significativas (INOCA). Se analizó la prevalencia de los distintos endotipos y la concordancia entre 2 métodos diagnósticos basados en la termodilución.
Métodos: Se incluyeron de forma prospectiva 60 pacientes con INOCA a quienes se realizó un test de vasorreactividad con acetilcolina intracoronaria, medida del flujo absoluto (Q) y la resistencia microvascular mínima (R) por termodilución continua y, por último, se calcularon la reserva de flujo coronario (RFC) y el índice de resistencia microvascular (IRM) por termodilución con bolos. Se consideraron como patológicos los puntos de corte establecidos de RFC < 2 e IRM ≥ 25.
Resultados: El procedimiento diagnóstico funcional invasivo permitió clasificar a los pacientes en 4 subgrupos: disfunción microvascular (40%), vasoespasmo epicárdico (17%), trastorno mixto (20%) y estudio normal (23%). No se observó correlación entre Q y RFC. Mediante curvas ROC se estimó una R > 435 UW como el punto de corte óptimo para identificar pacientes con IRM ≥ 25, con un área bajo la curva de 0,67 (IC95%, 0,51-0,82; p = 0,04).

* **Corresponding author.**
E-mail address: pau@comv.es (P. Federico Zaragoza).

Received 23 January 2023. Accepted 17 March 2023. Online 7 June 2023.

Conclusiones: El estudio invasivo de la vasorreactividad y la microcirculación fue factible y seguro. La prevalencia de vasoespasmo y de disfunción microvascular en pacientes con INOCA fue elevada. El análisis conjunto de RFC, IRM y Q permitió desenmascarar un subtipo de disfunción microvascular caracterizado por un flujo coronario basal anormalmente elevado. La concordancia entre la resistencia microvascular obtenida por termodilución continua respecto al método de referencia fue baja, por lo que se requieren futuros estudios para determinar la utilidad de esta técnica.

Palabras clave: Disfunción microvascular. Vasoespasmo. Acetilcolina. Termodilución continua. Resistencia microvascular. INOCA.

Abbreviations

CFR: coronary flow reserve; **INOCA:** ischemia with nonobstructive coronary artery disease; **IMR:** index of microcirculatory resistance; **Q:** absolute coronary blood flow; **R:** coronary microvascular resistance.

INTRODUCTION

Over the past few years, the term INOCA (ischemia with nonobstructive coronary arteries) has established to define patients with signs or symptoms of ischemic heart disease without angiographically significant obstructive coronary artery disease.[1] In these patients, coronary microvascular or epicardial vessel dysfunction could be the pathophysiological mechanism triggering the symptoms and ischemic impairment.[2]

Currently, the invasive study of microvascular function in patients with INOCA is a recommendation IIa according to the clinical practice guidelines of the European Society of Cardiology.[3] What it does is measure the parameters that show its functional or structural status like coronary flow reserve (CFR) or index of microcirculatory resistance (IMR).[4]

Recently, the possibility of measuring absolute coronary blood flow (Q) and microvascular resistance (R) by continuous thermodilution with the infusion of a physiological saline solution through a specific coronary microcatheter has been described. This technique has potential advantages like its independence from the operator or not needing pharmacologically induced hyperemia.[5]

The objective of this study is to estimate the prevalence of the different endotypes of patients with INOCA and analyze the correlation between the measurements obtained by continuous thermodilution and the traditional method of intracoronary boluses of physiological saline solutions.

METHODS

This was a prospective and consecutive study of 60 referred patients due to symptoms or signs of myocardial ischemia without angiographically significant coronary artery stenosis on the visual estimate (< 50%) or after functional assessment (resting full-cycle ratio [RFR] > 0.89 or fractional flow reserve [FFR] > 0.80). Severe valvular heart disease, acute coronary syndrome, decompensated heart failure, and any clinical or anatomical condition where the study of microcirculation and vasoreactivity would be considered unnecessary were excluded.

All microcirculation and vasoreactivity studies were scheduled and second-staged. Nitrates and calcium antagonists were withdrawn prior to conducting the tests.

The coronary angiography was performed based on the routine clinical practice via radial access. A spasmolytic cocktail of 200 µg of nitroglycerin was administered. The target artery was the left main coronary artery.

The study was approved by the center ethics research committee and the patients' written informed consent was obtained.

Vasoreactivity test

First, the vasoreactivity test was performed. Patient monitoring included precordial leads, and baseline angiograms were performed using 2 different projections. The sequential administration of acetylcholine was followed by increasing doses of 2 µg, 20 µg, and 100 µg in intracoronary bolus for 2 min. In the presence of significant bradycardia, the injection was interrupted, and if considered appropriate, it was re-administered at a slower rate. A follow-up angiogram was performed after every dose. In the presence of severe symptoms, changes to the echocardiogram or epicardial spasm 200 µg of intracoronary nitroglycerin were administered.

The test was considered positive based on the criteria established by the COVADIS (Coronary vasomotor disorders international study) group: epicardial spasm in the presence of chest pain, changes to the echocardiogram, and constriction ≥ 90%, and microvascular spasm in the presence of chest pain, and changes to the echocardiogram without epicardial spasm ≥ 90%.[6]

Indices obtained with continuous thermodilution

After the administration of unfractionated heparin (70 IU/kg), a pressure-temperature sensor guidewire Pressure Wire X (Abbott, United States) was inserted and pressures at the catheter distal border were equalized. The guidewire was advanced until it reached the left anterior descending coronary artery distal segment.

Resting full-cycle ratio was registered to confirm the lack of hemodynamically significant epicardial stenoses (RFR > 0.89).

Afterwards, a specific Rayflow (Hexacath, France) microcatheter for intracoronary infusion was placed in the left anterior descending coronary artery proximal segment. After confirmation that the guidewire sensor was, at least, 3 cm distal to the tip of the microcatheter, the intracoronary infusion of a physiological saline solution at room temperature and at a dose of 20 mL/min was started using an injector pump to induce hyperemia.

Pressure-temperatures curves were registered using Coroventis software (Abbott, United States). When the distal temperature drop

Figure 1. Measurements obtained by continuous thermodilution: DP, distal pressure; Q, absolute coronary blood flow; Q_i, infusion flow (mL/min); R, microvascular resistance; T, distal temperature; T_i, infusion temperature.

was stabilized, the sensor was withdrawn up to the tip of the microcatheter to determine the infusion temperature.

Afterwards, the injection of the physiological saline solution stopped, and Q (L/min) and R (Wood units) values were obtained automatically (figure 1).

Indices obtained with bolus thermodilution of a physiological saline solution

After completion of the continuous thermodilution study, and once the Rayflow microcatheter was removed, the pressure-temperature guidewire was repositioned in its previous location, and thermodilution curves were registered using the Coroventis software after the vigorous manual injection of 3 intracoronary boluses of 3 mL of a physiological saline solution. Measurements were taken at rest and after inducing hyperemia with a peripheral intravenous bolus of regadenoson (400 µg) resulting in the calculation of CFR and IMR.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median [interquartile range]. The categorical ones were expressed as absolute value or percentage. ROC (Receiver operating characteristic) curves were used to estimate the optimal cut-off values for the continuous variables Q and R. The cut-off values established as pathological for CFR < 2 and IMR ≥ 25 were used as the reference framework. Once dichotomized, the variables Q and R were compared to the CFR and IMR values using chi-square tests. One-way ANOVA was used to compare the different quantitative variables. The statistical analysis was performed using the SPSS v 20 statistical software package (IBM, United States). *P* values < .05 were considered statistically significant.

RESULTS

Study patients

Table 1 shows the baseline characteristics of the 60 patients included in the study. Women (55%) were predominant. Also, there was a high prevalence of cardiovascular risk factors. Most showed typical angina-like clinical signs (76%) and had tested positive to an ischemia test performed before the coronary angiography (60%).

The baseline coronary angiography confirmed that 37% of the patients showed parietal irregularities consistent with atheromatous disease, and 22% had slow coronary flow. The FFR and RFR values were normal in all the cases studied.

Coronary vasoreactivity

As shown on table 2, 60% of the cases (36/60) had a positive response to acetylcholine in the vasoreactivity test. A total of 32% of the cases (19/60) showed severe epicardial vasoconstriction, and 23% (14/60) met the criteria for microvascular spasm. In 3 patients (5%), microvascular spasm was observed concomitantly with the medium dose (20 µg), and epicardial spasm with the high dose (100 µg), which added to the impaired indices of microvascular function was consistent with a mixed endotype.

Indices of microvascular function

Both studies—bolus thermodilution and continuous infusion thermodilution—were performed uneventfully in all of the patients. Table 2 shows the values of the measurements of microvascular function obtained with both techniques.

In the continuous infusion study, a median of absolute flow in the left anterior descending coronary artery of 170 mL/min [138-219 mL/min] was described while the median of microvascular resistance was 496 WU [381-654 WU].

A total of 18% of the patients (11/60) had a reduced CFR (CFR < 2) while 33% (20/60) showed elevated resistances (IMR ≥ 25).

The group of patients with microvascular dysfunction due to low CFR with normal IMR (7/60, 12%) with respect to cases with microvascular dysfunction due to high IMR with normal CFR (16/60, 27%) had a clinical profile with a lower mean age (61 ± 11 vs 66 ± 8), and a higher predominance of women (86% vs 58%) although this tendency was not statistically significant.

Table 1. Clinical and angiographic characteristics (N = 60)

Age (years)	63 ± 10
Women	33 (55%)
Hypertension	39 (65%)
Diabetes	21 (35%)
Dyslipidemia	35 (58%)
Smoking (current or past)	28 (47%)
Previous percutaneous revascularization	4 (7%)
Previous myocardial infarction	3 (5%)
Left ventricular systolic dysfunction	4 (7%)
Ejection fraction (%)	63 ± 8
Clinical presentation	
Exertional angina	19 (32%)
Resting angina	13 (22%)
Mixed angina	14 (23%)
Other	14 (24%)
Ischemia test	
Ergometry	19 (32%)
Isotopic scintigraphy	18 (30%)
Dobutamine stress echocardiography	3 (5%)
None	20 (33%)
Coronary angiography	
Atheromatous disease	22 (37%)
Slow flow	13 (22%)

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

Table 2. Procedural data

Pathological vasoreactivity testing	36 (60%)
Epicardial vasospasm	19 (32%)
Microvascular vasospasm	14 (23%)
Combined vasospasm	3 (5%)
Structural microvascular dysfunction (IMR ≥ 25)	20 (33%)
Isolated	5 (8%)
Associated with epicardial spasm	8 (13%)
Associated with microvascular spasm	4 (7%)
Associated with combined spasm	3 (5%)
CFR < 2	11 (18%)
CFR < 2.5	17 (28%)
RFR	0.93 [0.91-0.94]
FFR	0.90 [0.87-0.93]
Q (mL/min)	170 ([138-219]
R (WU)	496 [381-654]
CFR	3.0 [2.3-4.2]
IMR	20 [12-28]

Data are expressed as no. (%) or median [interquartile range].
CFR, coronary flow reserve; FFR, fractional flow reserve; IMR, index of microvascular resistance; Q, absolute coronary blood flow; R, microvascular resistance; RFR: resting full-cycle ratio.

Table 3. Mean transit times obtained by bolus thermodilution

	Overall (N = 60)	CFR < 2 (N = 11)	CFR < 2 Q > 170 (N = 7)	CFR < 2 Q < 170 (N = 4)
Baseline MTT	1.13 ± 0.70	0.48 ± 0.45*	0.31 ± 0.15*	0.77 ± 0.68
Hyperemic MTT	0.36 ± 0.25	0.35 ± 0.28	0.25 ± 0.14	0.51 ± 0.41

Values (in seconds) are expressed as mean ± standard deviation.
CFR, coronary flow reserve; MTT, mean transit time; Q, absolute coronary blood flow.
* $P < .05$ for comparison with the rest of the sample.

Table 3 shows the mean transit times (MTT) of bolus thermodilution tests. The cases with low CFR showed significantly shorter baseline MTT (0.48 ± 0.45 vs 1.13 ± 0.70), especially the subgroup of patients with low CFR and high Q (0.31 ± 0.15 vs 0.77 ± 0.68).

Figure 2 shows data of coronary flow estimated by MTT measurement divided into 3 groups based on CFR and IMR results. We should mention that patients with low CFR without elevated resistances had significantly high resting flows and hyperemic flows without significant differences compared to the rest while in patients with low CFR and elevated resistances, the opposite phenomenon was described.

Endotypes

Figure 3A shows the percentages of endotypes based on the result of the acetylcholine test and the measurements of CFR and IMR. The most common pattern was microvascular dysfunction (24/60, 40%) followed by the normal study (14/60, 23%). In 20% of the patients (12/60), microvascular dysfunction overlapped with epicardial vasospasm while in 17% of the patients (10/60) isolated epicardial vasospasms were seen.

Table 4 shows how the mechanisms of vasomotor and microvascular dysfunction overlap in many cases.

The association between epicardial vasospasm and structural microvascular dysfunction (IMR ≥ 25) was the most prevalent combination in cases of mixed disorder (11/12). In turn, this endotype, in continuous thermodilution measurements, showed significant differences compared to the normal pattern, with reduced absolute flow values and elevated resistances (figure 3B) indicative of more serious structural and functional damage.

Concordance among the different indices of microvascular function

The ROC curve analysis of absolute coronary blood flow (Q) with respect to CFR < 2 determined an optimal cut-off value of 170 mL/min (a 64% sensitivity, and a 52% specificity) with an area under the curve of 0.50 (95% confidence interval [95%CI], 0.33-0.66; $P = .97$), therefore showing no diagnostic utility.

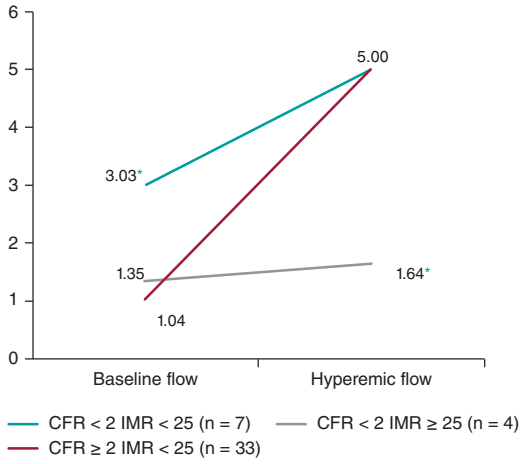


Figure 2. Baseline and hyperemic mean flow estimated based on the MTT (1/MTT) and grouped based on the CFR and IMR results. Values are expressed as s^{-1}. CFR, coronary flow reserve; IMR, index of microvascular resistance; MTT, mean transit time.
* $P < .05$.

Given the recent proposal to consider the cut-off value of CFR < 2.57,[7] the analysis was performed using this threshold as the reference. In addition, no significant concordance was seen (area under the curve of 0.45 [95%CI, 0.30-0.61; $P = .56$]).

Regarding R with respect to IMR, an area under the curve of 0.67 (95%CI, 0.51-0.82; $P = .04$) was obtained, which was indicative of a weak yet significant diagnostic concordance (figure 4). The estimated optimal cut-off value was 435 WU, which was consistent with an 81% sensitivity and a 57% specificity. A total of 66% of cases with IMR ≥ 25 were categorized correctly using this index.

The absence of an association between Q and CFR was confirmed in correlation tests (Spearman's rho correlation coefficient = -0.02; 95%CI, -0.24-0.25; $P = .99$). However, a weak yet significant correlation was seen between Q and hyperemic MTT (Spearman's rho = -0.28; 95%CI, -0.01-0.51; $P = .04$), and between R and IMR (Spearman's rho = 0.28; 95%CI, 0.04-0.51; $P = .03$).

Complications

While the vasoreactivity test was being performed, 3 cases of transient bradycardia (5%) without clinical repercussions and 2 episodes of atrial fibrillation (4%) were reported, 1 of them self-limited while the other required sedation and electrical cardioversion. After the administration of regadenoson, most patients experienced some degree of discomfort, which was well-tolerated and reversed with the administration of 100 mg of intravenous theophylline. No other complications or adverse effects were reported.

DISCUSSION

This study confirms that a high percentage of patients with symptoms or signs of INOCA show microvascular dysfunction or vasospasm in invasive functional testing, and that it is feasible and safe to perform (figure 5).

The percentage of patients with microcirculation or vasomotility alterations found in our study (77%) is consistent with former studies of patients with angina without obstructive coronary artery disease (64% to 89%[8-11]).

Vasoreactivity test

Some groups systematically use a dose of 200 µg of intracoronary acetylcholine to perform the vasoreactivity test; in our study, the high dose was established at 100 µg according to the COVADIS group, the CorMicA protocol, and the technical document of the Spanish Society of Cardiology Working Group on Cardiac Catheterization and Interventional Cardiology, which highlights its high sensitivity and specificity rates (90% and 99%, respectively).[12] As a matter of fact, the high prevalence of positive results seen in our study in the acetylcholine test (60%) is similar to that reported in other series (57% to 71%[13-15]). In a recent study of 110 patients, Feenstra et al.[11] revealed that 62% of the patients had a pathological acetylcholine test that confirmed the presence of epicardial vasospasm and microvascular spasm (36% and 26%, respectively).

In our study, the complications associated with the vasoreactivity test in our study are not very many: 2 cases of atrial fibrillation (4%), which is consistent with the incidence rate reported by the CorMIcA trial (5%).[9]

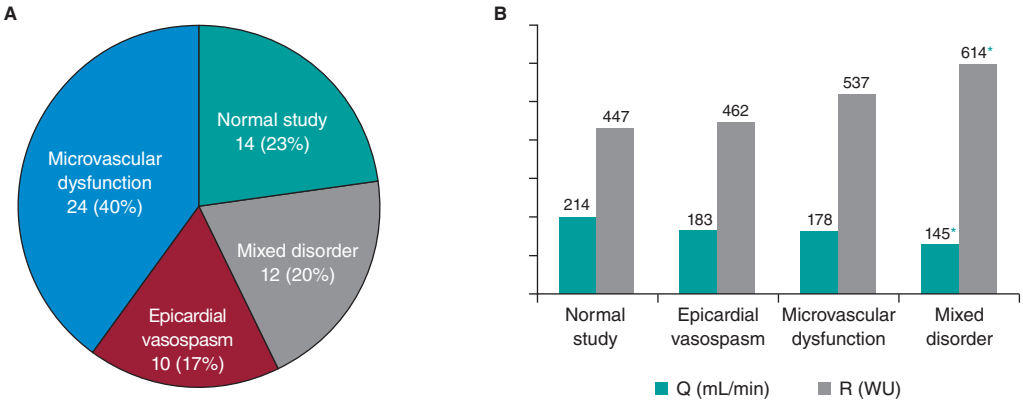


Figure 3. A: endotype-based classification. Values are expressed as absolute number and percentage. **B:** mean values of absolute flow and microvascular resistance grouped by endotypes. Q, absolute coronary blood flow; R, microvascular resistance.
* $P < .05$ with respect to normal study.

Table 4. Results of the acetylcholine test and bolus thermodilution study (N = 60)

Epicardial spasm	Microvascular spasm	IMR ≥ 25	CFR < 2	Endotype	Cases
–	–	–	–	Normal	14 (23.3%)
+	–	–	–	Epicardial vasospasm	10 (16.7%)
–	+	–	–	Microvascular dysfunction	9 (15.0%)
–	–	+	–	Microvascular dysfunction	5 (8.3%)
–	–	–	+	Microvascular dysfunction	5 (8.3%)
–	+	+	–	Microvascular dysfunction	3 (5.0%)
–	+	–	+	Microvascular dysfunction	1 (1.6%)
–	+	+	+	Microvascular dysfunction	1 (1.6%)
+	–	+	–	Mixed disorder	6 (10.0%)
+	+	+	–	Mixed disorder	2 (3.3%)
+	–	+	+	Mixed disorder	2 (3.3%)
+	–	–	+	Mixed disorder	1 (1.6%)
+	+	+	+	Mixed disorder	1 (1.6%)

Data are expressed as no. (%)
CFR, coronary flow reserve; IMR, index of microvascular resistance.

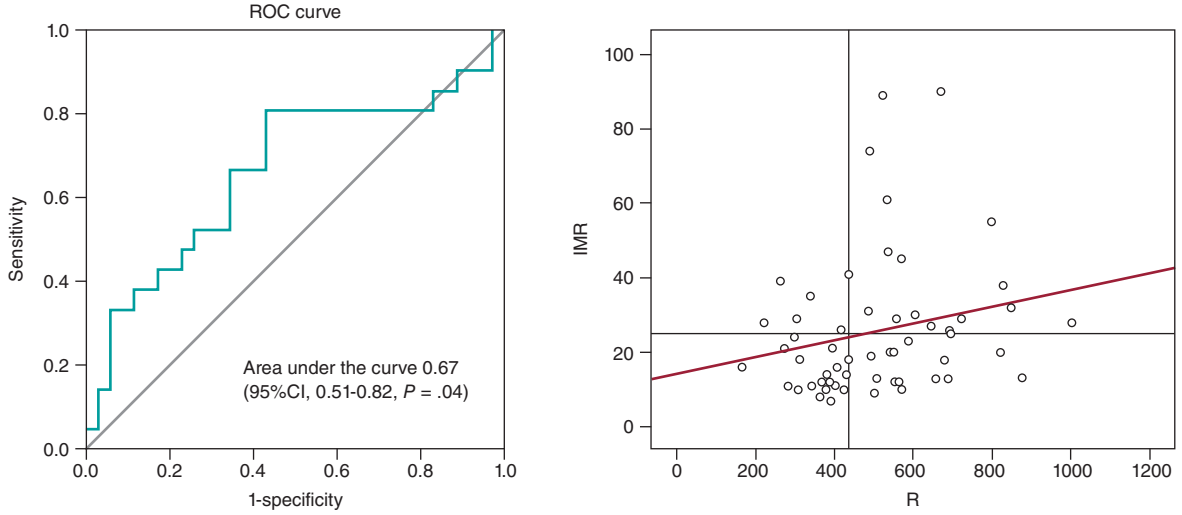


Figure 4. Analysis of the R cut-off value > 435 WU to predict IMR ≥ 25, and scatter plot showing the correlation between IMR and R. IMR, index of microvascular resistance; R, microvascular resistance.

Prevalence of endotypes

The most common endotype in our patients was isolated microvascular dysfunction (40%), but not as much as in the CorMicA trial (52%). These differences could be explained by the discrepancy seen in the percentage of completely normal angiographies (22% in the CorMicA vs 63% in our study) due to the possible association between non-obstructive atheromatous disease and microvascular dysfunction.[16,17]

The prevalence of the remaining endotypes is similar to that reported in the CorMicA trial: isolated epicardial vasospasm (17% vs 17%), and mixed disorder (20% vs 21%). A recent meta-analysis that included 14 427 patients with INOCA also shows similar percentages.[18]

Indices of microvascular function obtained through bolus thermodilution

The analysis of the MTT obtained with this technique (figure 2), a parameter that correlates inversely with the direct measurement of coronary flow,[19] reveals an interesting finding that is consistent with the data published by Nardone et al.[20]: patients with low CFR have 2 differentiated phenotypes based on the IMR. On the one hand, cases with reduced CFR and elevated resistances have normal baseline flow and low hyperemic flow, which would be indicative of an insufficient vasodilation response. However, in patients with normal resistances, a reduced CFR would be indicative of an abnormally elevated resting flow with hyperemic flow in the normal range. This phenomenon can also be observed in the analysis of patients with high Q (table 3) in whom a reduced CFR can be

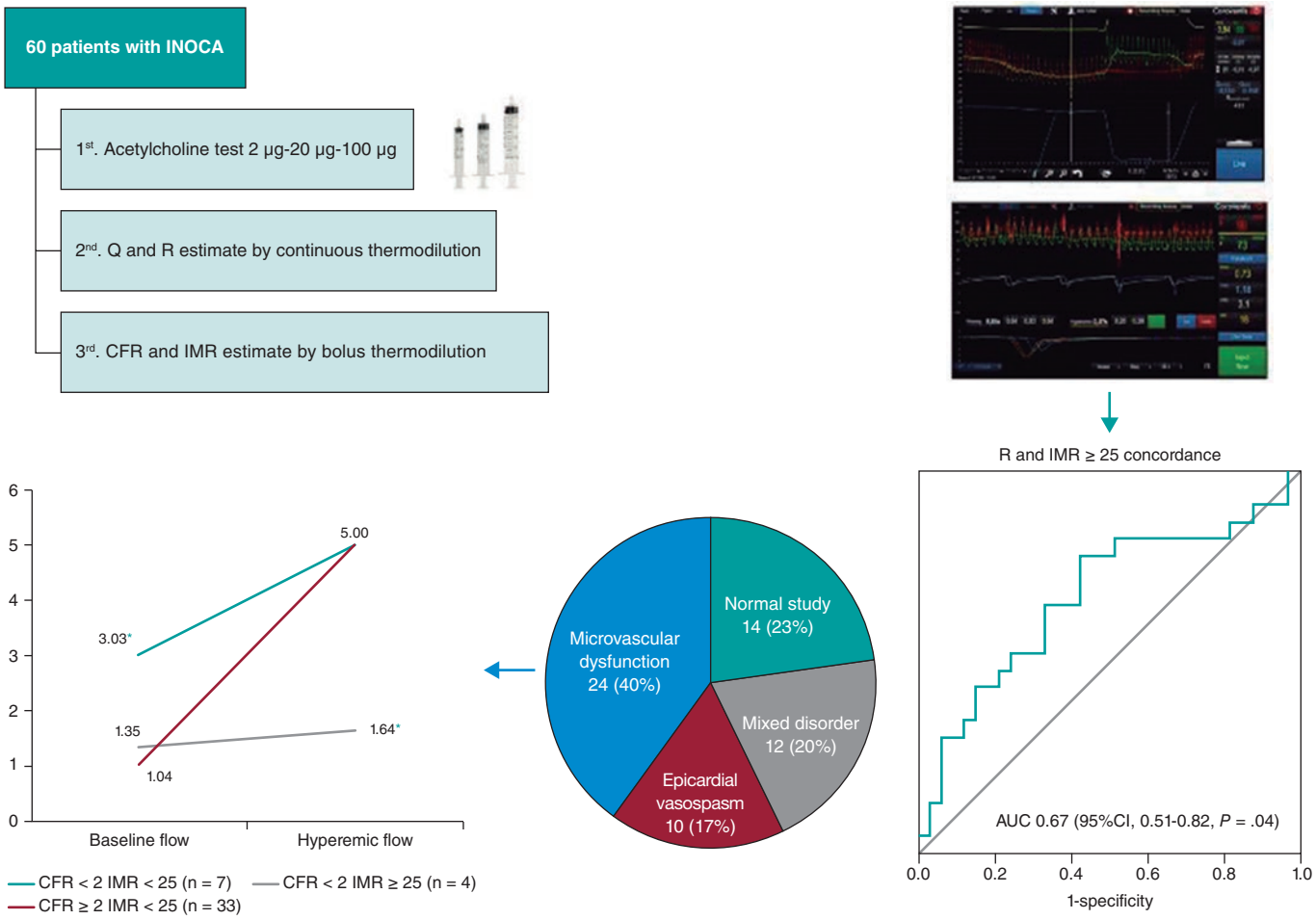


Figure 5. Study design, endotype-based classification, and analysis using the ROC curve. AUC, area under the curve; CFR, coronary flow reserve; IMR, index of microvascular resistance; INOCA, ischemia with nonobstructive coronary artery disease; Q, absolute coronary blood flow; R, microvascular resistance. * $P < .05$.

attributed to elevated baseline flow instead of an insufficient hyperemic response.

Therefore, this subgroup probably shows inefficient or dysregulated baseline myocardial flows. This characteristic, of indeterminate cause, could have important therapeutic implications like a lack of response to vasodilator drugs.

Indices of microvascular function obtained by continuous thermodilution

The continuous thermodilution technique has evolved to the point of quantifying Q and R with a microcatheter and specific software in a simple and precise fashion. The main advantages of this method are its independence from an operator, reproducibility, and induction of hyperemia with a physiological saline solution without the need for pharmacological agents.[21-24] However, its main limitation is the lack of normal reference values.

In our study, the lack of a correlation between Q and CFR could be justified by the variations described of baseline myocardial flow. Estimating the CFR requires estimating the baseline coronary flow while Q is a measurement that is representative of hyperemic flow.

The weak concordance seen in this study between Q and hyperemic MTT and between R and IMR shows how difficult it is to establish valid cut-off values for patient comparison with these indices.

With an optimal cut-off value of R in our study of 435 WU (an 81% sensitivity, and a 57% specificity), a total of 66% of cases with IMR ≥ 25 were properly categorized with this index. This value is somewhat lower compared to the one shown by Rivero et al.,[25] who analyzed 120 patients and found that an R > 500 WU properly categorized 80% of the cases with IMR ≥ 25. Konst et al.[26] studied 84 patients with INOCA using both thermodilution techniques only to find no correlation between the Q-R combo and IMR.

The differences seen may be explained by the fact that the quantitative variability of Q and R values among individuals mostly depends on myocardial mass. However, in positron emission tomography studies, considerable ranges were seen even after adjusting for flow and resistance values for myocardial mass. Therefore, it has been speculated that the most plausible hypothesis is the natural variation of hyperemic myocardial perfusion among individuals.[27]

Therefore, indices like CFR estimated by continuous thermodilution and microvascular resistance reserve are currently in the pipeline. They correlate the absolute values of flow and resistance seen during hyperemia with those obtained at rest. Nonetheless,

these new parameters will still need validation in future studies.[28,29]

Limitations

The data presented here should be interpreted while understanding that this is an observational, single-center study with a small sample size. Therefore, results may be biased by confounding factors associated with a study of this nature.

The left anterior anterior descending coronary artery was considered as the pre-specified target vessel. However, in the routine clinical practice, it may be appropriate to assess other arteries in the presence of negative tests and high clinical suspicion.[1]

The optimal sequence in invasive functional studies has not been established yet.[1] In our case, we chose to perform the acetylcholine test first to minimize the instrumentation of the artery and avoid further guidewire-induced vasoreactivity. However, the spasm and symptoms seen during the provocation test, although transient, could interfere with subsequent measurements of microvascular function. The possibility of determining CFR by continuous thermodilution was established at the beginning of our study, and it was assumed that a comparison of the CFRs obtained with both techniques would have been more appropriate.

In most bolus thermodilution studies, intravenous adenosine is used to induce hyperemia. However, we chose regadenoson because it is easy to use, following our previous experience, and because evidence says it is equivalent to adenosine.[30,31]

Finally, we should not overlook that this is an invasive study so potential risks associated with the examination should be weighed in. To this date, however, conducting this study has not impacted prognosis.

CONCLUSIONS

The invasive study of coronary vasoreactivity and microcirculation is feasible and safe. These studies allow us to easily recognize different endotypes of patients with INOCA and help us optimize their treatment.

The analysis of CFR, IMR, and Q combined can unmask a subtype of microvascular dysfunction characterized by an abnormally high baseline coronary flow.

The new indices obtained by continuous thermodilution show low concordance with respect to the reference indices. Therefore, future studies will be required to determine the utility of this technique.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors contributed substantially to the study idea, design, and data mining process. In addition, all approved the manuscript final version for publication.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THE TOPIC?

- The invasive diagnosis of microvascular dysfunction and coronary vasospasm have proven useful to improve the quality of life of patients without obstructive coronary artery disease on the coronary angiography.
- Indices of microvascular dysfunction obtained by continuous thermodilution offer potential advantages since are they are independent from the operator, reproducible, and do not require pharmacologically induced hyperemia.

WHAT DOES THIS STUDY ADD?

- Invasive coronary functional diagnosis is feasible and safe and highlights the high prevalence of microcirculation and vasomotility alterations in patients without obstructive coronary artery disease.
- The combined analysis of the different indices may be useful to characterize cases with decreased CFR.
- Future studies are needed to establish the utility of microvascular function measurements obtained by continuous thermodilution.

REFERENCES

1. Kunadian V, Chieffo A, Camici PG, et al. An EAPCI Expert Consensus Document on Ischaemia with Non-Obstructive Coronary Arteries in Collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. *Eur Heart J.* 2020;41:3504-3520.
2. Camici PG, Crea F. Coronary microvascular dysfunction. *N Engl J Med.* 2007;356:830-840.
3. Knuuti J, Wijns W, Saraste A, et al. ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41:407-477.
4. Ford TJ, Ong P, Sechtem U, et al. COVADIS Study Group. Assessment of Vascular Dysfunction in Patients Without Obstructive Coronary Artery Disease: Why, How, and When. *JACC Cardiovasc Interv.* 2020;13:1847-1864.
5. Xaplanteris P, Fournier S, Keulards DCJ, et al. Catheter-Based Measurements of Absolute Coronary Blood Flow and Microvascular Resistance: Feasibility, Safety, and Reproducibility in Humans. *Circ Cardiovasc Interv.* 2018;11:e006194.
6. Beltrame JF, Crea F, Kaski JC, et al., On Behalf of the Coronary Vasomotion Disorders International Study Group (COVADIS). International standardization of diagnostic criteria for vasospastic angina. *Eur Heart J.* 2015;38:2565-2568.
7. Demir OM, Boerhout CKM, de Waard GA, et al. Comparison of Doppler Flow Velocity and Thermodilution Derived Indexes of Coronary Physiology. *JACC Cardiovasc Interv.* 2022;15:1060-1070.
8. Suda A, Takahashi J, Hao K, et al. Coronary functional abnormalities in patients with angina and nonobstructive coronary artery disease. *J Am Coll Cardiol.* 2019;74:2350-2360.
9. Ford TJ, Stanley B, Good R, et al. Stratified medical therapy using invasive coronary function testing in angina: the CorMicAtrial. *J Am Coll Cardiol.* 2018;72:2841-2855.
10. Sara JD, Widmer RJ, Matsuzawa Y, Lennon RJ, Lerman LO, Lerman A. Prevalence of Coronary Microvascular Dysfunction Among Patients With Chest Pain and Nonobstructive Coronary Artery Disease. *JACC Cardiovasc Interv.* 2015;8:1445-1453.
11. Feenstra RGT, Boerhout CKM, Woudstra J, et al. Presence of Coronary Endothelial Dysfunction, Coronary Vasospasm, and Adenosine-Mediated Vasodilatory Disorders in Patients With Ischemia and Non obstructive Coronary Arteries. *Circ Cardiovasc Interv.* 2022;15:e012017.
12. Gutiérrez E, Gómez-Lara J, Escaned J, et al. Valoración de la función endotelial y provocación de vasoespasmo coronario mediante infusión

intracoronaria de acetilcolina. Documento técnico de la ACI-SEC. *REC Interv Cardiol*. 2021;3:286-296.
13. Aziz A, Hansen HS, Sechtem U, Prescott E, Ong P. Sex-Related Differences in Vasomotor Function in Patients With Angina and Unobstructed Coronary Arteries. *J Am Coll Cardiol.* 2017;70:2349-2358.
14. Seitz A, Gardezy J, Pirozzolo G, et al. Long-Term Follow-Up in Patients With Stable Angina and Unobstructed Coronary Arteries Undergoing Intracoronary Acetylcholine Testing. *J Am Coll Cardiol Interv.* 2020;13:1865-1876.
15. Ong P, Athanasiadis A, Borgulya G, et al. Clinical usefulness, angiographic characteristics, and safety evaluation of intracoronary acetylcholine provocation testing among 921 consecutive white patients with unobstructed coronary arteries. *Circulation.* 2014;129:1723-1730.
16. Melikian N, Vercauteren S, Fearon WF, et al. Quantitative assessment of coronary microvascular function in patients with and without epicardial atherosclerosis. *EuroIntervention*. 2010;5:939-945.
17. Sharaf B, Wood T, Shaw L, et al. Adverse outcomes among women presenting with signs and symptoms of ischemia and no obstructive coronary artery disease: findings from the National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation (WISE) angiographic corelaboratory. *Am Heart J*. 2013;166:134-141.
18. Mileva N, Nagumo S, Mizukami T, et al. Prevalence of Coronary Microvascular Disease and Coronary Vasospasm in Patients With Nonobstructive Coronary Artery Disease: Systematic Review and Meta-Analysis. *J Am Heart Assoc.* 2022;11:e023207.
19. De Bruyne B, Pijls NH, Smith L, et al. Coronary thermodilution to assess flow reserve: experimental validation. *Circulation.* 2001;104:2003-2006.
20. Nardone M, McCarthy M, Ardern CI, et al. Concurrently Low Coronary Flow Reserve and Low Index of Microvascular Resistance Are Associated With Elevated Resting Coronary Flow in Patients With Chest Pain and Nonobstructive Coronary Arteries. *Circ Cardiovasc Interv.* 2022;15:e011323.
21. Van't Veer M, Adjedj J, Wijnbergen I, et al. Novel monorail infusion catheter for volumetric coronary blood flow measurement in humans: invitro validation. *EuroIntervention*. 2016;12:701-707.
22. Rivero F, Bastante T, Cuesta J, García-Guimaraes M, Maruri-Sánchez R, Alfonso F. Volumetric Quantification of Coronary Flow by Using a Monorail Infusion Catheter: Initial Experience. *Rev Esp Cardiol*. 2018;71:1082-1084.
23. Everaars H, de Waard GA, Schumacher SP, et al. Continuous thermodilution to assess absolute flow and microvascular resistance: validation in humans using [15O] H2O positron emission tomography. *Eur Heart J.* 2019;40:2350-2359.
24. Keulards DCJ, Van't Veer M, Zelis JM, et al. Safety of absolute coronary flow and microvascular resistance measurements by thermodilution. *EuroIntervention.* 2021;17:229-232.
25. Rivero F, Gutiérrez-Barrios A, Gomez-Lara J, et al. Coronary microvascular dysfunction assessed by continuous intracoronary thermodilution: A comparative study with index of microvascular resistance. *Int J Cardiol.* 2021;333:1-7.
26. Konst RE, Elias-Smale SE, Pellegrini D, et al. Absolute Coronary Blood Flow Measured by Continuous Thermodilution in Patients With Ischemia and Nonobstructive Disease. *J Am Coll Cardiol.* 2021;77:728-741.
27. Fournier S, Keulards DCJ, van't Veer M, et al. Normal values of thermodilution-derived absolute coronary blood flow and microvascular resistance in humans. *EuroIntervention.* 2021;17:e309-e316.
28. Gutiérrez-Barrios A, Izaga-Torralba E, Rivero Crespo F, et al. Continuous Thermodilution Method to Assess Coronary Flow Reserve. *Am J Cardiol.* 2021;141:31-37.
29. De Bruyne B, Pijls NHJ, Gallinoro E, et al. Microvascular Resistance Reserve for Assessment of Coronary Microvascular Function: JACC Technology Corner. *J Am Coll Cardiol.* 2021;78:1541-1549.
30. Federico P, Martínez L, Castelló T, Pomar F, Peris E. Regadenoson intravenoso frente a adenosina intracoronaria para la medida de la reserva fraccional de flujo. *REC Interv Cardiol.* 2019;1:77-82.
31. Gill GS, Gadre A, Kanmanthareddy A. Comparative efficacy and safety of adenosine and regadenoson for assessment of fractional flow reserve: A systematic review and meta-analysis. *World J Cardiol*. 2022;14:319-328.

REC Interv Cardiol. 2023;5(4):279-286
https://doi.org/10.24875/RECICE.M23000381

Original article

Design of the ROLLERCOASTR trial: rotational atherectomy, lithotripsy or laser for the management of calcified coronary stenosis

Alfonso Jurado-Román,[a,*] Antonio Gómez-Menchero,[b] Ignacio J. Amat-Santos,[c,d] Juan Caballero-Borrego,[e] Soledad Ojeda,[f] Raymundo Ocaranza-Sánchez,[g] Santiago Jiménez-Valero,[a] Guillermo Galeote,[a] and Raúl Moreno[a]

[a] *Servicio de Cardiología, Hospital Universitario La Paz, Madrid, Spain*
[b] *Servicio de Cardiología, Hospital Universitario Juan Ramón Jiménez, Huelva, Spain*
[c] *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[d] *Servicio de Cardiología, Hospital Clínico Universitario, Valladolid, Spain*
[e] *Servicio de Cardiología, Hospital Universitario San Cecilio, Granada, Spain*
[f] *Servicio de Cardiología, Hospital Universitario Reina Sofía, Córdoba, Spain*
[g] *Servicio de Cardiología, Hospital Universitario Lucus Augusti, Lugo, Spain*

ABSTRACT

Introduction and objectives: Coronary calcification is one of the leading factors that affect negatively the safety and effectiveness of percutaneous coronary intervention. Several calcium modification techniques exist. However, there is a lack of randomized evidence on the therapy of choice in this scenario.
Methods: The ROLLERCOASTR is a prospective, multicenter, randomized clinical trial designed to compare the safety and efficacy profile of 3 plaque modification techniques in the moderate-to-severe coronary calcification setting: rotational atherectomy (RA), excimer laser coronary angioplasty (ELCA), and intravascular lithotripsy (IVL). The study primary endpoint is stent expansion evaluated by optical coherence tomography. An intention-to-treat analysis will be conducted with an alpha coefficient of 0.05 between the reference group (RA) and the remaining 2 groups (ELCA and IVL). An analysis of the study primary endpoint per protocol will be conducted for consistency purposes. If the non-inferiority hypothesis is confirmed, a superiority 2-sided analysis will be conducted. Both the clinical events committee and the independent core laboratory will be blinded to the treatment arm. Assuming an α error of 0.05, an β error of 0.2 (80% power), a margin of irrelevance (ε) of 7, and losses of 10% due to measurement difficulty or impossibility to complete the intervention, we estimate a sample size of 56 cases per group. The study secondary endpoints are device success, procedural success, crossover rate among the different techniques used, and the occurrence of major adverse cardiovascular events at 1-year follow-up.
Conclusions: The ROLLERCOASTR trial will evaluate and compare the safety and effectiveness of 3 plaque modification techniques: RA, ELCA, and IVL in patients with calcified coronary stenosis. This trial was registered at clinicaltrials.gov with identifier NCT04181268.

Keywords: Percutaneous coronary intervention. Calcified plaques. Laser. Lithotripsy. Rotational atherectomy. Optical coherence tomography.

Diseño del estudio ROLLERCOASTR: aterectomía rotacional, litotricia o láser para el tratamiento de estenosis coronarias calcificadas

RESUMEN

Introducción y objetivos: La calcificación coronaria es uno de los principales factores que inciden negativamente en la seguridad y la eficacia del intervencionismo coronario percutáneo. Existen varias técnicas de modificación del calcio, pero falta evidencia de estudios aleatorizados sobre la terapia de elección en este escenario.
Métodos: El ROLLERCOASTR es un estudio prospectivo, multicéntrico y aleatorizado, diseñado para comparar la seguridad y la eficacia de 3 técnicas de modificación de la placa en el contexto de calcificación coronaria moderada o grave: aterectomía rotacional (AR), aterectomía coronaria con láser láser excimer (ACLE) y litotricia intracoronaria (LIC). El objetivo primario es la expansión del *stent* evaluada mediante tomografía de coherencia óptica. Su análisis se hará por intención de tratar, con un α de 0,05 entre el grupo de referencia (AR) y cada uno de los otros grupos (ACLE y LIC). Se realizará también un análisis del objetivo primario por

*** Corresponding author.**
E-mail address: alfonsojuradoroman@gmail.com (A. Jurado-Román).
@AJuradoRoman

Received 19 February 2023. Accepted 28 March 2023. Online 22 May 2023.

protocolo para mantener la coherencia. Si se confirma la hipótesis de no inferioridad, se realizará un análisis bilateral de superioridad. El comité de eventos clínicos y el laboratorio central independiente no conocerán la rama de tratamiento. Asumiendo un error α de 0,05, un error β de 0,2 (80% de potencia), un margen de irrelevancia (ε) del 7% y un 10% de pérdidas por dificultad de medición o imposibilidad de completar la intervención, se estima un tamaño de muestra de 56 casos en cada grupo. Los objetivos secundarios son el éxito del dispositivo, el éxito del procedimiento, la tasa de cruce entre técnicas y la presentación de eventos cardiovasculares adversos importantes al año de seguimiento.
Conclusiones: El estudio ROLLERCOASTR evaluará y comparará la seguridad y la eficacia, en pacientes con estenosis coronaria calcificada, de 3 técnicas de modificación de placa: AR, ACLE y LIC. Este ensayo se ha registrado en Clinicaltrials.gov: NCT04181268.

Palabras clave: Intervencionismo coronario percutáneo. Placas calcificadas. Láser. Litotricia. Aterectomía rotacional. Tomografía de coherencia óptica.

Abbreviations

DES: drug-eluting stent. **ELCA**: excimer laser coronary angioplasty. **IVL:** intravascular lithotripsy. **OCT:** optical coherence tomography. **PCI:** percutaneous coronary intervention. **RA:** rotational atherectomy.

INTRODUCTION

Percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation is the most frequent mode of coronary revascularization.

Calcified coronary lesions pose a challenge to perform successful PCI.[1] Coronary calcification impedes PCI by multiple mechanisms like limiting DES lesion crossing, altering the drug elution kinetics, and interfering with optimal stent expansion. In addition, inadequate stent expansion is a powerful predictor of stent thrombosis and restenosis.[2-6] Coronary calcification also increases PCI-related procedural complications (dissection, perforation, myocardial infarction), and late adverse clinical outcomes like restenosis, repeat revascularization, stent fracture, and thrombosis.[1] The optimal approach for the management of calcified stenosis requires taking into account the characteristics of the lesion, calcium distribution, and the mechanism of action of every plaque-modification device. In this regard, intracoronary imaging techniques such as intravascular ultrasound and optical coherence tomography (OCT) are essential not only to evaluate the severity of calcification and its pattern, but also to optimize stenting.[7]

Currently, plaque-modification techniques can be categorized into *a) balloon-based* technologies (cutting/scoring balloons, non-compliant and super high-pressure balloons, and intravascular lithotripsy (IVL), and *b) non-balloon-based* technologies (rotational atherectomy [RA], orbital atherectomy, and excimer laser coronary angioplasty [ELCA]).[8,9]

The widespread use of these techniques and devices has been limited due to the risk of complications, the operator's experience, and the corresponding use of health resources. Over the past few decades, RA has been the therapy of choice for resistant calcified lesions. However, the development of new technologies such as IVL or the improvement of classical therapies such as ELCA has generated uncertainty on the optimal tool to modify calcified plaques as non-randomized comparisons between these techniques have been drawn.

The objective of this randomized trial is to assess the efficacy and safety profile of intensive plaque modification with RA, IVL or ELCA before DES implantation.

METHODS

Patients and study design

The ROLLERCOASTR (Rotational atherectomy, lithotripsy or laser for the treatment of calcified stenosis) is an investigator-initiated, multicenter, prospective, and randomized clinical trial that includes 6 large volume sites. Also, it includes men and women aged ≥ 18 years with a clinical indication for PCI (stable or unstable ischemic heart disease) in vessels with reference diameters ≥ 2.5 and ≤ 4.0 mm and moderate-to-severe calcification estimated by coronary angiography. The main study exclusion criteria are ST-segment elevation acute coronary syndrome as clinical presentation, cardiogenic shock, inability to tolerate dual antiplatelet therapy for, at least, 6 months for those who are not on oral anticoagulation, impossibility to obtain informed consent from the patient or conduct, at least, a 1-year follow-up.

Patients who meet all the inclusion criteria and none of the exclusion ones will be randomized on a 1:1:1 ratio to either lesion preparation with RA, ELCA or IVL. Randomization will on a web-based platform. The complete inclusion and exclusion criteria are shown on table 1 while the study flowchart is described on figure 1.

Study primary and secondary endpoints

The objective of this study is to evaluate and compare the results of RA, IVL, and ELCA for the management of calcified coronary lesions. This comparison will be made by assessing the angiographic and OCT findings after the implementation of these plaque modification techniques, and DES implantation and optimization.

The primary endpoint is the comparison between RA (reference group) vs ELCA and RA vs IVL in the percentage of stent expansion measured using OCT. As secondary endpoints we'll be analyzing the device success (successful stent implantation with minimum stent area ≥ 5.5 mm^2, final TIMI grade-3 flow, and no need for another plaque preparation strategy), procedural success (device success and no severe procedural complications like cardiovascular death, perioperative target vessel myocardial infarction, need for new target lesion revascularization, stent thrombosis, stroke or vessel perforation with extravasation [types II or III]), crossover from the assigned plaque modification technique to a different one, and occurrence of major adverse

Table 1. Study inclusion and exclusion criteria

Inclusion criteria
≥ 18 years old
Diameter stenosis ≥ 70% or fractional flow reserve < 0.8/non-hyperemic indexes < 0.89
Reference vessel diameter ≥ 2.5 and ≤ 4 mm
Moderate or severe calcification estimated by coronary angiography
Patients with stable coronary artery disease or non-ST-segment elevation acute coronary syndrome
Culprit lesions at native vessels or coronary bypasses
Exclusion criteria
Inability to tolerate a 6-month course of dual antiplatelet therapy in patients naïve to oral anticoagulation
ST-segment elevation acute coronary syndrome
Cardiogenic shock
Impossibility to obtain informed consent from the patient or his legal representative
Impossibility to conduct, at least, a 1-year follow-up

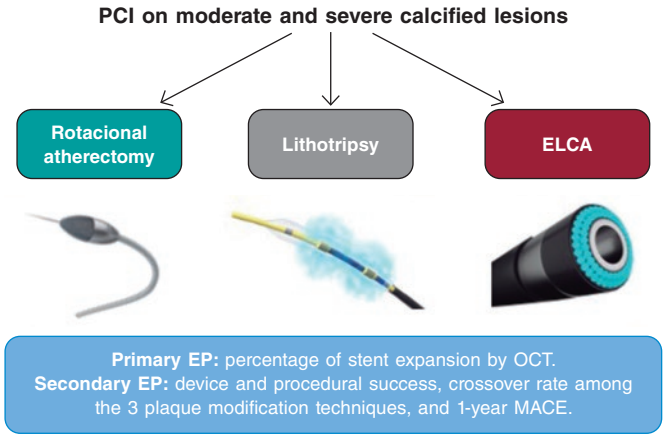


Figure 1. Study flowchart. ELCA, excimer laser coronary angioplasty; EP, endpoint; MACE, major adverse cardiovascular events; OCT, optimal coherence tomography; PCI, percutaneous coronary intervention.

cardiovascular events at 1-year follow-up (cardiovascular death, target vessel myocardial infarction, target lesion revascularization or stent thrombosis). We'll also be analyzing device success regarding the type of calcified plaque (concentric, eccentric, calcium nodule). The study primary and secondary endpoints are shown on table 2.

Devices

- RA: Rotablator or RotaPro System (Boston Scientific, Unites States).
- Coronary laser: Coronary laser-emitting device (CVX-300 ELCA System, Spectranetics Inc., United States).
- Intracoronary lithotripsy: Shockwave System, (Shockwave Medical, United States).

Table 2. Study main endpoints

Primary endpoint
Percentage of stent expansion measured by OCT
Key secondary endpoints
Device success (successful stent implantation with minimum stent area ≥ 5.5 mm^2, final TIMI grade-3 flow, and no need for another plaque preparation strategy)
Device success depending on the type of the calcific plaque: concentric, eccentric or nodular
Procedural success (device success in the absence of procedural severe complications)
Crossover from the assigned plaque modification technique to a different one
1 year-MACE (CD, TVMI, TLR or ST)

CD, cardiac death; MACE, major adverse cardiovascular events; OCT, optical coherence tomography; ST, stent thrombosis; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

- OCT system: OCT Imaging system (Abbott Vascular, United States)
- Stents: new-generation DES are mandatory (those currently being used in participant centers during the inclusion period).

Procedure

The angioplasty will be performed following the recommendations established by the current clinical practice guidelines on the management of coronary revascularization.[10] After crossing the lesion with the angioplasty guidewire, a first OCT assessment should be performed. If necessary, balloon dilatation is allowed to cross the OCT catheter. After this first OCT pullback, the use of a plaque modification technique will be required (RA, laser or lithotripsy) on a randomized basis. Afterwards, a second OCT assessment is advised to analyze the effects of the therapy. Finally, the angioplasty will be completed with the implantation of a new-generation DES. Pre or postdilatation will be left to the operator's criterion. After stenting (in the absence of postdilatation) or after the last postdilatation (if performed), a final OCT pullback will be performed to assess the final stent expansion.

Rotational atherectomy technique

The lesion will be crossed using the RotaWire (Boston Scientific, Unites States) directly or microcatheters or coaxial balloons. The RotaWire type (RotaWire Extra Support and RotaWire Floppy) will be used based on the characteristics of the plaque, the support required, and the operator's preferences. Afterwards, the rotational atherectomy technique will be used based on the current recommendations.[11] A 0.5:0.6 ratio between the burr and the vessel is advised. The rotational speed recommended is between 135 000 rpm and 180 000 rpm. Decelerations > 5000 rpm should be avoided. The burr should be advanced gradually with easy back-and-forth moves. Rotablation time should be < 20 seconds with pauses in between each cycle. Once rotablation has been performed, the burr should be removed with the Dynaglide mode on.

Intracoronary lithotripsy technique

The Shockwave balloon (Shockwave Medical, Inc., United States) is a 12 mm-long angioplasty balloon with 2.5 mm to 4 mm diameters.

It can be mounted over a 0.014 in guidewire. Mechanical energy is transmitted to the lesion when the Shockwave balloon contacts the artery intima layer and cracks superficial and deep calcium layers. Therefore, the Shockwave balloon/reference vessel diameter ratio should be 1:1.[12] Performing an OCT assessment prior to selecting the size of the balloon is also advised. Predilatation with balloons of smaller diameters is allowed to facilitate the passage of the lithotripsy balloon.

Once the Shockwave balloon is on the lesion, it is inflated at a pressure of 4 atm . Up to 80 pulses per balloon can be administrated (8 runs of 10 pulses). After every run (≤ 10 pulses), the Shockwave balloon is inflated at 6 atm and, after deflation, a new cycle can be applied if necessary. A minimum of 20 pulses per lesion is advised.

Laser technique

The size of the ELCA catheter will be selected considering the diameter of the target vessel on a 0.5-0.6 ratio with respect to its diameter.[13] However, 0.9 mm catheters will be prioritized because of their greater crossing capabilities and capacity to emit laser energy with greater fluence (80 mJ/mm^2) at the maximum pulse repetition rate (80 Hz). Regarding the device settings, it is recommended to start by applying a 60 mJ/mm^2 fluence and a 60 Hz pulse repetition frequency that can go up to 80 mJ/mm^2 and 80 Hz based on the operator's criterion. Energy pulses will be released while the catheter slowly moves forward through the lesion at a rate of 0.5 mm/s, thus allowing proper energy absorption and plaque modification. Retrograde application is also feasible, especially in severe lesions with antegrade resistance. Saline-infusion technique is advised. Both blood and iodinated contrast contain non-aqueous cellular macromolecules like proteins that absorb most of the energy released by the laser creating microbubbles that increase the chances of traumatic dissection.[14] On the contrary, the saline solution facilitates the passage of light from the tip of the catheter to the tissue without interferences or microbubbles at that level. Therefore, the saline solution infusion technique is used to safely control the energy that is being released, and minimize the risk of dissection.[15] In order to wash out the blood from the catheter-based tissue interface the catheter needs to be properly intubated and the saline solution properly infused during laser application. The application of laser to blood or contrast is allowed in selected cases of uncrossable or undilatable lesions and left to the operator's criterion.[16] At the end of the procedure, parameters like the number of pulses administered, the time of therapy, fluence, and repetition rate will need to be collected.

Crossover

Combination of several plaque modification techniques is permitted as they have shown to be complementary in some cases.[17,18] If a different plaque preparation technique is required, the technique should be changed based on why the first technique failed (table 3). This switch is consistent with the routine clinical practice. All the material and techniques used will be registered for further analysis.

Table 3. Crossover of plaque modification techniques

Failed early technique	Reason for failure	2nd technique
Rotational atherectomy	Uncrossable lesion with the rotablation olive-shaped burr	ELCA
	Undilatable lesion (suboptimal balloon expansion after rotablation)	Lithotripsy
Lithotripsy	Uncrossable lesion with Shockwave balloon (despite predilatation, if necessary)	Rotational atherectomy
	Undilatable lesion (suboptimal balloon expansion after lithotripsy)	ELCA
ELCA	Uncrossable lesion with ELCA	Rotational atherectomy
	Undilatable lesion (suboptimal balloon expansion after ELCA)	Lithotripsy

ELCA, excimer laser coronary angioplasty.

Optical coherence tomography image acquisition and stent optimization protocol

Intravascular OCT is performed using a commercially available system (the ILUMIEN OPTIS, OPTIS Integrated, OPTIS Mobile systems, OPTISIntegrated Next, OPTISMobile Next Abbott Vascular) that incorporates a rapid exchange catheter (Dragonfly OPTIS, Dragonfly OpStar Imaging Catheter; Abbott Vascular) and an integrated pullback system (18-36 mm/s). It acquires images at high axial resolution (~15 µm) with blood displacement. A total of 3 pullbacks are advised before and after using the plaque modification technique (to describe the calcified lesion and the effects of each modality over it, respectively), and optimizing the DES implanted. The automated OCT-angiography co-registration (where available) will be used, and recommendations for PCI guidance with OCT[19] will be left to the operator's criterion. Stent expansion can be estimated using 2 methods (figure 2): 1) dual method: it identifies the stented region and splits it in half. Minimum lumen expansion in the stented area (EXP) is estimated for each half (minimum stent area in each segment divided by the proximal or distal reference area x 100). The center point can be moved by the user (both the minimum stent area and the EXP recalculate automatically); 2) tapered mode: reference lumen profile is estimated based on the distal and proximal reference frame mean diameter and side branch mean diameter in between. The software automatically displays the minimum stent area and identifies the frame with the minimum lumen expansion in the stented area (EXP). A colored expansion indicator automatically pops up when a stent is detected. Automatic detection: minimum stent area frame/Automatic detection of minimum expansion frame (EXP).

With stent lengths > 50 mm, the dual method is preferred. With stent lengths < 50 mm the tapered method is often used. If the dual method is used, the stent expansion percentage of both segments is recorded being considered for analysis the lowest of the 2.

Follow-up and clinical definitions

In-hospital and follow-up outcomes were prespecified in the online database, complied with the requirements set forth by the Spanish Data Protection Act, and were only accessible to participant operators and study coordinators.

After each PCI, electrocardiographic and cardiac biomarker seriation will be performed. Clinical assessment will be conducted 1, 6, 12 months after PCI. Angiographic follow-up will be only clinically driven in patients with new symptoms, ventricular function worsening or new ischemia in non-invasive tests.

Calcification is defined as moderate if radiopacities are noted only during the cardiac cycle before contrast injection, and severe if

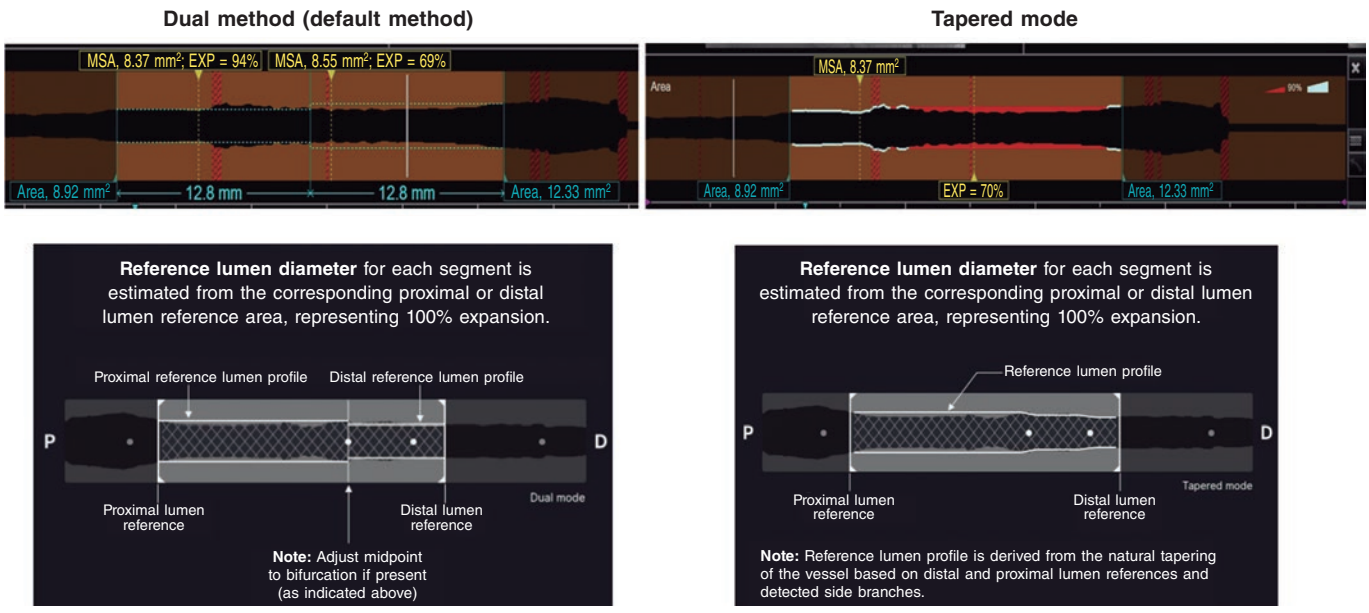


Figure 2. Stent expansion estimate by optical coherence tomography. EXP, stented area. MSA, minimum stent area. Modified with permission from Abbott Vascular from User Manual of Ultreon 1.0, and User Instructions of AptiVue Software.

radiopacities are noted without cardiac motion before contrast injection often compromising both sides of the arterial lumen.

Device success is defined as successful stent implantation with minimum stent areas ≥ 5.5 mm^2 by OCT, final TIMI grade-3 flow, and no need for another plaque preparation strategy.

Procedural success is defined as device success and no severe procedural complications: cardiovascular death, perioperative target vessel myocardial infarction, need for new target lesion revascularization, stent thrombosis, stroke or vessel perforation with extravasation [types II or III]).

Other procedural complications included ventricular arrhythmias or hemodynamic instability during PCI, major bleeding (bleeding requiring transfusion, vasopressors, surgery or percutaneous intervention), and flow limiting dissection.

Major cardiovascular adverse events include cardiovascular death, target vessel myocardial infarction, stent thrombosis or target lesion revascularization. All deaths were considered cardiac unless other specific causes were documented. Myocardial infarction was defined according to the current recommendations made,[20] and only those associated with the targer lesion, perioperative or at follow-up were considered. Target lesion revascularization or stent thrombosis were defined according to the criteria established by the Academic Research Consortium.[21]

Primary outcome assessment will be conducted in a central core laboratory by looking at the OCT imaging after stenting. All medical data will be codified anonymously and stored, and confidentiality will be protected at any time in observance of the current legislation. Both the clinical events committee and the independent core laboratory will be blinded to the treatment arm.

Secondary outcome assessment will be performed by assessing both the angiography and the OCT in a central core laboratory and through on-site or phone clinical follow-up sessions with the patients.

Statistical considerations

Sample size determination

This is a non-inferiority study. We expect to obtain similar outcomes regarding stent expansion using rotational atherectomy, laser, and intracoronary lithotripsy. The sample size was estimated based on the design of the trial and the results of former studies.[22-24] There are no standard criteria to define stent expansion in the routine clinical practice. In a recent expert consensus document, stent expansion > 80%[19] was considered appropriate. However, most former studies did not reach this threshold. In the ILUMIEN II trial, the mean stent expansion measured by OCT was 72.8% with a standard deviation of 12.6.[24] To calculate the size of the sample, we assume an α error of 0.05 and a β error of 0.2 (80% power), a margin of irrelevance (ε) of 7, and losses of 10% due to measurement difficulty or impossibility to complete the intervention. With these parameters we estimate a sample size of 56 cases per group.

Statistical analysis

The study primary endpoint analysis will be conducted by lesion and intention-to-treat with a 1-sided Student *t* test and an alpha coefficient of 0.05 between the reference group and the other groups (ELCA, and IVL). An analysis of the primary endpoint per protocol will be conducted and presented for consistency purposes. If the hypothesis of non-inferiority is confirmed, a 2-sided superiority analysis will be conducted. Clinical endpoints will be analyzed by patient.

Quantitative variables following a normal distribution will be expressed as median ± standard deviation. Those not following such distribution will be expressed as median and minimum and maximum values. Qualitative variables will be expressed as absolute values and frequencies.

P values < .05 will be considered statistically significant, and the 95% confidence interval of the study variables will be estimated.

The Kolgomorov-Smirnov test will be used to confirm the adjustment of variables to normal distribution. Regarding mean comparisons, the Student *t* test or the non-parametric Mann-Whitney *U* test (in case of qualitative dichotomous variables), and the ANOVA test or the non-parametric Kruskal Wallis test (in case of qualitative non-dichotomous variables) will be used. Regarding the bivariate analysis of qualitative variables, the chi-square test or Fisher's exact test will be used. If necessary, the linear correlation among the different quantitative variables will be performed using Pearson correlation coefficient or Spearman's correlation.

Regarding the multivariate analysis, the Cox regression analysis with forward, stepwise selection will be used drawing event-free survival curves using the Kaplan-Meier estimator. Variables will be considered potential predictors of risk in the multivariate model in the presence of a statistically significant correlation in the univariate analysis or a trend towards significance. The SPSS statistical software (version 20.0, SPSS Inc) will be used for all the estimates.

Organization and ethical concerns

The study protocol has been approved at each participant center by its internal ethics committee. All patients will have to give their informed written consent prior to their participation. The study is an investigator-initiated trial and follows the good clinical practice guidelines applicable to epidemiological studies. The rights and integrity of participants shall be guaranteed at all time while data confidentiality shall be safeguarded in observance of EU directives, the Declaration of Helsinki, as well as local rules and regulations. The ROLLERCOASTR trial is registered at clinicaltrials.gov wit identifier NCT04181268. The study promoter is Fundación EPIC. The study is supported by unrestricted grants from Fundación EPIC. The steering committee is the trial main decision-making committee and has final word on the medical and scientific approach to the trial. The clinical events committee includes interventional cardiologists who don't participate in the trial and are blinded to the randomized therapy. The clinical events committee will be responsible for developing specific criteria for the adjudication of the study clinical events and endpoints as per protocol. All members of the clinical events committee will be blinded to the study primary outcomes.

DISCUSSION

At least a third of all coronary lesions requiring PCI show significant calcification.[9] As a matter of fact, this is probably one of the greatest challenges interventional cardiologists face to this date. Different tools are available to prepare calcified plaques. These techniques are increasingly used in the routine clinical context based on the operator's experience or availability[25] since there are barely any comparative studies on this regard.

The role of rotational atherectomy is to facilitate stenting in calcified non-dilatable lesions. The technology has evolved for over 20 years now, and lots of patients have been treated with it. The setback is that it has a longer learning curve compared to other plaque modification techniques and requires a specific guidewire. The evidence available on RA in the calcified lesion setting shows higher procedural success rates compared to conventional or modified balloons with almost the same clinical outcomes. However, even the most recent trials have important limitations as a limited use of intracoronary imaging techniques and new-generation DES.[22,23]

The arrival of laser to treat atherosclerosis goes back to the 1980s to treat lower limb ischemia at the beginning, and then coronary artery disease.[26] However, both catheters and the techniques were rudimentary, and complications were a common thing. The early randomized clinical trials that compared ELCA to RA or balloon angioplasty (before the stent era) did not show favorable outcomes.[27] The refinement of this technology followed by the introduction of safe laser-based techniques has improved its results. However, no direct comparisons have been drawn over the past few years. Although, traditionally, severe calcification has been a non-favorable scenario for ELCA, this technique has repeatedly obtained good results in settings in which calcium is a common finding: balloon failure (uncrossable or undilatable lesions), in-stent restenosis, underexpanded stents or chronic total coronary occlusions.[13] Excimer laser releases energy in the UV range in very short pulses (nanoseconds). Billions of molecules per pulse are broken. Absorption depth is 50 µm, thus reducing the risk of collateral tissue damage (compared to previous infrared lasers). Laser ablates the atherosclerotic material mediated by 3 different mechanisms: *photochemical* (fracture of molecular bonds): the UV light pulse hits the plaque and is highly absorbed with each photon generated carrying sufficient energy to break molecular bonds; *photothermal* (tissue vaporization): molecular bonds also vibrate during the absorption process resulting in heat. Intracellular water is vaporized leading to cell rupture and the creation of a vapor bubble, and *photokinetic* (clearance of byproducts): the rapid expansion and collapse of the vapor bubble further breaks down the plaque, but it also helps clear byproducts of ablation like water, gases, and small particles. Laser effect is amplified especially when it acts directly on blood or a contrast agent. Therefore, to reduce the risk of coronary artery dissection, laser ablation is often performed during the continuous infusion of saline solution.[13] One advantage of laser is its short learning curve. It can be used through conventional 0.014 in guidewires in a rapid-exchange fashion and conventional 6-Fr guiding catheters. In addition, most of these particles are small enough to be cleared by the reticuloendothelial system, thus minimizing the risk of distal microembolization (1 more advantage compared to other plaque modification techniques).[13]

Lithotripsy is the latest technology that has become available to treat heavily calcified lesions. It emits pulsatile mechanical waves through emitters integrated in a semi-compliant balloon that is initially inflated at 4 atm. Afterwards, energy pulses are applied, and the vibrations produced interact with the atherosclerotic plaque breaking down both the superficial and deep calcium deposits.[9] This effect on deep calcium deposits is one of the greatest advantages of lithotripsy over other techniques. Also, this technique learning curve is short since it's based on a well-known coronary balloon technology. The DISRUPT CAD trials[12] have demonstrated the safety and efficacy profile of this technique treating heavily calcified lesions and its use has grown exponentially ever since. The main limitation of this technique is that, as it is a balloon-based technology with a smaller diameter of 2.5 mm, extremely tight stenoses can hamper its use as a first-line therapy, thus needing predilatation with lower profile balloons, and even with RA[17] or laser[18] combined to overcome this problem.

Intracoronary imaging modalities allow more accurate assessments of coronary artery disease compared to conventional angiography and give us essential information for PCI planning. This is particularly relevant during the management of calcified and complex lesions impacting the results of the angioplasty and the patient's prognosis[28] by optimizing DES implantation, thus leading to better stent expansion, vessel wall apposition, and eventually a greater luminal area. The OCT has greater spatial resolution[9] compared to the intracoronary ultrasound and has proven useful showing the effect of plaque modification therapies and stent optimization. All these reasons and the lack of use of intracoronary imaging techniques in previous plaque modification techniques has led us to using OCT to assess the study primary endpoint: percentage of stent expansion.

The ROLLERCOASTR trial will compare the 3 strategies most used in the routine clinical practice to treat lesions with moderate-to-severe calcifications. In addition, it will provide us with information on the effect of each of these strategies and the specific settings where they can be more useful. To this end, an intracoronary imaging study with an OCT will be performed to know the specific substrate of calcification and the type of plaque on which the therapy is performed as well as the effects this therapy will have. The study hypothesis is that the 3 modalities complement each other and have different effects depending on the characteristics of the lesion. At manuscript submission, a total of 135 patients have been included.

CONCLUSIONS

The ROLLERCOASTR is a prospective, multicenter, randomized clinical trial designed to compare the safety and efficacy profile of 3 plaque modification techniques in the moderate-to-severe coronary calcification setting: RA, ELCA, and IVL. The study primary endpoint is stent expansion evaluated by OCT. The secondary endpoints are device success, procedural success, crossover rate among techniques, and the occurrence of major adverse cardiovascular events at 1-year follow-up (cardiac death, target vessel myocardial infarction, need for new target lesion revascularization or stent thrombosis). We will also be describing the effects of the 3 imaging modalities in calcified lesions with OCT. Enrollment will end in 2023.

FUNDING

The study is supported by unrestricted grants from Fundación EPIC.

AUTHORS' CONTRIBUTIONS

A. Jurado-Román: conceptualization, original draft, review, and editing. A. Gómez-Menchero, I.J. Amat-Santos, J. Caballero-Borrego, S. Ojeda, and R. Ocaranza-Sánchez: drafting, review, and editing. S. Jiménez-Valero, G. Galeote, and R. Moreno: conceptualization, drafting, review, and editing.

CONFLICTS OF INTEREST

S. Ojeda and R. Moreno are associate editors of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. S. Ojeda has received consulting fees and participated on Medtronic and Edwards Lifesciences Data Safety Monitoring Board or Advisory Boards, and payment or honoraria for lectures, presentations, speakers bureaus, manuscript drafting or educational events organized by Philips, Biomenco, and World Medica. R. Moreno has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript drafting or educational events organized by Medtronic Inc, Boston scientific, Abbott vascular, Biosensors, Biotronik, Edwards Lifesciences, AMGEN, Astra Zeneca, Daiichi Sankyo New Vascular Therapies, and Biosensors. A. Jurado-Román has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript drafting or educational events organized by Boston Scientific, Shockwave, Philips, Biotronik, Biomenco, Abbott, and Medtronic. A. Gómez-Menchero, J. Caballero-Borrego, R. Ocaranza, G. Galeote, and S. Jiménez-Valero declared no conflicts of interest whatsoever. I. Amat-Santos has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript drafting or educational events organized by Boston Scientific.

WHAT IS KNOWN ABOUT THE TOPIC?

- Coronary calcification worsens the safety and efficacy of percutaneous coronary intervention.
- Several calcium modification techniques are currently available. However, there is a lack of randomized evidence on the therapy of choice in this scenario.

WHAT DOES THIS STUDY ADD?

- The ROLLERCOASTR is a multicenter randomized study that compared 3 advanced plaque modification techniques in the coronary calcification setting: rotational atherectomy, excimer laser, and lithotripsy.
- The study primary endpoint is stent expansion evaluated by optical coherence tomography.
- Secondary endpoints are device success (overall and depending on the type of calcific plaque), procedural success, crossover rate, and the occurrence of major adverse cardiovascular events at 1-year follow-up.

REFERENCES

1. Bourantas CV, Zhang YJ, Garg S, et al. Prognostic implications of coronary calcification in patients with obstructive coronary artery disease treated by percutaneous coronary intervention: a patient-level pooled analysis of 7 contemporary stent trials. *Heart Br.* 2014;100:1158-1164.
2. Mori S, Yasuda S, Kataoka Y, Morii I, Kawamura A, Miyazaki S. Significant association of coronary artery calcification in stent delivery route with restenosis after sirolimus-eluting stent implantation. *Circ J.* 2009;73:1856-1863.
3. Tzafriri AR, Garcia-Polite F, Zani B, et al. Calcified plaque modification alters local drug delivery in the treatment of peripheral atherosclerosis. *J Control Release.* 2017;264:203-210.
4. Wiemer M, Butz T, Schmidt W, Schmitz KP, Horstkotte D, Langer C. Scanning electron microscopic analysis of different drug eluting stents after failed implantation: from nearly undamaged to major damaged polymers. *Catheter Cardiovasc Interv*. 2010;75:905-911.
5. Kobayashi Y, Okura H, Kume T, et al. Impact of target lesion coronary calcification on stent expansion. Circ J. 2014;78:2209-2214.
6. Lee MS, Shah N. The Impact and Pathophysiologic Consequences of Coronary Artery Calcium Deposition in Percutaneous Coronary Interventions. *J Invasive Cardiol*. 2016;28:160-167.
7. di Mario C, Koskinas KC, Räber L. Clinical Benefit of IVUS Guidance for Coronary Stenting: The ULTIMATE Step Toward Definitive Evidence? *J Am Coll Cardiol.* 2018;72:3138-1341.
8. Barbato E, Shlofmitz E, Milkas A, Shlofmitz R, Azzalini L, Colombo A. State of the art: evolving concepts in the treatment of heavily calcified and undilatable coronary stenoses - from debulking to plaque modification, a 40-year-long journey. *EuroIntervention.* 2017;13:696-705.
9. De Maria GL, Scarsini R, Banning AP. Management of Calcific Coronary Artery Lesions: Is it Time to Change Our Interventional Therapeutic Approach? *JACC Cardiovasc Interv.* 2019;12:1465-1478.
10. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J.* 2019;40:87-165.
11. Barbato E, Carrié D, Dardas P, et al. European expert consensus on rotational atherectomy. *EuroIntervention*. 2015;11:30-36.
12. Kereiakes DJ, Di Mario C, Riley RF, et al. Intravascular Lithotripsy for Treatment of Calcified Coronary Lesions: Patient-Level Pooled Analysis of the Disrupt CAD Studies. *JACC Cardiovasc Interv.* 2021;14:1337-1348.
13. Rawlins J, Din JN, Talwar S, O'Kane P. Coronary Intervention with the Excimer Laser: Review of the Technology and Outcome Data. *Interv Cardiol*. 2016;11:27-32.
14. Baumbach A, Haase KK, Rose C, Oberhoff M, Hanke H, Karsch KR. Formation of pressure waves during in vitro excimer laser irradiation in

whole blood and the effect of dilution with contrast media and saline. *Lasers Surg Med*. 1994;14:3-6.
15. Tcheng JE. Saline infusion in excimer laser coronary angioplasty. *Semin Interv Cardiol SIIC*. 1996;1:135-41.
16. Latib A, Takagi K, Chizzola G, et al. Excimer Laser LEsion modification to expand non-dilatable stents: the ELLEMENT registry. *Cardiovasc Revasc Med*. 2014;15:8-12.
17. Jurado-Román A, Gonzálvez A, Galeote G, Jiménez-Valero S, Moreno R. RotaTripsy: Combination of Rotational Atherectomy and Intravascular Lithotripsy for the Treatment of Severely Calcified Lesions. *JACC Cardiovasc Interv*. 2019;12:e127-129.
18. Jurado-Román A, García A, Moreno R. ELCA-Tripsy: Combination of Laser and Lithotripsy for Severely Calcified Lesions. *J Invasive Cardiol*. 2021;33:E754-755.
19. Räber L, Mintz GS, Koskinas KC, et al. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions. *EuroIntervention*. 2018;14:656-677.
20. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol*. 2018;72:2231-2264.
21. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344-2351.
22. de Waha S, Allali A, Büttner HJ, et al. Rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: Two-year clinical outcome of the randomized ROTAXUS trial. *Catheter Cardiovasc Interv*. 2016;87:691-700.
23. Abdel-Wahab M, Toelg R, Byrne RA, et al. High-Speed Rotational Atherectomy Versus Modified Balloons Prior to Drug-Eluting Stent Implantation in Severely Calcified Coronary Lesions. *Circ Cardiovasc Interv*. 2018;11:e007415.
24. Maehara A, Ben-Yehuda O, Ali Z, et al. Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound: The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention). *JACC Cardiovasc Interv*. 2015;8:1704-1714.
25. Romaguera R, Ojeda S, Cruz-González I, Moreno R. Spanish Cardiac Catheterization and Coronary Intervention Registry. 30th Official Report of the Interventional Cardiology Association of the Spanish Society of Cardiology (1990-2020) in the year of the COVID-19 pandemic. *Rev Esp Cardiol*. 2021;74:1095-1105.
26. Bittl JA, Sanborn TA, Tcheng JE, Siegel RM, Ellis SG. Clinical success, complications, and restenosis rates with excimer laser coronary angioplasty. The Percutaneous Excimer Laser Coronary Angioplasty Registry. *Am J Cardiol*. 1992;70:1533-1539.
27. Appelman YE, Piek JJ, Strikwerda S, et al. Randomised trial of excimer laser angioplasty versus balloon angioplasty for treatment of obstructive coronary artery disease. *Lancet*. 1996;347:79-84.
28. Ahn JM, Kang SJ, Yoon SH, et al. Meta-analysis of outcomes after intravascular ultrasound-guided versus angiography-guided drug-eluting stent implantation in 26,503 patients enrolled in three randomized trials and 14 observational studies. *Am J Cardiol*. 2014;113:1338-1347.

REC Interv Cardiol. 2023;5(4):287-296
https://doi.org/10.24875/RECICE.M23000386

Original article

Left atrial appendage occlusion vs oral anticoagulants in AF and coronary stenting. The DESAFIO registry

José Ramón López-Mínguez,[a] Estrella Suárez-Corchuelo,[a] Sergio López-Tejero,[b] Luis Nombela-Franco,[c] Xavier Freixa-Rofastes,[d] Guillermo Bastos-Fernández,[e] Xavier Millán-Álvarez,[f] Raúl Moreno-Gómez,[g] José Antonio Fernández-Díaz,[h] Ignacio Amat-Santos,[i] Tomás Benito-González,[j] Fernando Alfonso-Manterola,[k] Pablo Salinas-Sanguino,[c] Pedro Cepas-Guillén,[d] Dabit Arzamendi,[f] Ignacio Cruz-González,[b] and Juan Manuel Nogales-Asensio[a]

[a] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de Badajoz, Badajoz, Spain*
[b] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca (IBSAL), Salamanca, Spain*
[c] *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[d] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Instituto Cardiovascular, Hospital Clínico San Carlos Madrid, Spain*
[e] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Clínico de Barcelona, Barcelona, Spain*
[f] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Álvaro Cunqueiro, Vigo, Pontevedra, Spain*
[g] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de la Santa Creu i Sant Pau, Barcelona, Spain*
[h] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de La Paz, IdiPAZ, Madrid, Spain*
[i] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de Puerta de Hierro, Majadahonda, Madrid, Spain*
[j] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain*
[k] *Sección de Cardiología Intervencionista, Servicio de Cardiología, Hospital Universitario de León, León, Spain*

ABSTRACT

Introduction and objectives: The treatment of patients with non-valvular atrial fibrillation (NVAF) who need coronary stenting is challenging. The objective of the study was to determine whether left atrial appendage occlusion (LAAO) could be a feasible option and benefit these patients. To this end, we studied the impact of LAAO plus antiplatelet drugs vs oral anticoagulants (OAC) (including direct OAC) plus antiplatelet drugs in these patients' long-term outcomes.
Methods: The results of 207 consecutive patients with NVAF who underwent coronary stenting were analyzed. A total of 146 patients were treated with OAC (75 with acenocoumarol, 71 with direct OAC) while 61 underwent LAAO. The median follow-up was 35 months. Patients also received antiplatelet therapy as prescribed by their cardiologist. The study received the proper ethical oversight.
Results: Age (mean 75.7 years), and the past medical history of stroke were similar in both groups. However, the LAAO group had more unfavorable characteristics (history of coronary artery disease [CHA_2DS_2-VASc], and significant bleeding [BARC ≥ 2] and HAS-BLED). The occurrence of major adverse events (death, stroke/transient ischemic events, major bleeding) and major cardiovascular events (cardiac death, stroke/transient ischemic attack, and myocardial infarction) were significantly higher in the OAC group compared to the LAAO group: 19.75% vs 9.06% (HR, 2.18; P = .008) and 6.37% vs 1.91% (HR, 3.34; P = .037), respectively.
Conclusions: In patients with NVAF undergoing coronary stenting, LAAO plus antiplatelet therapy produced better long-term outcomes compared to treatment with OAC plus antiplatelet therapy despite the unfavorable baseline characteristics of the LAAO group.

Keywords: Stents. Atrial appendage. Atrial fibrillation. Anticoagulants.

*** Corresponding author.**
Email address: lopez-minguez@hotmail.com (J.R. López-Mínguez).

Received 6 February 2023. Accepted 19 April 2023. Online 12 June 2023.

Cierre de la orejuela izquierda frente a anticoagulantes orales en FA e implante de *stents* coronarios. Registro DESAFIO

RESUMEN

Introducción y objetivos: El tratamiento de los pacientes con fibrilación auricular no valvular (FANV) que requieren implante de *stents* coronarios es un desafío. El objetivo del estudio fue investigar si el cierre de la orejuela izquierda (COI) podría ser una opción posible y beneficiosa para estos pacientes. Para ello, se analiza el impacto del COI más tratamiento antiagregante plaquetario (AP) en comparación con la combinación de anticoagulantes orales (ACO), incluidos los ACO directos, y tratamiento AP en los resultados a largo plazo de estos pacientes

Métodos: Se analizaron los resultados de 207 pacientes con FANV sometidos consecutivamente a implante de *stents* coronarios. Recibieron ACO 146 pacientes (74 acenocumarol, 71 ACO de acción directa) y en 61 se realizó COI. La mediana de seguimiento fue de 35 meses. Los pacientes también recibieron tratamiento AP por prescripción de su cardiólogo. El estudio recibió la debida supervisión ética.

Resultados: La edad (media: 75,7 años) y el antecedente de accidente vascular cerebral fueron similares en ambos grupos, aunque el grupo de COI presentó más características desfavorables (antecedente de enfermedad de las arterias coronarias [CHA_2DS_2-VASc], antecedente de hemorragias significativas [BARC ≥ 2] y HAS-BLED). La aparición de acontecimientos adversos graves (muerte, accidente vascular cerebral, accidente isquémico transitorio, hemorragia grave) y cardiovasculares graves (muerte de causa cardiaca, accidente vascular cerebral, accidente isquémico transitorio, infarto de miocardio) fue significativamente mayor en el grupo de ACO que en el de COI: 19,75 frente a 9,06% (HR = 2,18; p = 0,008) y 6,37 frente a 1,91% (HR = 3,34; p = 0,037), respectivamente.

Conclusiones: La combinación de COI y tratamiento AP en pacientes con FANV conlleva mejor pronóstico clínico a largo plazo que el tratamiento con ACO y terapia AP, a pesar de las características basales desfavorables del grupo de COI.

Palabras clave: *Stent*. Orejuela. Fibrilación auricular. Anticoagulantes.

Abbreviations

AP: antiplatelet drugs; **LAAO:** left atrial appendage occlusion; **NVAF:** non-valvular atrial fibrillation; **OAC:** oral anticoagulants; **PCI:** percutaneous coronary intervention; **TIA:** transient ischemic attack.

INTRODUCTION

Patients with atrial fibrillation (AF) who undergo percutaneous coronary intervention (PCI) with coronary stenting are a subset in whom antithrombotic treatment is particularly complex. In this challenging scenario, anticoagulant therapy is the treatment of choice for stroke prevention while dual antiplatelet therapy (DAPT) is the treatment of choice for preventing stent thrombosis and future coronary events. Combining both drug types, however, increases the risk of bleeding.[1]

This problem will only rise in prominence since the rate of AF and coronary artery disease increases with age and elderly patient populations continue to grow.[2]

The rate of coronary artery disease in patients with non-valvular atrial fibrillation (NVAF) is as high as 30%. As a matter of fact, nearly 20% of the patients undergo coronary revascularization, especially PCI.[3] Furthermore, approximately 6% to 8% of the patients admitted due to acute coronary syndrome (ACS) have AF.[4] The higher mortality rates seen in these patients (between 2- and 3-fold at 5 years) may also be related, among other factors, to the need for combined anticoagulant and antiplatelet (AP) drug therapies and the high rate of associated bleeding events.[5] In fact, the effect post-discharge bleeding has on all-cause mortality at 2 years has been associated with higher crude all-cause mortality rates (13.0% vs 3.2%; $P < .0001$; hazard ratio [HR], 5.03; $P < .0001$) with an effect size greater than that of myocardial infarction after discharge (HR, 1.92; $P < .009$).[6]

Left atrial appendage occlusion (LAAO) has been shown to reduce bleeding compared to oral anticoagulants (OAC) in patients with a high risk of bleeding.[7-9] This strategy may also allow patients to continue DAPT possibly reducing ischemic events with fewer bleeding events compared to the anticoagulant-AP therapy combo.

Our objective was to determine whether LAAO could be a feasible option and benefit these patients. To this end, we studied the impact of LAAO plus AP versus OAC (including direct OAC [DOAC]) plus AP in these patients' long-term outcomes regarding mortality prevention, ischemic and hemorrhagic events (figure 1).

METHODS

This was a multicenter, observational study of 2 historical cohorts of patients. Back in 2021, 11 Spanish centers were asked to participate in a registry of patients who had received LAAO with an indication for OAC withdrawal in the presence of a high risk of bleeding when this indication coexisted with that of DAPT following intracoronary stenting. Inclusion went on through March 2021. Patients treated with LAAO were compared to a consecutive series of patients with an indication for anticoagulation, treated with intracoronary stenting, without LAAO, collected from March 2014 through March 2021, a period that was partially coincidental with the inclusion period of patients with LAAO. Procedural data were obtained from the hospital registries and cath labs of participant centers.

The use of antithrombotic treatment and the indication for LAAO were left to the treating cardiologist's criterion. In all patients, closure device implantation was indicated for the primary prevention of thrombotic and hemorrhagic events. Exclusion criteria were *a)* formal contraindication to anticoagulant therapy; *b)* patient with previous percutaneous atrial appendage closure outside the PCI time frame specified in the study; *c)* LAAO indicated due to significant bleeding or thromboembolic event after initiation of post-PCI

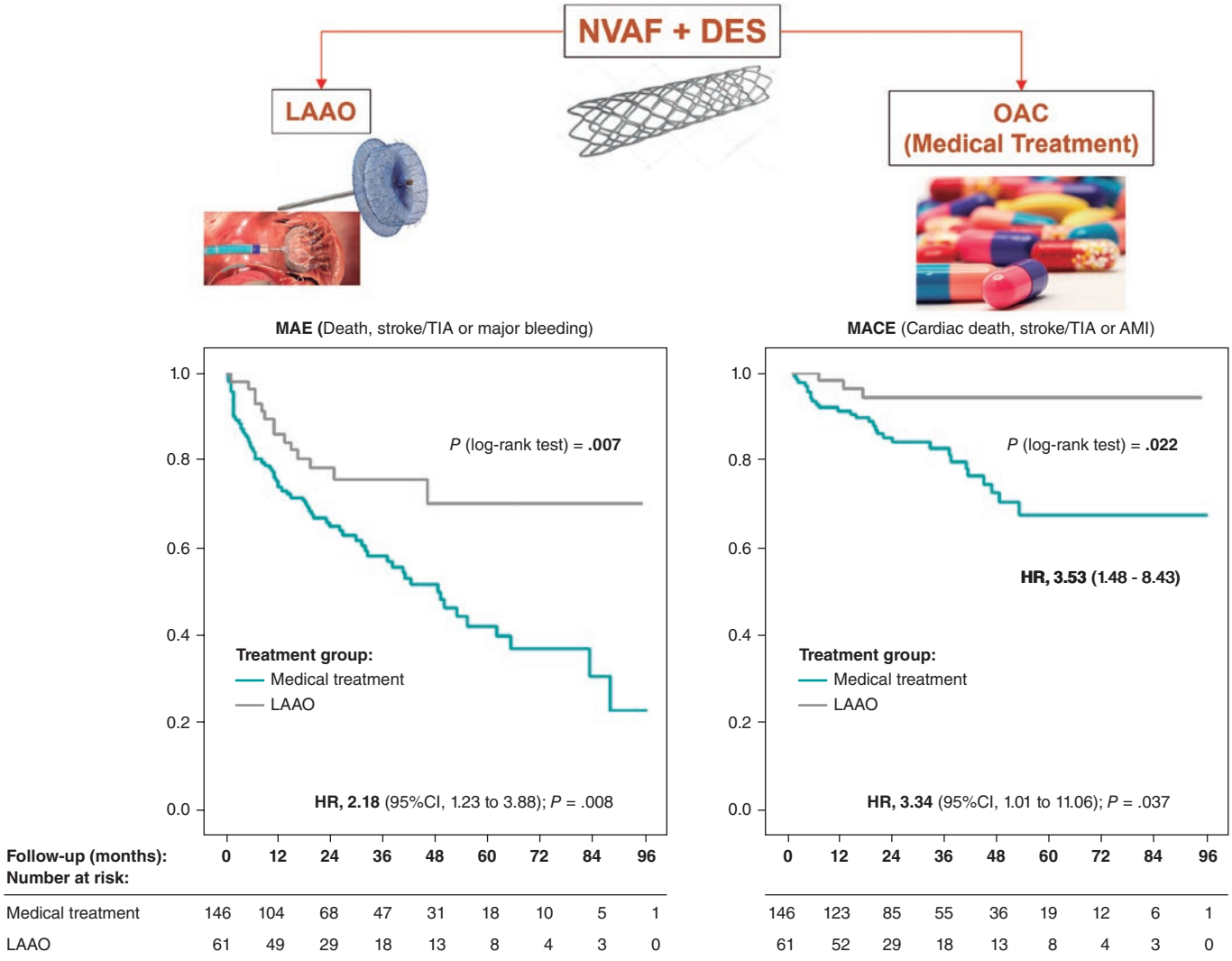


Figure 1. Central illustration. AMI, acute myocardial infarction; CI, confidence interval; DES, drug-eluting stent; HR, hazard ratio; LAAO, left atrial appendage occlusion; MACE, major adverse cardiovascular events; MAE, major adverse events; NVAF, non-ventricular atrial fibrillation; OAC, oral anticoagulants; TIA, transient ischemic attack.

antithrombotic therapy; *d)* refusal to be included in the study or sign the written informed consent; *e)* impossibility to obtain the clinical follow-up. It is important to clarify that, being a real-life study as it was, patients with previous bleeding were included, but that, at the time, their cardiologists did not consider requesting a LAAO and thus, when the PCI was performed, they had the option of being assessed for LAAO. However, if a patient underwent LAAO before or after PCI due to bleeding, they were not considered study eligible.

Patients in the medical treatment group were all included consecutively at the coordination center to ensure data quality, as they were the largest group and could pose a greater challenge regarding follow-up. The presence of digitized medical records at regional level in the coordination center, and the thoroughness of follow-up ensured high-quality data collection for these patients.

Percutaneous coronary intervention and left atrial appendage closure

The indication for LAAO was established by the treating clinician after coronary anatomy was determined. LAAO was performed during the peri-PCI period (before, at the time of or within a 6-month time frame after PCI). The implantation technique, type of device, and post-implantation antithrombotic treatment were selected and left to the operator's criterion. As an indication IIb, the inclusion of these patients was limited and generally followed a strategy of avoiding the withdrawal of antiplatelet therapy and/or fear of bleeding with antithrombotic combination. They were consecutive but several months could pass between one and the other due to these circumstances.

Follow-up and outcome definitions

All patients were clinically followed after PCI, even in the arm in which the LAAO is subsequently performed. At follow-up, the appearance of the following events was prospectively collected: death, hemorrhage, stroke or transient ischemic attack, and acute myocardial infarction (AMI). Composite endpoints were defined as major adverse events (defined as the primary endpoint) including death, major bleeding or stroke/transient ischemic attack, and major adverse cardiovascular events including cardiac death, stroke/transient ischemic attack, and AMI. Hemorrhages were classified according to the Bleeding Academic Research Consortium (BARC)

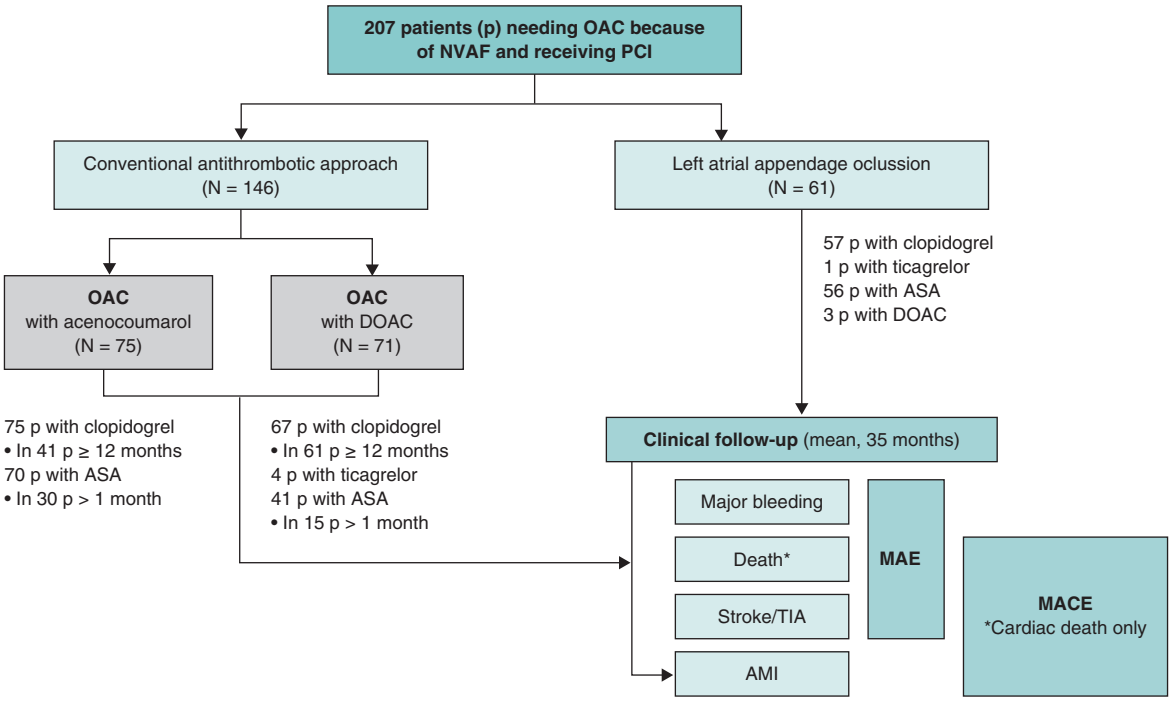


Figure 2. Study flowchart. AMI, acute myocardial infarction; ASA, acetylsalicylic acid; DOAC, direct oral anticoagulants; MACE, major adverse cardiovascular events; MAE, major adverse events; NVAF, non-valvular atrial fibrillation; OAC, oral anticoagulants; p, patients; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

guidelines.[10] Only BARC ≥ 2 hemorrhages classified as relevant, and BARC ≥ 3 hemorrhages as major (fatal bleeding, and/or symptomatic bleeding in a critical area or organ such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial or intramuscular with compartment syndrome, and/or bleeding causing hemoglobin levels drop ≥ 2 g/L [1.24 mmol/L] or requiring transfusion of ≥ 2 units of whole blood or red cells) were recorded.

There was no loss in the LAAO group while only 5 patients from the medical treatment group (3.4%) were lost (without known event) before the study completion date.

Statistical methods

Continuous variables were expressed as mean ± SD or median (25^{th}–75^{th} percentiles) depending on data distribution. The categorical ones were compared using chi-square or Fisher's exact test while numerical variables were analyzed using the Student *t* test or the Mann-Whitney *U* test. The observed adjusted incidence rate regarding the density of events (number of events at follow-up divided by the sum of person-time of the at-risk population) are expressed as 100 patient-years. Event-free survival was analyzed using the Kaplan-Meier and Cox methods. All data were analyzed using the SPSS V.22.0 statistical software package.

Ethical aspects

The DESAFIO (DES implantation in patients with atrial fibrillation followed by LAA occlusion device) study protocol was approved by the independent ethics committees of the participant hospitals, and all patients gave their written informed consent to participate in this study. All procedures comply with the Declaration of Helsinki. The authors' center approved the data analysis. Registration was not deemed necessary since this is an observational study.

RESULTS

Overall, 146 patients received conventional antithrombotic treatment with OAC (75 with the vitamin K antagonist [VKA] acenocoumarol, and 71 with DOAC) while 61 patients underwent LAAO. The median follow-up after PCI was 35 months (figure 2).

The characteristics of both groups are shown on table 1, and classified according to their possible impact on ischemic-thrombotic or hemorrhagic events.

There were no significant differences in variables such as age (mean, 75.5 years), high blood pressure, diabetes, sex, permanent or paroxysmal AF or past medical history of stroke or thromboembolism between the 2 groups. There were, however, more unfavorable characteristics in the LAAO group with significant differences being reported in the past medical history of coronary disease (43.2% vs 75.4%; $P < .001$), CHA_2DS_2-VASc (4.07 ± 1.70 vs 4.56 ± 1.53; $P = .033$), relevant bleeding (BARC ≥ 2) (8.9% vs 49.2%; $P < .001$), high bleeding risk (defined as previous bleeding or HAS-BLED ≥ 3) (19.9% vs 62.3%; $P < .001$), and HAS-BLED score (1.63 ± 1.09 vs 2.49 ± 1.18; $P < .001$) between the OAC and the LAAO group, respectively. As shown on table 1, 36% of the patients from the LAAO group had GI bleeding vs 6.8% of the patients from the medical treatment group.

Table 2 shows the PCI-related characteristics of both groups, and table 3 the different bleeding types and their classification. A total of 41% of the patients from the COI group showed GI bleeding compared to 6.8% of the patients from the group on medical therapy as shown on table 3.

In the intervention group, this was the timeline association between LAAO and PCI: in 4 (6.6%) patients, LAAO was performed a median of 35 days before PCI; in 4 (6.6%), during the same procedure, while in 53 patients (86.9%), it was performed a median of

Table 1. Baseline characteristics

	MT (N = 146)	Acenocoumarol (N = 75)	DOAC (N = 71)	LAAO (N = 61)	P[a]	P[b]
Age	75.7 ± 8.8	75.1 ± 8.8	76.4 ± 8.8	75.8 ± 8.9	.947	.664
Age ≥ 75 years	88 (60.3)	41 (54.7)	47 (66.2)	36 (59.0)	.866	.359
Age, 65-74 years	36 (24.7)	23 (30.7)	13 (18.3)	17 (27.9)	.629	.206
Female sex	41 (28.1)	22 (29.3)	19 (26.8)	14 (23.0)	.446	.703
Thrombotic characteristics						
Paroxysmal AF	79 (54.1)	38 (50.7)	41 (57.7)	27 (44.3)	.196	.301
Permanent AF	66 (45.5)	37 (49.3)	30 (42.9)	34 (55.7)	.180	.249
Chronic heart failure	28 (19.2)	15 (20.0)	13 (18.3)	18 (29.5)	.103	.257
High blood pressure	121 (82.9)	65 (86.7)	56 (78.9)	55 (90.2)	.180	.171
DM	71 (48.6)	33 (44.0)	38 (53.5)	24 (39.3)	.222	.243
History of stroke/TIA/TE	27 (18.5)	11 (14.7)	16 (22.5)	15 (24.6)	.320	.303
History of stroke/TIA	24 (16.4)	9 (12.0)	15 (21.1)	15 (24.6)	.172	.145
Previous CAD	63 (43.2)	36 (48.0)	27 (38.0)	46 (75.4)	< .001	< .001
Previous AMI	25 (17.1)	12 (16.0)	13 (18.3)	24 (39.3)	.001	.003
Previous PCI	45 (30.8)	27 (36.0)	18 (25.4)	42 (68.9)	< .001	< .001
Previous APE	14 (9.6)	5 (6.7)	9 (12.7)	14 (23.0)	.010	.021
Previous APE/AMI/revasc	59 (40.4)	32 (42.7)	27 (38.0)	48 (78.7)	< .001	< .001
$CHADS_2$	2.48 ± 1.31	2.35 ± 1.24	2.62 ± 1.39	2.67 ± 1.34	.340	.292
CHADS-VASc	4.07 ± 1.70	3.92±1.68	4.11 ± 1.75	4.56 ± 1.53	.033	.082
Bleeding characteristics						
BP > 160 mmHg	14 (9.6)	8 (10.7)	6 (8.5)	10 (16.4)	.163	.347
Liver or kidney failure	38 (26.0)	23 (30.7)	15 (21.1)	22 (36.1)	.147	.156
Dialysis	4 (2.7%)	4 (5.3)	0	7 (11.5)	.017	.014
Previous stroke/TIA	24 (16.4)	9 (12.0)	15 (21.1)	15 (24.6)	.172	.145
Previous bleeding	13 (8.9)	9 (12.0)	4 (5.6)	30 (49.2)	< .001	< .001
High bleeding risk	29 (19.9)	19 (25.3)	10 (14.1)	37 (60.7)	< .001	< .001
Labile INR	10 (6.8)	8 (10.7)	2 (2.8)	6 (9.8)	.463	.158
Age > 65	124 (84.9)	64 (85.3)	60 (84.5)	53 (86.9)	.716	.927
Anti-inflammatory drugs	9 (6.2)	5 (6.7)	4 (5.6)	11 (18.0)	.008	.030
Alcohol/drug abuse	5 (3.4)	2 (2.7)	3 (4.2)	2 (3.3)	.999	.872
HAS-BLED	1.63 ± 1.09	1.72 ± 1.24	1.54 ± 0.91	2.49 ± 1.18	< .001	< .001

Data from the groups in brackets are expressed as percentages. AF, atrial fibrillation; AMI, acute myocardial infarction; APE, acute pulmonary edema; BP, blood pressure; CAD, coronary artery disease; DM, diabetes mellitus; DOAC, direct oral anticoagulants; INR, international normalized ratio; LAAO, left atrial appendage. occlusion; MT, medical treatment; PCI, percutaneous coronary intervention; revasc, revascularization; TE, thromboembolism; TIA, transient ischemic attack.
[a] LAAO vs MT.
[b] LAAO vs acenocoumarol vs DOAC.

75 days after the PCI. The Amplatzer Amulet (Abbott, United States), WATCHMAN (Boston Scientific, United States), and LAmbre (Lifetech Scientific, China) devices were used in 50 (82%), 9 (14.8%), and 2 (3.2%) patients, respectively.

Regarding the antithrombotic regimen used between the PCI and LAAO, 30 patients received triple antiplatelet therapy while 23 received DAPT. After LAAO, most remained on DAPT (table 4).

Clinical outcomes

The rates of major adverse events and major adverse cardiovascular events were significantly higher in the OAC group: 19.75% vs 9.06% (HR, 2.18; $P = .008$) and 6.37% vs 1.91% (HR, 3.34; $P = .037$) (table 5, figure 3A), respectively. The median follow-up was 29.6 and 23.3 months for the medical and LAAO groups, respectively (table 6).

Table 2. Percutaneous coronary intervention: indications and type

	MT (N = 146)	Acenocoumarol (N = 75)	DOAC (N = 71)	LAAO (N = 61)	P[a]	P[b]
PCI indication						
Stable angina	15 (10.3)	6 (8.0)	9 (12.7)	12 (19.7)	.067	.132
NSTEACS	94 (64.4)	55 (73.3)	39 (54.9)	43 (70.5)	.397	.044
STEACS	37 (25.3)	14 (18.7)	23 (32.4)	6 (9.8)	.012	.005
Number of diseased vessels	1.76 ± 0.77	1.71 ± 0.71	1.82 ± 0.83	2.02 ± 1.06	.091	.116
Number of vessels treated	1.32 ± 0.52	1.36 ± 0.56	1.27 ± 0.48	1.30 ± 0.53	.782	.575
Number of lesions treated	1.50 ± 0.78	1.45 ± 0.72	1.55 ± 0.83	1.48 ± 0.77	.835	.736
Number of stents	1.71 ± 0.96	1.64 ± 0.78	1.75 ± 1.10	1.69 ± 1.04	.984	.827
PCI on LMCA	11 (7.5)	7 (9.3)	4 (5.6)	6 (9.8)	.582	.617
PCI on proximal LAD	37 (25.3)	15 (20.0)	23 (31.0)	19 (31.1)	.391	.227
PCI on bifurcation	3 (2.1)	2 (2.7)	1 (1.4)	2 (3.3)	.601	.772
PCI due to restenosis/stent thrombosis	3 (2.1)	1 (1.3)	2 (2.8)	1 (1.6)	1	.793
PCI due to overlapping stents	20 (13.7)	2 (2.7)	18 (25.4)	8 (13.1)	.911	< .001
PCI due to recurrent AMI	2 (1.4)	1 (1.3)	1 (1.4)	6 (9.8)	.009	.016

Data from the groups in brackets are expressed as percentages. AMI, acute myocardial infarction; DES, drug-eluting stent; LAD, left anterior descending coronary artery; DOAC, direct oral anticoagulants; LAAO, left atrial appendage occlusion; LMCA, left main coronary artery; MT, medical treatment; NSTEACS, non-ST-segment elevation acute coronary syndrome; STEACS, ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention.
[a] LAAO vs MT.
[b] LAAO vs Acenocoumarol vs DOAC.

Table 3. Past medical history of bleeding prior to percutaneous coronary intervention in each group

	MT (N = 146)	Acenocoumarol (N = 75)	DOAC (N = 71)	LAAO (N = 61)	P[a]	P[b]
Characteristics						
Need for transfusion	5 (3.4)	4 (5.3)	1 (1.4)	13 (21.3)	< .001	< .001
Need for admission	6 (4.1)	5 (6.7)	1 (1.4)	23 (37.7)	< .001	< .001
Hb drop by 3-5 g/dL	4 (2.7)	3 (4.0)	1 (1.4)	11 (18.0)	< .001	< .001
Hb drop > 5 g/dL	0	0	0	5 (8.2)	.002	.002
BARC score						
Type 2	9 (6.2)	4 (5.3)	3 (4.2)	8 (13.1)	.097	< .001
Type 3a	5 (3.4)	5 (6.7)	1 (1.4)	10 (16.4)	.002	< .001
Type 3b	0	0	0	6 (9.8)	.002	< .001
Type 3c	0	0	0	6 (9.8)	.001	.004
Type of bleeding						
Intracranial	0	0	0	6 (9.8)	.001	.001
GI	10 (6.8)	8 (10.7)	2 (2.8)	25 (41.0)	< .001	< .001
Other	3 (2.1)	1 (1.3)	2 (2.8)	2 (3.3)	.267	.463

Data from the groups in brackets are expressed as percentages. BARC, Bleeding Academic Research Consortium guidelines; DES, drug-eluting stent; DOAC, direct oral anticoagulants; GI, gastrointestinal; Hb, hemoglobin; LAAO, left atrial appendage occlusion; MT, medical treatment; PCI, percutaneous coronary intervention.
[a] LAAO vs MT.
[b] LAAO vs acenocoumarol vs DOAC.

Table 4. Antiplatelet therapy after percutaneous coronary intervention or left atrial appendage closure

	Acenocoumarol (N = 75)	DOAC (N = 71)	LAAO (N = 61)	*P*
ASA	70 (93.3)	41 (57.7)	56 (91.8)	< .001
ASA > 1 month	39 (57.1)	15 (29.7)	31 (50.8)	< .001
Clopidogrel	75 (100)	67 (94.4)	57 (93.4)	.091
Clopidogrel ≥ 6 months	41 (57.7)	61 (92.4)	28 (57.1)	< .001
Ticagrelor	0	4 (5.6)	1 (1.6)	.077
DOAC	0	71 (100)	3 (4.9)	–
1 month-triple antiplatelet therapy	39 (57.1)	15 (29.7)	0	< .001
6 month-triple antiplatelet therapy	3 (4)	5 (7)	0	< .001
DT > 6 months	54 (72)	65 (91.5)	1 (1.6)	< 0.001

Data from the groups in brackets are expressed as percentages. ASA, acetylsalicylic acid; DOAC, direct oral anticoagulants; DT, double therapy (anticoagulation + antiplatelet); LAAO, left atrial appendage occlusion.

Table 5. Major adverse events and major adverse cardiovascular events at follow-up

	MT (N = 146; 449 p-y)	Acenocoumarol (N = 75; 277 p-y)	DOAC (N = 71; 175 p-y)	LAAO (N = 61; 158 p-y)	HR (95%CI)	*P*[a]	*P*[b]
Overall death	49 (10.84)	35 (12.68)	14 (7.99)	11 (6.95)	1.56 (0.81-3.01)	.184	.081
Cardiac death	4 (0.89)	2 (0.72)	2 (1.14)	1 (0.63)	1.41 (0.17-14.05)	.691	.850
Stroke/TIA	19 (4.59)	11 (4.31)	8 (5.05)	2 (1.27)	3.59 (0.84-15.54)	.084	.150
AMI	4 (0.91)	4 (1.52)	0	1 (0.63)	1.44 (0.19-15.40)	.628	.167
PCI	7 (1.68)	5 (2.08)	2 (1.14)	1 (0.63)	2.67 (0.29-20.09)	.415	.314
Bleeding BARC ≥ 2	42 (11.56)	28 (13.14)	14 (9.33)	7 (4.57)	2.53 (1.22-6.05)	.014	.002
Bleeding BARC ≥ 3	31 (7.99)	22 (9.48)	9 (5.77)	6 (3.88)	2.06 (0.93-5.36)	.072	.011
Overall death/stroke - TIA/BARC ≥ 2 bleeding	76 (23.52)	47 (24.54)	29 (21.79)	15 (9.80)	2.40 (1.38-4.17)	.002	.001
Overall death/stroke - TIA/bleeding BARC ≥ 3 (MAE)	68 (19.75)	43 (20.43)	25 (18.02)	14 (9.06)	2.18 (1.23-3.88)	.008	.004
Cardiac death/stroke/TIA/AMI (MACE)	25 (6.37)	15 (6.16)	10 (6.32)	3 (1.91)	3.34 (1.01-11.06)	.037	.069

Data from the groups in brackets are expressed as percentages. Absolute values and percentages are expressed per 100 patient-years. AMI, acute myocardial infarction; DOAC, direct oral anticoagulants; BARC, Bleeding Academic Research Consortium guidelines; LAAO, left atrial appendage occlusion; MACE, major adverse cardiovascular events; MAE, major adverse events; p, patients; PCI, percutaneous coronary intervention TIA, transient ischemic attack; y, years.
[a] MT vs LAAO.
[b] LAAO vs acenocoumarol vs DOAC.

The rates of death, stroke/acute cerebrovascular event, and relevant bleeding, expressed as 100 patient-years, were higher in the group of patients treated with OAC compared to the LAAO group. Since the rate of stroke was higher than expected in the OAC group, the possible reasons for this observation were further investigated. Out of the 19 patients reported with stroke, at least, 13 had some predisposing condition that could have increased risk: *a)* treatment withdrawal due to surgery: 3 cases; *b)* treatment withdrawal due to bleeding: 2 cases; and *c)* under-dosing: 9 cases (4 of which were in the VKA group with an international normalized ratio < 2).

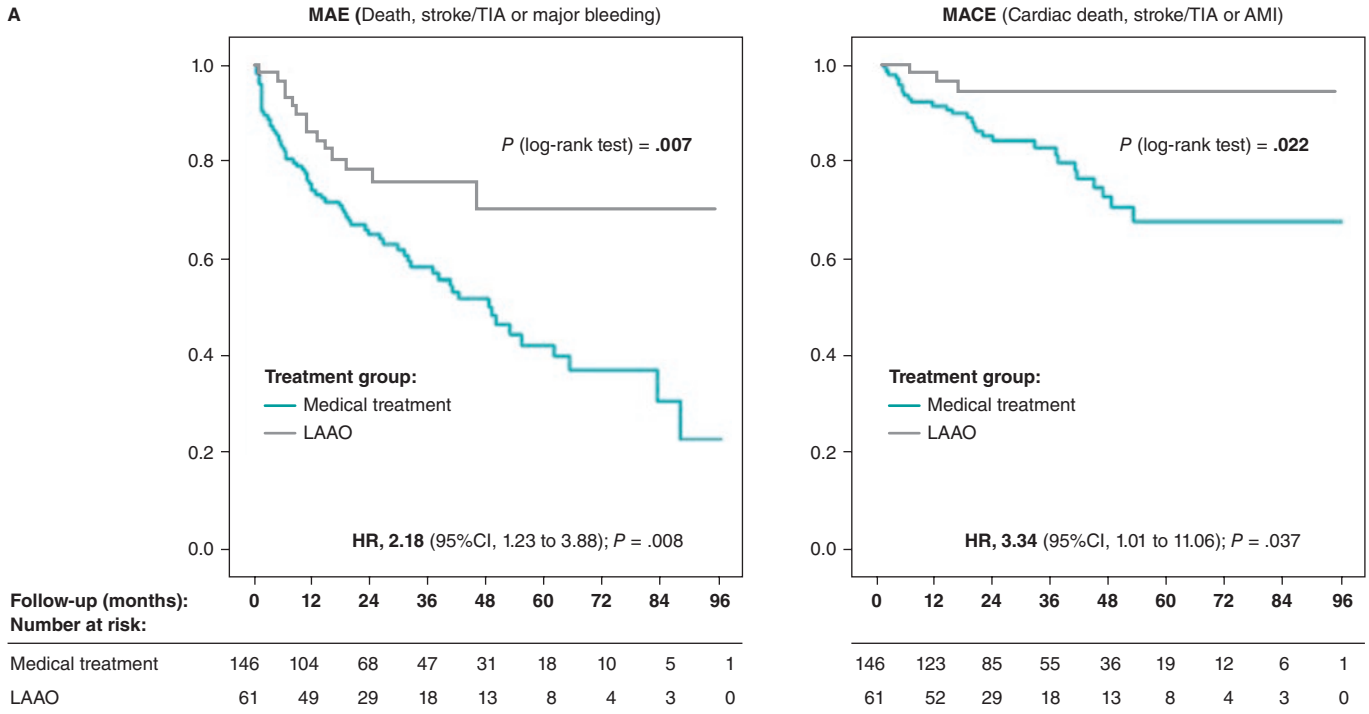
Figure 3B shows significant bleeding differences between the LAAO and the OAC group. Table 5 shows bleeding events by group; a favorable trend was found in the LAAO group even compared to DOAC regarding relevant bleeding.

In the multivariate analysis (Cox regression), only the HAS-BLED score (HR, 1.30; 95%CI, 1.04-1.62; $P = .019$) and medical treatment allocation (HR, 3.42; 95%CI, 1.57-7.42; $P = .002$) were independent predictors of major adverse events. On the other hand, the CHA_2DS_2-VASc score (HR, 1.24; 95%CI, 1.01-1.53; $P = .043$), and medical treatment allocation (HR, 3.71; 95%CI, 1.11-12.37; $P = .033$) were independent predictors of major adverse cardiovascular events.

In the LAAO population the following procedural complications were reported: 1 patient with an arteriovenous fistula who did not require vascular surgery, 2 patients with pericardial effusion, 1 patient who required pericardiocentesis, and 1 patient with bronchospasm after extubation that resolved uneventufully with medical treatment.

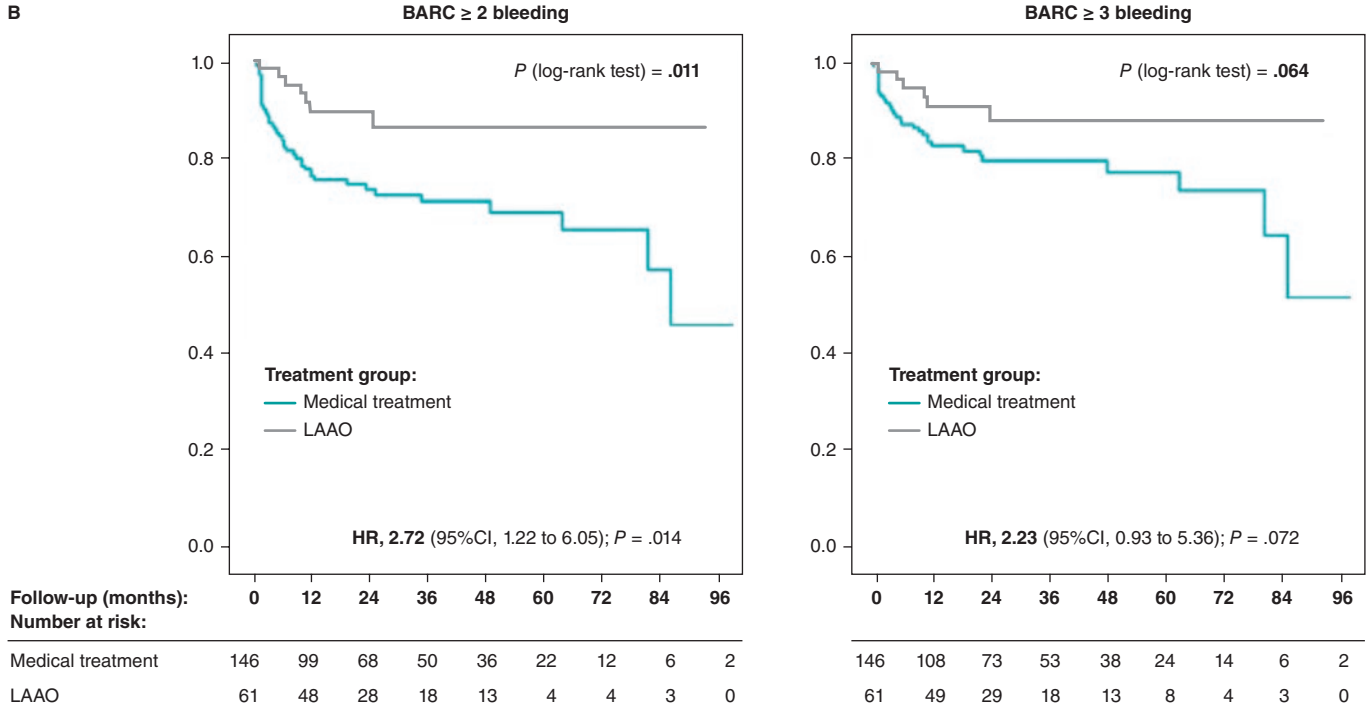
DISCUSSION

Out study main finding was that, in patients with NVAF treated with coronary stents, LAAO plus AP showed better long-term outcomes compared to OAC (including DOAC) plus AP. These



Follow-up (months): Number at risk:	0	12	24	36	48	60	72	84	96
Medical treatment	146	104	68	47	31	18	10	5	1
LAAO	61	49	29	18	13	8	4	3	0

Follow-up (months): Number at risk:	0	12	24	36	48	60	72	84	96
Medical treatment	146	123	85	55	36	19	12	6	1
LAAO	61	52	29	18	13	8	4	3	0



Follow-up (months): Number at risk:	0	12	24	36	48	60	72	84	96
Medical treatment	146	99	68	50	36	22	12	6	2
LAAO	61	48	28	18	13	4	4	3	0

Follow-up (months): Number at risk:	0	12	24	36	48	60	72	84	96
Medical treatment	146	108	73	53	38	24	14	6	2
LAAO	61	49	29	18	13	8	4	3	0

Figure 3. Kaplan-Meier curves for major adverse events and major cardiovascular events-free survival (A) and bleeding events-free survival (B) at follow-up. AMI, acute myocardial infarction; BARC, Bleeding Academic Research Consortium; CI, confidence interval; HR, hazard ratio; LAAO, left atrial appendage occlusion; MACE, major adverse cardiovascular events; MAE, major adverse events; TIA, transient ischemic attack.

findings are significant considering the adverse characteristics of the LAAO group. The benefit of LAAO was maintained against both the acenocoumarol and DOAC subgroups. Regarding safety, there were significantly fewer hemorrhages (BARC 2 and 3) with LAAO compared to the acenocoumarol group. No significant differences regarding hemorrhages were reported between the LAAO and the DOAC group although there were fewer events in the LAAO arm, especially BARC ≥ 2.

Table 6. Rates of events at 12 and 36 months

	TM (146 p)	LAAO (61 p)
MAE at 12 m	37 (30.5)	8 (14.13)
MAE at 36 m	54 (20.5)	13 (10.8)
Overall MAE	68 (19.75)	14 (9.06)
MACE at 12 m	11 (8.28)	2 (3.41)
MACE at 36 m	18 (5.92)	3 (2.43)
Overall MACE	25 (6.37)	3 (1.91)

Rates are expressed as absolute number of events (100 patient-years). Data from the groups in brackets are expressed as percentages. m, months; MACE, major adverse cardiovascular events; MAE, major adverse events; p, patients.

In recent years, 4 studies on DOAC and several meta-analyses showed that DAPT (DOAC plus P2Y12, usually clopidogrel) is associated with fewer hemorrhages compared to triple antiplatelet therapy (warfarin + clopidogrel + aspirin). Also that this treatment is rarely associated with worse outcomes in ischemic-thrombotic events.[11-16] These results are undoubtedly important and have shaped the new recommendations published by scientific societies on the management of these patients.[17]

However, bleeding rates remain very high in this population. In addition, in former studies, the combination of VKAs plus aspirin has already been a less effective strategy compared to DAPT.[1]

The major PIONEER[11] and REDUAL[14] studies reported a mean annual rate of bleeding after a 12-month follow-up with DAPT consisting of DOAC plus clopidogrel of 16.9% and 20.2%, respectively. Of note, data from the AUGUSTUS trial on apixaban are limited to 6 months only, which would explain, at least partially, the lower rate of bleeding reported.[11,12,14,15]

Earlier studies comparing DAPT with aspirin and clopidogrel in patients without AF showed significantly lower rates of bleeding compared to the combination of VKAs plus aspirin.[18]

The clinical follow-up of most DOAC studies has been short (from the 6 months of the AUGUSTUS[15] trial to the 14 months of the REDUAL[14]). Our study reported on a 35-month follow-up. Although bleeding events are known to be more common within the first year for both groups, we saw that beyond the first year, curves diverged favoring the LAAO group (figure 3B). This had already been shown in large LAAO registries.[19] As these treatments are lifelong, the risk of recurrent bleeding and the possibility of future surgical procedures in patients > 70-75 years who need to stop using OAC underline the need for assessing other possible therapeutic alternatives. The rate of thromboembolic events, especially stroke, is known to be significant within the first few days after OAC discontinuation.[20]

Similarly, recurrent ACS in patients who have already had coronary events is not rare. In the Melbourne registry of 9615 patients, 12% required hospitalization 1 year after ACS.[21] Some of these patients require a new PCI, which again brings back the dilemma of using a combined treatment or not.

Importantly, the exclusion criteria specified in these studies limit the applicability of results to the general population of hospitalized patients. It is estimated that the results of these trials could be generalized to less than two-thirds of the patients in the routine clinical practice.[22]

In most studies of DOAC in patients with AF undergoing PCI, the history of previous bleeding is not recorded except for, indirectly, in patients with a past medical history of previous GI bleeding and, in any case, these patients are largely misrepresented. Thus, 1.3% had a past medical history of GI bleeding in the DOAC plus clopidogrel subgroup of the PIONEER study compared to 5% in the warfarin plus clopidogrel group of the WOEST study.[14,23] In our study, 10.7%, 2.8%, and 41% of the patients from the OAC, DOAC, and LAAO groups, respectively, had a past medical history of GI bleeding. Unsurprisingly, since the study was not randomized, cardiologists ordered the LAAO strategy more frequently in patients with a past medical history of bleeding.

Although these 4 studies do report HAS-BLED scores, the predictive value of this parameter, while of use, is much lower compared to the past medical history of bleeding, especially in patients with a history of bleeding and age > 75 years as seen in large LAAO studies.[24,25]

Finally, ischemic events showed significance favorable to the DAPT group vs dual antithrombotic therapy (1.6% vs 6.2%; $P = .01$; and 0.5% vs 2.7%: $P = .01$), respectively.[1]

Limitations

The number of patients was small, and our study was not randomized. Therefore, our results should only be considered hypothesis generating in this pilot study. Despite being an observational study with no control of confounding bias in its design, most of the baseline variables were equally distributed among the groups being the hemorrhagic and thrombotic risks reported at baseline even more unfavorable in the LAAO group. However, a selection bias cannot be ruled out in patients from the LAAO group.

The rate of stroke in the medical treatment group was higher than expected from pivotal studies. This was probably the result of the associated comorbidities that increase the likelihood of readmissions due to invasive procedures that, in turn, require anticoagulant therapy modification as a bridging therapy to these procedures. This increases the long-term rate of stroke in this population compared to those who have undergone LAAO. However, it reflects real-world. Further studies are required to elucidate what the best therapeutic strategy is for these challenging patients.

CONCLUSIONS

In patients with NVAF treated with coronary stents, an LAAO strategy with AP provides superior long-term results regarding major adverse events and major adverse cardiovascular events compared to treatment with OAC (DOAC included) plus AP despite the more unfavorable characteristics reported in the LAAO group.

The benefit favorable to the LAAO group persisted over both VKA and DOAC groups. There were significantly fewer hemorrhagic events (BARC 2 and 3) following LAAO compared to the VKA group, but not between LAAO and DOAC (although there were fewer events in the LAAO arm, especially BARC ≥ 2).

FUNDING

This research received no specific grant from any funding agency from the public, commercial or non-profit sectors.

AUTHORS' CONTRIBUTIONS

The authors guarantee all researchers are responsible for the data contained in this study.

CONFLICTS OF INTEREST

F. Alfonso-Manterola, and R. Moreno-Gómez are associate editors of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. J.R. López-Mínguez received consulting fees for his job as a proctor for Abbott regarding left atrial appendage occlusion; L. Nombela-Franco received grants or contracts c as a proctor for Abbott, Edwards Lifesciences, and Products and Features, and lecture fees from Abbot, Edwards Lifesciences, and Boston Scientific; X. Freixa-Rofastes received consulting fees for his job as a proctor for Abbott and Boston Scientific; X. Millán-Alvárez received consulting fees from Abbott and Boston Scientific, and payment or honoraria for being involved in lectures, presentations, speakers bureaus, manuscript writing or educational events on behalf of Abbott; P. Salinas-Sanguino received speaking fees from Abbott and Boston Scientific, and other financial or non-financial interests as a proctor for Abbott; D. Arzamendi received consulting fees for his job as a proctor for Abbott and Boston Scientific; I. Cruz-González received consulting fees for his job as a proctor and/or consultant for Abbott, Boston Scientific, and Lifetech. The remaining authors declared no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- There is growing evidence that LAAO can be a potential therapeutic alternative to the use of OAC in patients with NVAF and a history of significant bleeding or high bleeding risk.
- LAAO has similar efficacy to OAC preventing the occurrence of thromboembolisms and associates minor bleeding risk especially 1 year after the procedure.

WHAT DOES THIS STUDY ADD?

- The study results suggest that LAAO is a favorable alternative to OAC in patients with NVAF with ischemic heart disease who require coronary stenting and AP-based therapies.
- The observations summarized herein demonstrate, in a real-world setting, that the combination of LAAO plus AP results in a lower rate of major adverse events and major adverse cardiovascular events compared to treatment with OAC plus AP.

ACKNOWLEDGEMENTS

Medical writing support was provided by Javier Arranz-Nicolás, PhD, from Medical Statistics Consulting (MSC), Valencia, Spain under the authors' guidance.

REFERENCES

1. Leon MB, Baim DS, Popma JJ, et al. A Clinical Trial Comparing Three Antithrombotic-Drug Regimens after Coronary-Artery Stenting. *N Engl J Med*. 1998;339:1665-1671.
2. Benjamin EJ, Virani SS, Callaway CW, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation*. 2018;137:e67-e492.
3. Kralev S, Schneider K, Lang S, Süselbeck T, Borggrefe M. Incidence and severity of coronary artery disease in patients with atrial fibrillation undergoing first-time coronary angiography. *PLoS One*. 2011;6:e24964-e24964.
4. González-Pacheco H, Márquez MF, Arias-Mendoza A, et al. Clinical features and in-hospital mortality associated with different types of atrial fibrillation in patients with acute coronary syndrome with and without ST elevation. *J Cardiol*. 2015;66:148-154.
5. Rohla M, Vennekate CK, Tentzeris I, et al. Long-term mortality of patients with atrial fibrillation undergoing percutaneous coronary intervention with stent implantation for acute and stable coronary artery disease. *Int J Cardiol*. 2015;184:108-114.
6. Généreux P, Giustino G, Witzenbichler B, et al. Incidence, Predictors, and Impact of Post-Discharge Bleeding After Percutaneous Coronary Intervention. *J Am Coll Cardiol*. 2015;66:1036-1045.
7. Busu T, Khan SU, Alhajji M, Alqahtani F, Holmes DR, Alkhouli M. Observed versus Expected Ischemic and Bleeding Events Following Left Atrial Appendage Occlusion. *Am J Cardiol*. 2020;125:1644-1650.
8. Osmancik P, Herman D, Neuzil P, et al. 4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation. *J Am Coll Cardiol*. 2022;79:1-14.
9. Reddy VY, Doshi SK, Kar S, et al. 5-Year Outcomes After Left Atrial Appendage Closure. *J Am Coll Cardiol*. 2017;70:2964-2975.
10. Mehran R, Rao SV, Bhatt DL, et al. Standardized Bleeding Definitions for Cardiovascular Clinical Trials. *Circulation*. 2011;123:2736-2747.
11. Cannon CP, Bhatt DL, Oldgren J, et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. *N Eng J Med*. 2017;377:1513-1524.
12. Capodanno D, Huber K, Mehran R, et al. Management of Antithrombotic Therapy in Atrial Fibrillation Patients Undergoing PCI. *J Am Coll Cardiol*. 2019;74:83-99.
13. Gargiulo G, Goette A, Tijssen J, et al. Safety and efficacy outcomes of double vs triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of non-vitamin K antagonist oral anticoagulant-based randomized clinical trials. *Eur Heart J*. 2019;40:3757-3767.
14. Gibson CM, Mehran R, Bode C, et al. Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI. *N Eng J Med*. 2016;375:2423-2434.
15. Lopes RD, Leonardi S, Wojdyla DM, et al. Stent Thrombosis in Patients With Atrial Fibrillation Undergoing Coronary Stenting in the AUGUSTUS Trial. *Circulation*. 2020;141:781-783.
16. Vranckx P, Valgimigli M, Eckardt L, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. *Lancet*. 2019;394:1335-1343.
17. Cheung CC, Nattel S, Macle L, Andrade JG. Management of Atrial Fibrillation in 2021: An Updated Comparison of the Current CCS/CHRS, ESC, and AHA/ACC/HRS Guidelines. *Can J Cardiol*. 2021;37:1607-1618.
18. Bertrand ME, Legrand V, Boland J, et al. Randomized Multicenter Comparison of Conventional Anticoagulation Versus Antiplatelet Therapy in Unplanned and Elective Coronary Stenting. *Circulation*. 1998;98:1597-1603.
19. López-Mínguez JR, Nogales-Asensio JM, Infante De Oliveira E, et al. Long-term Event Reduction After Left Atrial Appendage Closure. Results of the Iberian Registry II. *Rev Esp Cardiol*. 2019;72:449-455.
20. Yao X, Abraham NS, Alexander GC, et al. Effect of Adherence to Oral Anticoagulants on Risk of Stroke and Major Bleeding Among Patients With Atrial Fibrillation. *J Am Heart Assoc*. 2016;5:e003074.
21. Yudi MB, Clark DJ, Farouque O, et al. Trends and predictors of recurrent acute coronary syndrome hospitalizations and unplanned revascularization after index acute myocardial infarction treated with percutaneous coronary intervention. *Am Heart J*. 2019;212:134-143.
22. Lee S, Monz BU, Clemens A, Brueckmann M, Lip GYH. Representativeness of the dabigatran, apixaban and rivaroxaban clinical trial populations to real-world atrial fibrillation patients in the United Kingdom: a cross-sectional analysis using the General Practice Research Database. *BMJ Open*. 2012;2:e001768.
23. Dewilde WJM, Oirbans T, Verheugt FWA, et al. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. *Lancet*. 2013;381:1107-1115.
24. López-Mínguez JR, Nogales-Asensio JM, Infante De Oliveira E, et al. Major Bleeding Predictors in Patients with Left Atrial Appendage Closure: The Iberian Registry II. *J Clin Med*. 2020;9:2295.
25. Tarantini G, D'Amico G, Schmidt B, et al. The Impact of CHA2DS2-VASc and HAS-BLED Scores on Clinical Outcomes in the Amplatzer Amulet Study. *JACC: Cardiovasc Interv*. 2020;13:2099-2108.

REC Interv Cardiol. 2023;5(4):297-298
https://doi.org/10.24875/RECICE.M23000401

Debate. Percutaneous revascularization in dilated cardiomyopathy. Apropos of the REVIVED BCIS2 trial: the interventional cardiologist's view

A debate. Revascularización percutánea en miocardiopatía dilatada. A propósito del ensayo REVIVED BCIS2: visión del intervencionista

José F. Díaz Fernández*

Servicio de Cardiología, Hospital Universitario Virgen del Rocío, Sevilla, Spain

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M23000403

Question: What is your opinion of the REVIVED BCIS2 trial? Which, would you say, are its most positive and most debatable features?

Answer: The REVIVED BCIS2[1] is a prospective, multicenter, randomized, open-label trial of stable patients with severe left ventricular dysfunction (left ventricular ejection fraction [LVEF] ≤ 35%), extensive coronary artery disease with a British Cardiovascular Intervention Society (BCIS) risk score ≥ 6, and evidence of viability in at least 4 dysfunctional segments amenable to percutaneous coronary intervention (PCI). Patients were randomized in a 1:1 ratio to receive PCI along with optimal medical therapy (OMT), or OMT alone. The OMT included pharmacological therapy and implantable devices for the management of heart failure.

The primary endpoint was a composite of all-cause mortality or hospitalization over a minimum follow-up of 24 months. Secondary endpoints included 6- and 12-month echocardiographic measurements of LVEF (core lab), quality of life measurement through questionnaires such as the Kansas City Cardiomyopathy Questionnaire, the EuroQol Group 5-Dimensions 5-Level Questionnaire, and New York Heart Association Functional Class, cardiovascular death, acute myocardial infarction (AMI), appropriate defibrillator therapy (antitachycardia pacing or shock), unplanned revascularization, brain natriuretic peptide values, functional class, and major bleeding.

A total of 700 patients were included, of which 347 were randomized to PCI and 353 to OMT. The participants' mean age was 69 years, and 12% were women. The median follow-up was 41 months (importantly, randomization began back in 2013 and the study was published in 2022), and 40 hospitals in the United Kingdom participated in the trial. The participants received guideline-directed pharmacological therapy (93% received beta-blockers; 66% angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers, and 56% aldosterone antagonists). More than 30% of the participants in the 2 groups received a defibrillator or resynchronization device before or during the study period.

The primary endpoint was observed in 37.2% of the PCI group and 38% of those in the OMT group. LVEF was similar in the 2 groups both at 6 and 12 months. Although quality of life questionnaires favored PCI at 6 and 12 months, this improvement was attenuated at 24 months.

I believe the main strength of the study is that it is the first to compare this revascularization mode (PCI) with OMT in ischemic patients with LVEF ≤ 35%. Previously, we only had the STITCH[2] trial for this patient subgroup, which compared coronary revascularization surgery with OMT in a population of younger patients with less extensive coronary artery disease. This trial did not show any benefits associated with surgery in terms of overall 5-year mortality but did show benefits at the extended 10-year follow-up. Another important point is the efficacy of OMT in these patients today; in fact, the number of events was even lower than initially anticipated by the investigators.

Regarding debatable aspects, I'd say that, although the patients were selected on the basis of myocardial viability; until now viability testing has never been used to predict the effectiveness of revascularization.[2,3] And to be honest, it may not be the most suitable way to identify patients who will benefit from PCI in this population.[4] Additionally, most patients were asymptomatic (66%) or showed mild angina symptoms, which could undoubtedly have impacted the results.

* **Corresponding author.**
E-mail address: jfdiazf@yahoo.es (J. F. Díaz Fernández).
𝕏 @pepp183 @CorazonHuvr

Online 3 October 2023.

Q.: What was the patients' coronary artery disease profile? What do think of the use of an angiographic risk index like the BCIS in this trial compared with alternatives like the SYNTAX score, and especially functional assessment using pressure guidewires? How far do you think the causal relationship between coronary artery disease and dilated cardiomyopathy was clear?

A.: Compared with the STITCH[2] trial, the REVIVED BCIS2[1] trial included older patients with more extensive coronary artery disease and more contemporary medical treatment. However, the assessment of disease extent and the significance of coronary involvement according to the BCIS[5] score raises some questions. In fact, it's surprising that despite having mean scores of 10, almost half of the participants had 2-vessel disease, and the median number of vessels and lesions treated was 2,[6] which raises concerns about how many lesions were not revascularized. Also, it is unclear whether there could have been some selection bias, because some participants with more extensive coronary artery disease amenable to surgery might have been referred directly and not included in the study.

On the other hand, it seems obvious that lesion assessment with pressure guidewires would have provided the study with significant reliability. If we look at the BCIS score, lesions are defined as severe when stenosis is $\geq$ 70%. Especially in a population of mostly asymptomatic patients or those with mild angina symptoms and multivessel disease, it seems more than reasonable to select target lesions and vessels based on coronary physiology assessment.

Q.: What can you tell us about revascularization? Could the degree of complete revascularization or crossing over from OMT to PCI have impacted the results?

A.: As I mentioned, despite having extensive coronary artery disease according to the angiographic scale used, almost half of the participants had 2-vessel disease, and the median number of treated lesions was 2. Additionally, the authors mention that they have not yet analyzed whether the target vessels coincided with segments of affected viability, complicating interpretation of the results even more. Undoubtedly, if some lesions were left untreated while others without indications were indeed treated, the impact on the results is obvious. Also, as you mentioned in your question, unplanned revascularization was more frequent in the OMT group (10.5%) than in the PCI group (2.9%), which could explain why the PCI group showed better quality of life scores at 6 and 12 months, but not at 24 months when the impact of the higher rate of unplanned revascularizations in the OMT group may have been a factor.

Q.: Were there any benefits seen in any type of clinical event in the PCI group?

A.: Yes. The PCI group experienced fewer episodes of ventricular tachycardia or fibrillation than the OMT group, suggesting a lower ischemic burden and arrhythmic risk in the OMT group. Additionally, the number of defibrillators implanted after randomization was lower in the PCI group.

On the other hand, although the incidence of AMI was similar in the 2 groups (around 10%), almost half were perioperative in the PCI group, whereas none were perioperative in the OMT group, resulting in more spontaneous AMIs in the OMT group (9% vs 5%). This datum might be clinically relevant because the ISCHEMIA trial[7] revealed that spontaneous AMIs have a worse prognosis than perioperative AMIs.

As I mentioned previously, the PCI group also benefitted in terms of quality of life at 6 and 12 months, but not at 24 months.

Q.: Bearing in mind that coronary artery disease may have a causal relationship with cardiomyopathy, do you think there is a particular patient profile that could benefit from PCI or, at the least, merit further investigation of this link?

A.: Based on the REVIVED trial results, it's obvious that percutaneous revascularization in stable patients with severe LVEF depression, multivessel disease, and few or no angina symptoms provides little benefit. If we remember that lesion selection was purely angiographic (lesions with stenosis ≥ 70%), and that we just don't know if the treated lesions coincided with segments of abnormal viability, patients with severe left ventricular dysfunction, angina symptoms, angiographically significant lesions, and abnormal coronary physiology assessments (or left main coronary artery intravascular ultrasound assessments)[8] may constitute a group that could benefit from coronary angioplasty in terms of survival and quality of life.

FUNDING

None reported.

CONFLICTS OF INTEREST

None.

REFERENCES

1. Perera D, Clayton T, O'Kane PD, et al. Percutaneous revascularization for ischemic left ventricular dysfunction. *N Engl J Med.* 2022;387:1351-1360.
2. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. *N Engl J Med.* 2016;374:1511-1520.
3. Cleland JG, Calvert M, Freemantle N, et al. The heart failure revascularisation trial (HEART). *Eur J Heart Fail.* 2011;13:227-233.
4. Ryan M, Morgan H, Chiribiri A, Nagel E, Cleland J, Perera D. Myocardial viability testing: all STICHed up, or about to be REVIVED? *Eur Heart J.* 2022;43:118-126.
5. Perera MA, Stables R, Booth J, et al. The Balloon pump-assisted Coronary Intervention Study (BCIS-1): Rationale and design. *Am Heart J.* 2009;158:910-916.
6. Vergallo R, Liuzzo G. The REVIVED-BCIS2 trial: percutaneous coronary intervention vs. optimal medical therapy for stable patients with severe ischaemic cardiomyopathy. *Eur Heart J.* 2022; 43:4775-4776.
7. Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med.* 2020;382:1395-1407.
8. De Maria GL, Testa L, de la Torre Hernandez JM, et al. A multi-center, international, randomized, 2-year, parallel-group study to assess the superiority of IVUS-guided PCI versus qualitative angio-guided PCI in unprotected left main coronary artery (ULMCA) disease: Study protocol for OPTIMAL trial. *PLoS One*. 2022;17:e0260770.

REC Interv Cardiol. 2023;5(4):299-301
https://doi.org/10.24875/RECICE.M23000403

Debate. Percutaneous revascularization in dilated cardiomyopathy. Apropos of the REVIVED BCIS2 trial: the clinician's view

A debate. Revascularización percutánea en miocardiopatía dilatada. A propósito del ensayo REVIVED BCIS2: visión del clínico

Ángel Manuel Iniesta Manjavacas*

Servicio de Cardiología, Hospital Universitario La Paz, Instituto de Investigación Sanitaria del Hospital Universitario La Paz (IdiPAZ), Madrid, Spain

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M23000401

Question: What's your interpretation of the REVIVED BCIS2 trial? Which, would you say, are its most positive and debatable features?

Answer: The REVIVED BCIS2[1] trial randomized stable patients with ischemic dilated cardiomyopathy to undergo percutaneous coronary intervention (PCI) along with optimal medical therapy (OMT) or OMT alone without revascularization. The trial included patients with left ventricular ejection fraction ≤ 35%, extensive coronary artery disease, and viability in 4 or more segments amenable to PCI. The results proved that the 2 strategies offered comparable outcomes regarding the primary composite endpoint of all-cause mortality or hospitalization-related heart failure (37.2% vs 38.0%; hazard ratio, 0.99; 95% confidence interval, 0.78-1.27; P = .96). There were no differences in the changes in left ventricular ejection fraction recorded at 6 months and at 1 year, with improvement confirmed in both groups.[2] Previously, the STICH trial[2,3] had demonstrated that surgical revascularization combined with OMT provided long-term overall survival benefits in patients with ischemic dilated cardiomyopathy, despite an initial increase in surgery-related mortality. Therefore, it was believed that the REVIVED BCIS2 trial, with the lower perioperative risk associated with PCI, could equal or even exceed these benefits. However, things have changed since the publication of the STICH trial, including improvements in pharmacological therapy, greater use of devices such as implantable cardioverter-defibrillators and cardiac resynchronization therapy, closer follow-up of patients with heart failure, and widespread use of cardiac rehabilitation programs. The REVIVED BCIS2 trial proves that current OMT with the use of these resources in patients with ischemic dilated cardiomyopathy provides certain benefits regarding mortality and heart failure-related hospitalizations that are not enhanced by revascularization, at least with the percutaneous approach.

The most positive feature of this study is that it addresses an open question on the need for the systematic use of PCI in these patients and it does so with a methodologically appropriate clinical trial. The most debatable aspects are the definition of ischemic dilated cardiomyopathy and the achievement of complete revascularization. To characterize cardiomyopathy as ischemic, a BCIS-Jeopardy score[4] ≥ 6 was required, with 49% of the patients having 2-vessel disease, while the median number of lesions and vessels treated per patient in the PCI group was 2, and complete revascularization was achieved in 71% of the patients.[1]

Q.: The STICH trial[2] showed benefits beyond the 5- to 10-year mark, but in the REVIVED BCIS2 trial, the median follow-up was 3 to 4 years, although the patients' age in the 2 studies was very different. What do you make of this?

A.: In the STICH trial, the all-cause mortality curves (primary endpoint) began to separate at the 2-year follow-up, and the original publication of the study, with a median follow-up of 4.7 years, failed to show a significant reduction in the primary endpoint. What demonstrated the prognostic benefit of cardiac surgery in addition to OMT was extending the follow-up to 10 years (median, 9.8 years).[3] This reveals several points: on the one hand, the increased perioperative morbidity and mortality and, on the other hand, the long-term benefits of alleviating myocardial ischemia, leading, among other things, to lower rates of reinfarction and ventricular arrhythmias[5] This is especially relevant when treating younger patients, whose lower surgical risk and longer life expectancy allow us to actually see clinical benefits. Although PCI was not associated with higher perioperative mortality in the REVIVED BCIS2 trial, there were no significant separations of the primary endpoint curves during the study.

* **Corresponding author.**
E-mail address: a.m.iniesta84@gmail.com (A.M. Iniesta Manjavacas).
@angel84ma @CardiologiaLa

Online 3 October 2023.

We need to obtain data from a longer follow-up to detect any potential benefits associated with PCI. Additionally, the mean age of the REVIVED trial population was 70 years (compared with the median of 60 years in the STICH trial), making it less likely to achieve the same long-term benefits associated with surgical revascularization.

Q.: What was the clinical profile of these patients, and to what extent was their medical therapy optimized during randomization? Do you think they could have progressed to advanced stages of cardiomyopathy, and if so, could that have impacted the outcomes?

A.: The participants' clinical profile was typical of this kind of disease. Most were men (88%), and 56% of them had a history of hypertension, 41% had diabetes, and 53% had previous myocardial infarction: 67% were angina-free, 20% had a history of previous PCI, and 5% had undergone surgical revascularization. They were in a favorable functional class (74% were in NYHA class I or II), while only 33% had been hospitalized due to heart failure in the previous 2 years, and the median N-terminal pro-brain natriuretic peptide (NT-proBNP) was 1400 pg/mL. Therefore, their baseline characteristics do not support the assumption that they were in an advanced stage of the disease.[6] Although mortality during follow-up was high (32%), it was consistent with what we would expect of patients with ischemic dilated cardiomyopathy,[7,8] while the rate of heart failure-related hospitalizations was relatively low (15%). Based on their clinical profile, these patients would have been eligible for improvement with percutaneous revascularization. When the participants were randomized, 89% were on an angiotensin-converting enzyme inhibitor, combined with an angiotensin II receptor antagonist or sacubitril-valsartan, 91% were on beta-blockers, and 49% were on mineralocorticoid receptor antagonists. Although this is a well-optimized regimen, there is still room for improvement, because only 5% of the participants were on sacubitril-valsartan, half of them were not on aldosterone antagonists, and sodium-glucose co-transporter-2 inhibitors were not yet considered part of the foundational treatment of heart failure. Indeed, at the 2-year follow-up, only 20% were on sacubitril-valsartan and 55% were on mineralocorticoid receptor antagonists. Additionally, a low percentage of participants (23%) had a defibrillator or a cardiac resynchronizer.[1]

Q.: Do you agree that the trial questions the validity of viability tests? Although a 25% cutoff value for late gadolinium enhancement was established in cardiac magnetic resonance, in cases with 25% to 50% enhancement it was left to the local investigators' discretion to use another imaging modality, such as dobutamine echocardiography. Do you think places doubt on the criteria applied to the trial?

A.: The STICH trial viability subanalysis already cast doubt on the utility of detecting a viable myocardium through single-photon emission computed tomography or dobutamine echocardiography to predict favorable outcomes after revascularization.[9] The REVIVED BCIS2 also failed to demonstrate that viability-guided revascularization is able to reduce mortality or improve cardiac remodeling. In this trial, a larger number of dysfunctional—yet viable—myocardial segments were not associated with prognosis or with the possibility of improved ventricular function, whereas less myocardial scarring did predict a more favorable prognosis and a higher likelihood of reverse remodeling. This was independent of the baseline ejection fraction and extent of coronary artery disease.[10] The results should prompt us to revisit the notion of hibernating myocardium and avoid basing the coronary revascularization strategy solely on viability tests.[11] In this trial, cardiac magnetic resonance was the preferred imaging modality to assess viability (used in 71% of the patients). Considering segments with a maximum late enhancement of 25% as viable was a positive aspect, because participants with higher theoretical probabilities of improving after PCI were selected. Although another additional imaging modality could be used in patients with late enhancement between 26% and 50%, in practice, only 8 patients[1] received more than 1 viability test, so this does not seem to be an important point.

Q.: Considering the possibility that coronary artery disease can be concurrent with cardiomyopathy, without it necessarily being the main cause, do you think there is a specific patient profile that could benefit from PCI or, at the very least, could be worth further study?

A.: The subgroup analysis did not show any significant treatment interaction in the prespecified subgroups of interest.[1] However, data from the study allow us to speculate on which participants might benefit more from PCI. The trial included few patients with limiting angina, thus making the findings less applicable to these patients. The study showed differences in favor of PCI regarding quality of life at the 6- and 12-month follow-up (becoming equal at 2 years in the 2 groups), suggesting that PCI might be crucial for patients with angina.[5] Additionally, PCI-treated patients showed a trend toward fewer appropriate implantable cardioverter-defibrillator therapies,[1] indicating that revascularization could be more beneficial in individuals in whom ventricular arrhythmias are an issue. Other subgroups of interest would be patients with more extensive coronary artery disease, those with complete revascularization, and those with greater ventricular dysfunction. Future publication of these patients' outcomes could help in the decision-making process.[6]

Finally, while surgical revascularization should be the preferred strategy for patients with ischemic dilated cardiomyopathy,[7] PCI should still play a role in the management of young patients with significant coronary artery disease and high surgical risk or poor distal beds. With the current evidence available and contemporary OMT, a clinical trial should be conducted comparing 3 therapeutic strategies: isolated OMT, OMT along with surgical revascularization, and OMT alongside PCI in patients with ischemic dilated cardiomyopathy. The selection criteria should not consist of viability but rather the feasibility of achieving complete myocardial revascularization in regions at-risk, and follow-up should be long-term.

FUNDING

None reported.

CONFLICTS OF INTEREST

None.

REFERENCES

1. Perera D, Clayton T, O'Kane PD, et al. Percutaneous revascularization for ischemic left ventricular dysfunction. *N Engl J Med.* 2022;387:1351-1360.
2. Velazquez EJ, Lee KL, Deja MA, et al. Coronary-artery bypass surgery in patients with left ventricular dysfunction. *N Engl J Med*. 2011;364:1607-1616.
3. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. *N Engl J Med.* 2016;374:1511-1520.
4. Morgan H, Ryan M, Briceno N, et al. Coronary Jeopardy Score Predicts Ischemic Etiology in Patients With Left Ventricular Systolic Dysfunction. *J Invasive Cardiol.* 2022;34:E683-E685.
5. Ezad SM, Ryan M, Perera D. Can Percutaneous Coronary Intervention Revive a Failing Heart? *Heart Int.* 2022;16:72-74.

6. Vergallo R, Liuzzo G. The REVIVED BCIS2 trial: percutaneous coronary intervention vs. optimal medical therapy for stable patients with severe ischaemic cardiomyopathy. *Eur Heart J.* 2022;43:4775-4776.
7. Liga R, Colli A, Taggart DP, Boden WE, De Caterina R. Myocardial Revascularization in Patients With Ischemic Cardiomyopathy: For Whom and How. *J Am Heart Assoc.* 2023;12:e026943.
8. Perera D, Clayton T, Petrie MC, et al. Percutaneous Revascularization for Ischemic Ventricular Dysfunction: Rationale and Design of the REVIVED BCIS2 Trial: Percutaneous Coronary Intervention for Ischemic Cardiomyopathy. *JACC Heart Fail.* 2018;6:517-526.
9. Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction. *N Engl J Med.* 2011;364: 1617-1625.
10. Perera D. Effect of Myocardial Viability, Functional Recovery and ICP on Clinical Outcomes in the REVIVED BCIS2 Trial. En: American College of Cardiology 2023 Scientific Session; 2023 March 4-6; New Orleans, LA, USA. Available at: https://accanywhere.acc.org/media/c2f4157c-0bef-4d69-87b4-ac6ab6224e07. Accessed 9 Jul 2023.
11. Ryan M, Morgan H, Chiribiri A, Nagel E, Cleland J, Perera D. Myocardial viability testing: all STICHed up, or about to be REVIVED? *Eur Heart J.* 2022;43:118-126.

REC Interv Cardiol. 2023;5(4):302-310
https://doi.org/10.24875/RECICE.M23000390

Drug-eluting balloon angioplasty for bifurcated chronic total coronary occlusion

Angioplastia con balón farmacoactivo para una oclusión coronaria total crónica en bifurcación

Marcel Almendárez,[a,b,*] Rut Álvarez-Velasco,[a,b] Alberto Alperi García,[a,b] Pablo Avanzas,[a,b,c] Cesar Morís de la Tassa,[a,b,c] and Isaac Pascual[a,b,c]

[a] *Área de Gestión Clínica del Corazón, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*
[b] *Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Asturias, Spain*
[c] *Departamento de Medicina, Facultad de Medicina, Universidad de Oviedo, Oviedo, Asturias, Spain*

To the Editor,

This is the case of a 67-year-old woman admitted due to a 6-month history of exertional angina. Stress echocardiography showed severe anterior wall ischemia. The patient was referred for coronary angiography that revealed the presence of a chronic total coronary occlusion of the proximal left anterior descending coronary artery (LAD) immediately before the bifurcation with the first diagonal branch (D1) from the septal collaterals of the right coronary artery (figure 1A, video 1 of the supplementary data). The patient signed the written informed consent, and a chronic total coronary occlusion recanalization was performed 6 months after the index angiography.

Initial antegrade acess was planned given the lesion's favorable characteristics (Japan-chronic total occlusion score of 1). An ultrasound-guided dual angiography was performed with a 7-Fr AL1 guiding catheter (Cordis, United States) via femoral access for the right coronary artery, and a 7.5-Fr PB 3.5 SheathLess guiding catheter (Asahi Intecc, United States) for the left main coronary artery. The procedure was started with a Caravel microcatheter (Asahi Intecc, United States) loaded with a SION wire (Asahi Intecc, United States) that crossed the distal LAD plus a second wire that crossed the D1. The lesion was not heavily calcified, which is why it was predilated with a 2 mm x 12 mm semi-compliant Emerge balloon (Boston Scientific, United States) at 12 atmospheres. Despite using vasodilators, a narrow distal bed in the LAD and D1 was seen, and the use of stenting was ill-advised. Drug-eluting balloon (DEB) angioplasty for the bifurcation was decided. A 2.5 mm x 20 mm SeQuent Please Neo DEB up to a nominal pressure was used for the LAD for 60 seconds (Braun Melsungen, Germany), and a 2 mm x 20 mm DEB up to a nominal pressure was used for the D1 for 60 seconds. A final TIMI grade-3 flow was obtained when the procedure was completed (figure 1B, video 2 of the supplementary data). A small non-flow limiting dissection was managed conservatively in the mid-LAD after the D1.

The patient was scheduled for angiography and optical coherence tomography. Six months later, the study showed patency of recanalization and significant improvement of the distal vessel with a TIMI grade-3 flow (figure 1C). The optical coherence tomography confirmed the excellent results, and the complete resolution of the dissection in the mid-LAD (figure 2A-C, and video 3 of the supplementary data). The patient was free from angina at this follow-up.

The main reasons to avoid stenting were the size of both vessels, the possibility of side branch occlusion using provisional stenting, and the high probability of in-stent restenosis with a 2-stent technique considering the localization of the lesion. Arguably, good mid-term results were expected if a TIMI grade-3 flow was obtained in both branches, thus avoiding multiple layers of stents. For this reason, we corroborated this hypothesis in a 6-month angiographic and optical coherence tomography follow-up.

The BASKET-SMALL 2 randomized control trial proved to be non-inferior to DEB compared to second-generation drug-eluting stents for a composite endpoint of cardiac death, non-fatal myocardial infarction, and target vessel revascularization in de novo lesions for vessels < 3 mm.[1] Even better results were obtained in the randomized control trial PICCOLETO II where a DEB was compared to an everolimus-eluting stent showing less in-lesion late lumen loss at 6 months (0.04 vs 0.17 mm; $P = .03$).[2]

Several studies have evaluated different approaches to DEB in bifurcations. However, no randomized control trial has ever compared the use of DEB for the left main coronary artery and side branches to another strategy.[3] Observational analyses of 39 and 127 patients conducted by Shulz et al. and Bruch et al., respectively, concluded that a DEB-only approach was safe and effective to treat selected bifurcations (namely a side branch ≥ 2 mm) with low rates of restenosis and target lesion revascularization. Stenting as a bailout strategy was advised when flow-limiting dissection or excessive recoil occurred.[4,5]

Only a few cases describe the treatment of complex lesions such as a chronic total coronary occlusion with a DEB. Our case seems especially relevant considering that the occlusion involved a bifurcation and a small distal bed. This case highlights the feasibility of treating a bifurcated chronic total coronary occlusion when a narrow vessel is found with a DEB.

FUNDING

None whatsoever.

*** Corresponding author.**
E-mail address: marcel.almendarez@gmail.com (M. Almendárez).

Online 8 June 2023.

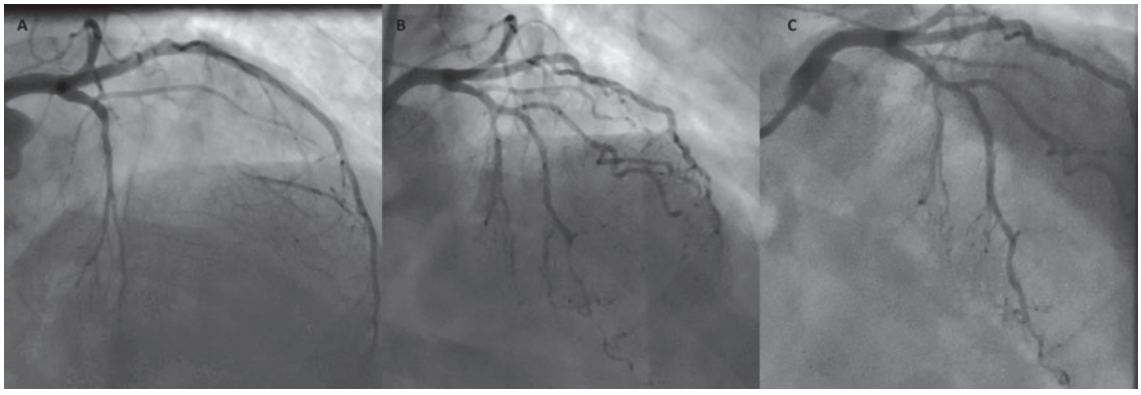


Figure 1. **A:** cranial view of chronic total coronary occlusion of proximal left anterior descending coronary artery (LAD). **B:** postoperative final angiographic result with a small non-flow limiting dissection in the mid-LAD treated conservatively. **C:** angiographic control at 6 months showed great outcomes using drug-eluting balloons. The distal vessel has increased its size with no signs of the small dissection whatsoever.

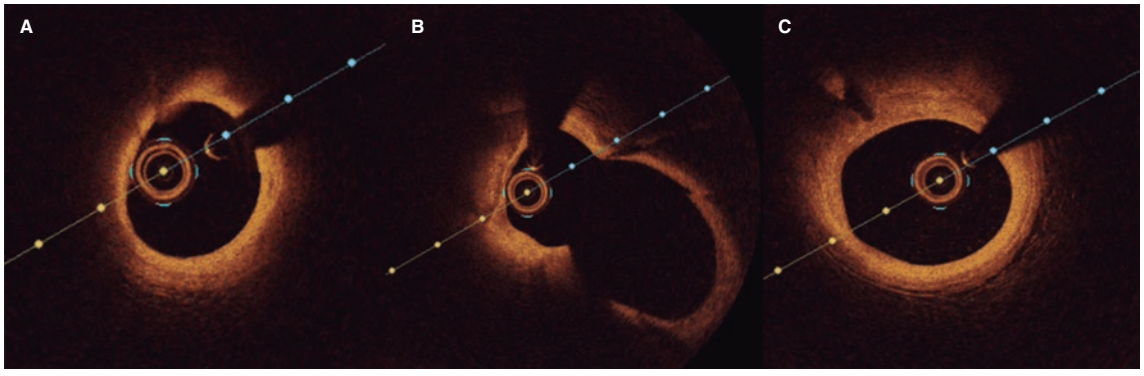


Figure 2. **A:** distal left anterior descending coronary artery (LAD) showing no signs of the previous dissection. **B:** LAD at the carina. **C:** proximal LAD before the bifurcation without any evidence of dissection by optical coherence tomography.

AUTHORS' CONTRIBUTIONS

Operator: I. Pascual. Original drafting of the manuscript: M. Almendárez, and R. Álvarez-Velasco. Revision and editing: P. Avanzas, and C. Morís de la Tassa. Figure edition: A. Alperi García.

CONFLICTS OF INTEREST

None.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M23000390.

REFERENCES

1. Jeger RV, Farah A, Ohlow MA, et al. Drug-coated balloons for small coronary artery disease (BASKET-SMALL 2): an open-label randomised non-inferiority trial. *Lancet*. 2018;392:849-856.
2. Cortese B, Di Palma G, Guimaraes MG, et al. Drug-Coated Balloon Versus Drug-Eluting Stent for Small Coronary Vessel Disease: PICCOLETO II Randomized Clinical Trial. *JACC Cardiovasc Interv*. 2020;13:2840-2849.
3. López-Mínguez JR, Navarro Romero R. Current state of knowledge on the use of drug-coated balloon in coronary bifurcation lesions. *REC Interv Cardiol*. 2023. https://doi.org/10.24875/RECICE.M22000341.
4. Bruch L, Zadura M, Waliszewski M, et al. Results From the International Drug Coated Balloon Registry for the Treatment of Bifurcations. Can a Bifurcation Be Treated Without Stents? *J Interv Cardiol*. 2016;29:348-356.
5. Schulz A, Hauschild T, Kleber FX. Treatment of coronary de novo bifurcation lesions with DCB only strategy. *Clin Res Cardiol*. 2014;103:451-456.

https://doi.org/10.24875/RECICE.M23000391

Atrial flow regulator and atrial septostomy in pediatric pulmonary hypertension: when procedure and device match

Regulador de flujo auricular y atrioseptostomía en hipertensión pulmonar en pediatría: cuando un procedimiento encuentra su dispositivo

Lisa Bianco,[a,*] Anna Sabaté-Rotés,[b] Alba Torrent-Vernetta,[c,d] and Pedro Betrián-Blasco[a]

[a] *Unidad de Hemodinámica Pediátrica, Hospital Vall d'Hebrón, Universitat Autònoma de Barcelona, Barcelona, Spain*
[b] *Servicio de Cardiología Pediátrica, Hospital Vall d' Hebrón, Universitat Autònoma de Barcelona, Barcelona, Spain*
[c] *Servicio de Alergia Pediátrica, Neumología Pediátrica y Fibrosis Quística, Hospital Vall d' Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain*
[d] *Centro de Investigación en Red de Enfermedades Raras (CIBERER), Instituto de Salud Carlos III, Spain*

To the Editor,

Despite recent improvements in the management of pediatric pulmonary hypertension (PH) and reduced overall mortality rates due to pathway-targeted therapy, there is currently no cure for most patients, and morbimortality remains high with lung transplant being the destination therapy for most.[1,2]

According to the clinical practice guidelines, the creation of a pre-tricuspid restrictive defect with atrial septostomy (AS) has no strong evidence but may be considered for patients in WHO/Ross III-IV functional class (FC) with syncope and/or severe right ventricular failure who remain unresponsive to maximal pharmacological treatment or as a bridging therapy to lung transplant.[1,2] There is relatively little experience among pediatric patients. However, the AS/PH drug combo has improved short-term outcomes like FC, syncope or survival.[3,4] When performed by experienced teams the rate of complications drops. However, it is still challenging in the context of high-risk patients. Main fatal events are related to a severe PH crisis or severe cyanosis due to unpredictable shunt size.

Different approaches have been described to create a restrictive AS. Balloon (or blade) septostomy shows early spontaneous closure, so implanting a device in the atrial septum would be a common way to prevent it. The use of a customized fenestrated closure device has been reported, but this shows a high rate of long-term occlusion and a less predictable diameter of the shunt. At our center, we often perform AS with a diabolo-shaped stent in the septum. This allows us to predict the diameter of the shunt, but it has a relatively higher risk of embolization and potential in-stent neointimal hyperplasia.[4] An alternative has appeared with the availability of the atrial flow regulator (AFR, Occlutech, Turkey), a self-expandable nitinol wire mesh device made up of 2 symmetric discs connected by a central fenestrated waist. It comes in 8 mm and 10 mm fenestration diameters (4 mm and 6 mm for compassionate use) with disc diameters of 21 mm and 23-mm, respectively, and 2 models (M/L) depending of the height of the central waist (5 mm and 10 mm) associated with the thickness of the atrial septum. A welded ball connector is located on his proximal disc to secure it to the delivery system. The AFR has been used in different scenarios including PH in adults and older children. Although data on smaller ones are more limited it's still promising.[5,6] Larger data are needed to support this evidence.

We report our first experience with 2 4-year-old twins (13 kg and 12.5 kg) with PH diagnosed due to recurrent syncope. Both showed severe PH with estimated supra-systemic systolic pulmonary artery pressure, right ventricular hypertrophy, and severe dilatation with preserved function without structural abnormalities. Pharmacological therapy (sildenafil, bosentan, and treprostinil) was started in both twins. Patient #1 had the worst evolution with the persistence of syncope, and up-titration of the medication was required while patient #2 had an impaired FC. The procedure (table 1) was performed on PH-targeted pharmacotherapy, mechanical ventilation on high doses of oxygen, and under fluoroscopy and transoesophageal echocardiography guidance with extracorporeal membrane oxygenation and cardiac surgery teams on standby. Invasive data confirmed the diagnosis. Puncture of the fossa ovalis was performed in patient #1 using a Brockenbrough needle (video 1 of the supplementary data). In patient #2, the left atrium was accessed through a patent foramen ovalis. In both cases, an AFR with an 8 mm fenestration size and model M was used, which was the smallest CE approved device. The atrial septum defect was dilated (video 2 of the supplementary data) with balloons that were smaller than recommended by the manufacturer (Advance balloon, Cook Medical, United States, 8 mm*2 cm in patient #1, and 7 mm*2 cm in patient #2) so that the central fenestration of AFR would be slightly constrained by the interatrial septum, thus allowing a shunt slightly under 8 mm. The remaining procedure is the same as an atrial septal defect closure with a standard device (figure 1, video 3 of the supplementary data). The shunt final sizes were 6.5 mm,and 6.3 mm in patients #1 and #2, respectively on the transoesophageal echocardiography. There were no further complications. Both patients were admitted to the intensive care unit for postoperative care where they remained < 24 hours. They were discharged on aspirin and PH-targeted treatment (sildenafil, bosentan, and treprostinil). Procedures were relatively straightforward, easier, and shorter compared to our diabolo-shaped stent series.[4]

At their last follow-up (after 9 and 8 months) both had good disease progression: the device was patent with a bidirectional but predominant left-to-right shunt (videos 4 to 6 of the supplementary data) without significant baseline desaturation (> 94%) or syncope and with normal FC. The N-terminal pro-B-type natriuretic peptide (pg/mL) levels were slightly lower in both patients (163 pg/mL to 159 pg/mL in patient #1 and 376 pg/mL to 157 pg/mL in #2). They are not

* **Corresponding author.**
E-mail address: asi.bianco@gmail.com (L. Bianco).

Online 12 June 2023.

Table 1. Procedural characteristics

	Patient #1	Patient #2
Sex	Male	Male
Age (years)	4	4
Weight (kg)	13	12.5
RA (mmHg)	4	6
LA (mmHg)	6	8
PA (mmHg)	63/42/51	69/24/46
Ao (mmHg)	72/40/56	80/39/56
Previous O_2 saturation (%)	98	98
Postoperative O_2 saturation (%)	94	96
Fenestration diameter on the TEE (mm)	6.5	6.3
AFR device (mm)		
Fenestration diameter	8	8
Waist height	5	5
Diameters of discs	21	21
Venous access	femoral	femoral
Maximum venous access size (Fr)	12	12
TS access	Brockenbrough needle	PFO
Balloon AS dilatation	Advance 35 LP 8 mm × 2 cm	Advance 35 LP 7 mm × 2 cm
Procedural time (min)	116	74
Fluoroscopy time (min)	25	12
Radiation dose (Gy/cm²)	14.8	5.9

AFR, atrial flow regulator; Ao, aortic systolic/diastolic/mean pressure; AS, atrial septum; LA, left atrial mean pressure; LP, low profile; PA, pulmonary artery systolic/diastolic/mean pressure; PFO, patent foramen ovalis; RA, right atrial mean pressure; TEE, transesophageal echocardiography; TS, transseptal.

currently listed for lung transplant and are still on triple therapy up-titrated according to weight gain.

Our data are consistent with those reported,[5,6] making the AFR a valid alternative also in small children with severe high-risk PH. Its main advantage is the possibility of creating a shunt of predictable size combined with greater technical ease and low risk of device migration.

The twin's parents gave their explicit informed written consent to publish the data and images, and to perform the procedure.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

L. Bianco participated in clinical data collection, and draft manuscript preparation with inputs from all the authors. P. Betrián Blasco performed the procedure and supervised the manuscript final version. A. Torrent Vernetta, and A. Sabaté Rotés were involved in the patient's healthcare plan and reviewed the manuscript. All authors approved the manuscript final version.

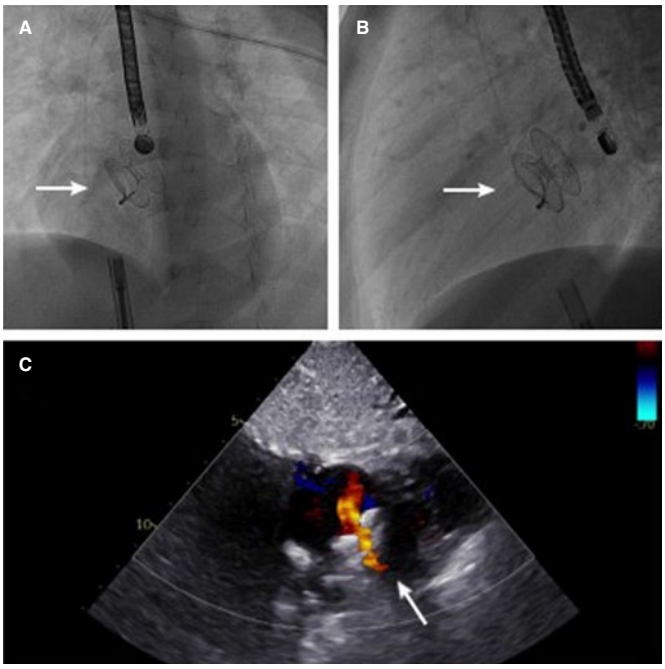


Figure 1. A and **B:** fluoroscopy frames at left anterior oblique (A) and lateral (B) projections showing the atrial flow regulator (AFR) device released in its target position in the interatrial septum (white arrow). **C:** transthoracic color Doppler echocardiography image at subcostal view of the AFR (white arrow).

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.M23000391.

REFERENCES

1. Hansmann G, Koestenberger M, Alastalo TP, et al. 2019 updated consensus statement on the diagnosis and treatment of pediatric pulmonary hypertension: The European Pediatric Pulmonary Vascular Disease Network (EPPVDN), endorsed by AEPC, ESPR and ISHLT. *J Heart Lung Transplant*. 2019;38:879–901.
2. Rosenzweig EB, Abman SH, Adatia I, et al. Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management. *Eur Respir J*. 2019;53:1801916.
3. Grady RM. Beyond transplant: Roles of atrial septostomy and Potts shunt in pediatric pulmonary hypertension. *Pediatr Pulmonol*. 2021;56:656–660.
4. Degano Iglesias LA, Sabaté Rotés A, Betrian Blasco P, Torrent Vernetta A, Moreno-Galdó A, Albert Brotons DC. Septostomía auricular en niños con hipertensión pulmonar. *Rev Esp Cardiol*. 2019;72:688–691.
5. Sivakumar K, Rohitraj GR, Rajendran M, Thivianathan N. Study of the effect of Occlutech Atrial Flow Regulator on symptoms, hemodynamics, and echocardiographic parameters in advanced pulmonary arterial hypertension. *Pulm Circ*. 2021;11:1–10.
6. Vanhie E, VandeKerckhove K, Haas NA, De Wolf D. Atrial flow regulator for drug-resistant pulmonary hypertension in a young child. *Catheter Cardiovasc Interv*. 2021;97:E830-E834.

https://doi.org/10.24875/RECICE.M23000392

Coronary malperfusion in acute type A aortic dissection

Hipoperfusión coronaria en la disección aórtica aguda tipo A

Cristina Morante Perea,[a,*] Tomás Cantón Rubio,[a] Luis Manuel Hernando Romero,[a] José Alfonso Buendía Miñano,[b] José Moreu Burgos,[a] and Luis Rodríguez Padial[a]

[a] *Servicio de Cardiología, Hospital Universitario de Toledo, Toledo, Spain*
[b] *Servicio de Cirugía Cardiaca, Hospital Universitario de Toledo, Toledo, Spain*

To the Editor,

Coronary malperfusion in patients with aortic dissection further worsens prognosis due to compromised myocardial blood flow. The incidence rate of coronary disease goes from 9% to 10% according to various registries.[1,2] Also, it can occur simultaneously at the beginning of dissection, during the patient transfer or in the middle of surgery. The management of these patients is still a matter of discussion. The optimal time of myocardial reperfusion is 90 min, a timeframe that cannot be guaranteed with surgical revascularization associated with aortic valve repair surgery.

This is the case of a 65-year-old man. The patient was a smoker with chronic kidney disease who was admitted to our center as a «myocardial infarction code» case due to suspected anterior ST-segment elevation acute coronary syndrome. The coronary angiography revealed the presence of a type A aortic dissection with coronary malperfusion due to left main coronary artery (LMCA) occlusion.

The patient had reported to his tertiary referral center with a 30-min history of oppressive retrosternal chest pain. Upon arrival at the emergency room, he remained symptomatic and hemodynamically unstable (pale, sweaty, low arterial blood pressure levels, 60/40 mmHg). The electrocardiogram showed anterior ST-segment elevation and aVR changes, which is why the «myocardial infarction code» was activated and the patient transferred to our center. The cardiac ultrasound revealed the presence of a severely depressed left ventricular ejection fraction (visual estimate of 10% to 15%) with changes in segmental contractility located in the anterior, septal, and lateral walls without pericardial effusion. A total of 300 mg of acetylsalicylic acid, 180 mg of ticagrelor, and vasoactive drugs were administered to the patient.

The patient was sent to the cath lab right away. Given the situation of established cardiogenic shock (stage D) and the potential need for percutaneous circulatory support systems (intra-aortic balloon pump, Impella, Abiomed, United States), the femoral access route was selected (bilateral common femoral artery puncture with 6-Fr introducers).

Initial complications were found in the selective catheterization of the left coronary artery via right femoral access and direct guide catheter insertion (due to highly suspected LMCA disease). Due to suspected type A aortic dissection, an aortogram was performed using a pigtail catheter that confirmed this suspicion and LMCA disease due to hematoma/intimal flap with subtotal occlusion (videos 1 and 2 of the supplementary data).

The criterion for remaining in the true lumen was the presence of an aortic pressure curve of normal morphological characteristics (non-damped) using a 0.35 in 260 cm Teflon-coated guidewire for catheter exchange.

Simultaneously, the cardiac surgery unit was contacted and it was decided to proceed with an emergency percutaneous revascularization as a bridging therapy until definitive surgical treatment. A 6-Fr JL4 guide catheter (Mach 1, Boston Scientific, United States) was used to facilitate the subselective catheterization of the LMCA and perform maneuvers to increase active support (deep intubations) if necessary (sacrificing greater passive support but with better maneuverability compared to other catheters). Once the stay inside the true lumen was confirmed, a 0.014 in angioplasty guidewire was advanced towards the distal third of the left anterior descending coronary artery. A hydrophilic, intermediate weight guidewire was used (SION black, Asahi, Japan).

Afterwards, a 3.5 mm x 16 mm drug-eluting stent was implanted with 50% protrusion of the device into the ascending aorta to simulate the «chimney stent» technique used in cases of damaged coronary ostia during transcatheter aortic valve implantations. The stent was deployed at low (nominal) pressure to minimize the risk of dissection of the LMCA uncovered by the stent and, at least initially, free from significant atherosclerotic disease.

This stabilized the patient's hemodynamic status significantly. The echocardiography confirmed the improvement of left ventricular systolic function.

An emergency computed tomography scan of the aorta revealed the presence of a Standford type A aortic dissection without damage to supra-aortic trunks or the rest of the aorta. Surgery was planned based on the patient's hemodynamic instability, high risk of bleeding, and baseline anatomy (dilated aortic root and ascending aorta). The goal was to use a surgical technique that would require the shortest possible time on extracorporeal circulation. Based on the previous considerations, the Bentall-Bono technique was used. Both the aortic root and the ascending aorta were replaced for a no. 25 Carboseal valved conduit (Palex Medical, Spain) followed by coronary ostia re-implantation. Intraoperatively, the roof of the left main coronary artery was ruptured and the stent malapposed to the arterial walls, which led to the removal and further reinforcement of both the roof of the LMCA and left coronary ostium with 6/0 sutures, and a pericardial patch, respectively. The total time on extracorporeal circulation was 12 min.

*** Corresponding author.**
E-mail address: Cristinamorante94@gmail.com (C. Morante Perea).
𝕏 @MorantePerea

Online 29 June 2023.

The patient did fine after the surgery, was successfully extubated, and eventually discharged from the hospital. Prior to being discharge, an echocardiogram confirmed the presence of preserved systolic function (left ventricular ejection fraction of 55%) with mild hypokinesis of the anterior septum and proper positioning and functioning of the valved conduit.

In conclusion, this patient was initially treated of an anterior ST-segment elevation acute coronary syndrome (KK-IV). During coronary angiography, however, he was diagnosed with a type A aortic dissection that led to coronary malperfusion due to the protrusion of the dissection flap into the left main coronary artery. An urgent decision was made for drug-eluting stent implantation into the LMCA, which improved perfusion to the left coronary tree and provided enough hemodynamic stabilization to proceed with cardiac surgery.

In a series by Uchida et al.[1] of 25 patients with type A aortic dissection and signs and symptoms of coronary malperfusion, 11 underwent preoperative coronary angiography while 9 went to surgery right away. In those treated with coronary angiography, if coronary flow was compromised following dissection, a drug-eluting stent was implanted. If ventricular function improved, emergency surgery was performed. Otherwise, veno-arterial extracorporeal membrane oxygenation cannulation was used after surgery. Patients who underwent coronary angiography had a better prognosis.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

C. Morante Perea, T. Cantón Rubio, and J.A. Buendía Miñano were all involved in the patient healthcare process, bibliographic search, and manuscript drafting. L.M. Hernando Romero, J. Moreu Burgos, and L. Rodríguez Padial participated in the rewiew process and final approval of 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/RECIC.M23000392.

REFERENCES

1. Uchida K, Karube N, Minami T, et al. Treatment of coronary malperfusion in type A acute aortic dissection. *Gen Thorac Cardiovas Surg.* 2018;66:621-625.
2. Czerny M, Schoenhoff F, Etz C, et al. The impact of pre-operative malperfusion on outcome in acute type A aortic dissection. Results from the GERAADA registry. *J Am Coll Cardiol.* 2015;65:2628-2635.

https://doi.org/10.24875/RECICE.M23000397

Co-registration assisted 3-vessel orbital atherectomy in de novo calcified multivessel coronary artery disease

Aterectomía orbital a 3 vasos guiada por corregistro en enfermedad coronaria multivaso calcificada

Asad Shabbir, David Chipayo, Adrián Jerónimo, Alejandro Travieso, Nieves Gonzalo, and Javier Escaned*

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

To the Editor,

Treatment of heavily calcified coronary artery disease (CAD) remains a technical challenge since a significant number of patients require some type or form of advanced plaque modification procedure in the cath lab. Therefore, interventional cardiologists should be aware of the complete array of plaque modification techniques available to prepare vessels to facilitate optimal stent deployment and expansion.[1] In the presence of proximal calcified disease in tortuous vessels, orbital atherectomy can be used as an alternative to rotational atherectomy thanks to its greater stability with reverse ablation, improved ease of use, and convenience as a result of a single-size burr that can be used to treat a wide range of vessel profiles. In addition, it appears to have a similar safety profile compared to rotational atherectomy.[2] We herein describe a case of 3-vessel proximal heavily calcified CAD where we demonstrate the feasibility of using orbital atherectomy to prepare all 3 epicardial vessels using a one-size burr guided by co-registered intravascular ultrasound (IVUS) and physiology prior to complete percutaneous revascularization in a single-staged procedure.

This is the case of a 73-year-old man with hypertension, type II diabetes mellitus, severe chronic obstructive pulmonary disease (forced expiratory volume in 1 second [FEV_1] of 29%), and atrial

* **Corresponding author.**
E-mail address: escaned@secardiologia.es (J. Escaned).
@AsadKShabbir @JEscaned

Online 17 July 2023.

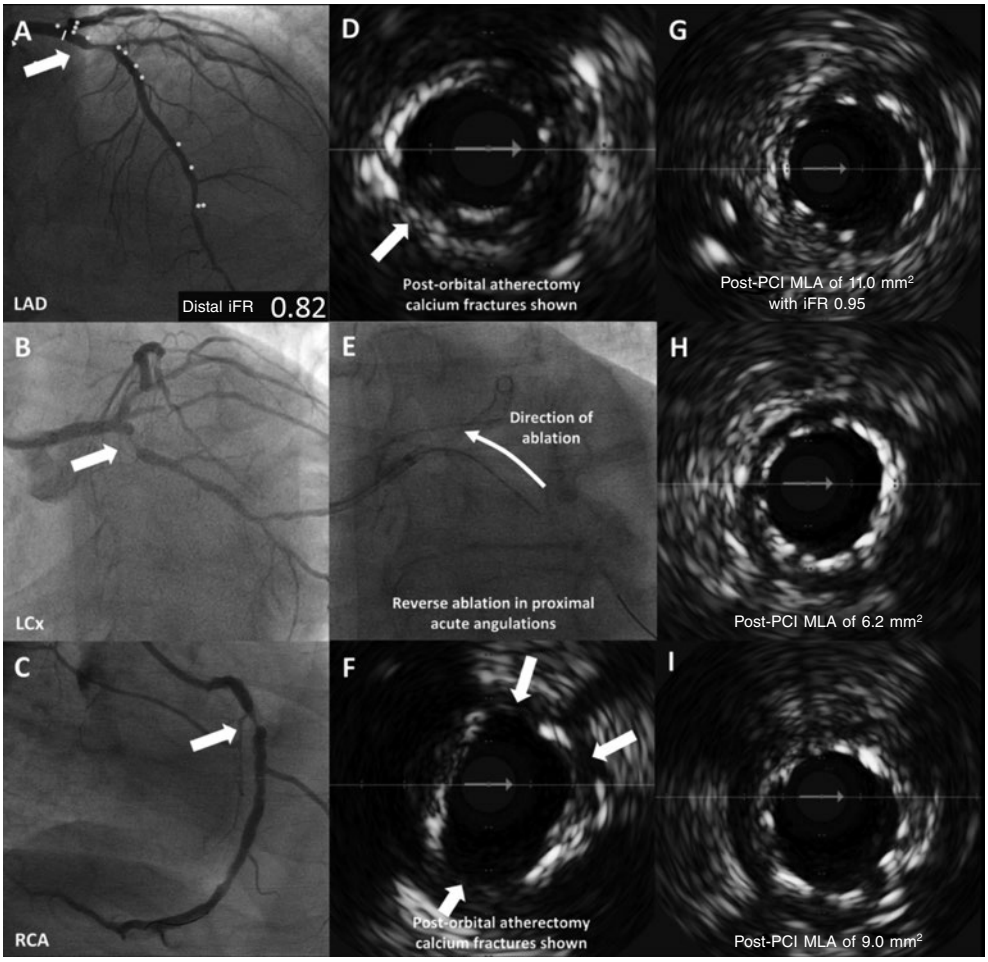


Figure 1. Baseline angiography with IVUS-guided orbital atherectomy showing the mechanisms of calcium modification with stent deployment and strut apposition. **A:** lesion in proximal LAD with iFR of 0.82. **B:** lesion in proximal LCx. **C:** lesion in proximal RCA. **D:** post-orbital IVUS-guided atherectomy with presence of calcium fractures (asterisks). **E:** reverse orbital atherectomy shown. **F:** post-orbital IVUS-guided atherectomy with presence of calcium fractures (asterisks). **G:** stent apposition in LAD with post-PCI MLA of 11.0 mm^2 and iFR of 0.95. **H:** stent apposition in LCx with MLA of 6.2 mm^2. **I:** stent apposition in RCA with MLA of 9.0 mm^2. iFR, instantaneous wave-free ratio; IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LCx, left circumflex artery; MLA, minimum lumen area; PCI, percutaneous coronary intervention; RCA, right coronary artery.

fibrillation that presented with exertional chest tightness. Clinical examination was unremarkable, and the clinical hematology and biochemistry were normal except for an N-terminal pro-B-type natriuretic peptide of 1365 pg/mL (normal reference range, < 125 pg/mL) and troponin I levels of 351 ng/L [normal reference range, 3-58 ng/L]. The electrocardiogram confirmed the presence of atrial fibrillation. The transthoracic echocardiography identified an impaired left ventricular systolic function with an ejection fraction of 43% with inferior hypokinesia. After giving his informed consent, the patient underwent invasive coronary angiography that revealed the presence of heavily calcified proximal 3-vessel CAD with diffuse atheroma (left anterior descending coronary artery [LAD] figure 1A; left circumflex artery [LCx] figure 1B; right coronary artery [RCA] figure 1C; diseased segments are highlighted with arrows). Disease distribution was anatomically complex (SYNTAX score, 30) and considering the patient's clinical status, the SYNTAX score II predicted a 4-year mortality rate associated with percutaneous coronary intervention (PCI) or coronary artery bypass graft of 8.3% and 17.7%, respectively. The patient eventually underwent a PCI as advised by the heart team.

Via right radial artery, the pre-PCI instantaneous wave-free ratio (iFR) of the least angiographically severe lesion in the LAD was positive at 0.82. Longitudinal vessel analysis was performed using IVUS with co-registration to better characterize the extent of the calcified disease in the LAD and the RCA. The LCx stenosis was uncrossable with the IVUS catheter before calcium modification. Therefore, intracoronary imaging prior to the procedure was not performed in this vessel. Given that > 270º of heavy calcification was present in the target vessel landing zones in both the LAD and the RCA, upfront orbital atherectomy was performed in all 3 arteries using a 1.25 mm burr (Diamondback 360, CSI, United States). The use of orbital atherectomy produced significant calcium debulking and fractures (LAD, figure 1D; RCA, figure 1F; calcium fractures are shown with arrows). After additional treatment with non-compliant balloons, sirolimus-eluting stents were deployed both to the LAD and the LCx (3.5 mm × 35 mm and 3.0 mm × 15 mm, respectively; Osiro, Biotronik, Germany) and an everolimus-eluting stent was deployed to the RCA (3.5 mm × 33 mm; XIENCE, Abbott, United States). The post-PCI IVUS of all 3 vessels confirmed complete strut apposition, and good minimum stent areas and lesion coverage. In addition to the post-PCI physiology of the LAD that confirmed good functional outcomes with an iFR of 0.95 (LAD, figure 1G; LCx, figure 1H; RCA, figure 1I) the final angiographic outcomes of the 3 target vessels are shown on figure 2 (LAD, figure 2A; LCx, figure 2B; RCA, figure 2C). A summary of the devices used to perform the procedure is shown on table 1.

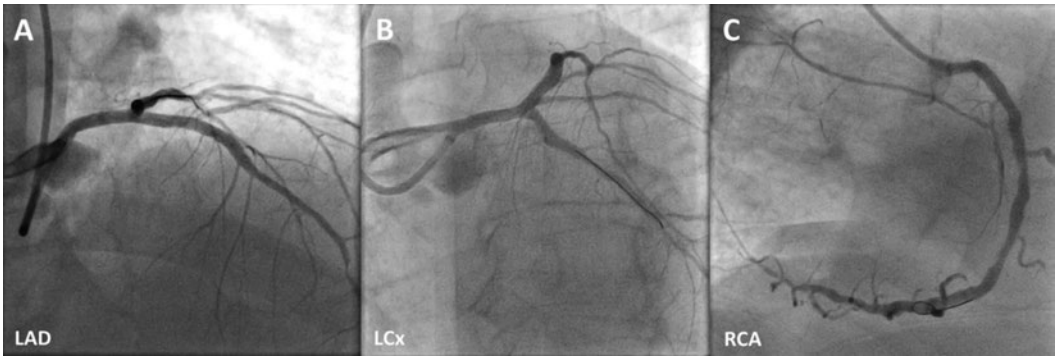


Figure 2. Final angiographic outcomes of LAD (A), LCx (B), and RCA (C) are shown. LAD, left anterior descending coronary artery; LCx left circumflex artery; RCA, right coronary artery.

Table 1. Devices used to perform PCIs

Vessel	Device
LAD	3.5 mm 7-Fr EBU guide catheter
	ViperWire coronary wire (Cardiovascular Systems Inc., United States)
	Sion Blue coronary wire (ASAHI Intecc Inc., Japan)
	OmniWire physiology and coronary guidewire (Philips, the Netherlands)
	FineCross microcatheter (Terumo Corporation, Japan)
	Diamondback 360 coronary orbital atherectomy system with 1.25 mm burr (Cardiovascular Systems Inc., United States of America)
	Eagle Eye IVUS catheter (Philips, the Netherlands)
	2.5 mm x 15 mm Trek balloon (Abbott, United States)
	NC Xperience 3.5 mm x 10 mm balloon (iVascular, Spain)
	3.5 mm x 35 mm Orsiro drug-eluting stent (Biotronik, Germany)
LCx	ViperWire coronary wire (Cardiovascular Systems Inc., United States)
	Sion Blue coronary wire (ASAHI Intecc Inc., Japan)
	Diamondback 360 coronary orbital atherectomy system with 1.25 mm burr (Cardiovascular Systems Inc., United States)
	Eagle Eye IVUS catheter (Philips, the Netherlands)
	2.5 mm x 15mm Trek balloon (Abbott, United States)
	3.0 mm x 15 mm NC Xperience balloon (iVascular, Spain)
	3.0 mm x 15 mm Orsiro drug-eluting stent (Biotronik, Germany)
RCA	ViperWire coronary wire (Cardiovascular Systems Inc., United States)
	Sion Blue coronary wire (ASAHI Intecc Inc., Japan)
	Diamondback 360 coronary orbital atherectomy system with 1.25mm burr (Cardiovascular Systems Inc., United States)
	Eagle Eye IVUS catheter (Philips, the Netherlands)
	3.0 mm x 12 mm Trek balloon (Abbott, United States)
	3.5 mm x 10 mm NC Xperience balloon (iVascular, Spain)
	3.5 mm x 33 mm XIENCE Skypoint drug-eluting stent (Abbott, United States)

EBU, extra-back up; IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LCx, left circumflex artery; NC, non-compliant; PCI, percutaneous coronary intervention; RCA, right coronary artery.

This case is an example of the feasibility of plaque modification with orbital atherectomy to multiple vessels in a patient with calcified CAD through intravascular imaging and physiology guidance, calcified plaque preparation with orbital atherectomy, and post-PCI assessments. These technologies are key to guarantee durable results and, collectively, add prognostic value.[3] Atherectomy in all 3 coronary vessels was justified given the extent of calcification. In addition, the use of orbital atherectomy (rather than rotational atherectomy) was carefully considered due to its unique features, specifically, reverse ablation (figure 1E) and variable debulking diameter thereby allowing the management of vessels of different diameters with the use of a one-size burr.[4,5] In selected cases, these features of orbital atherectomy can be particularly useful in ostial and/or angulated vessels particularly in the LCx as in this case where tortuosity may prevent adequate plaque modification of heavily calcified lesions, be subject to burr bias or limited by solely antegrade ablation, thus impacting guide catheter support and the overall procedural success.

Herein we highlighted the feasibility of performing co-registration assisted 3-vessel orbital atherectomy in heavily calcified proximal lesions, and demonstrated the performance of this technique in the management of complex disease with effective calcium ablation and fracture.

Informed and written consent from the patient were deemed necessary for publication purposes.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

A. Shabbir, and D. Chipayo both drafted the manuscript and prepared the images. A. Jerónimo conducted a critical review of the manuscript intellectual content and contributed substantially to it. A. Travieso also conducted a critical review of the manuscript intellectual content and contributed substantially to it. N. Gonzalo, and J. Escaned conceptualized the manuscript and conducted its critical review. All co-authors gave their final approval to the version that would eventually be published, and all take full responsibility for all aspects of the manuscript.

CONFLICTS OF INTEREST

A. Shabbir declared having received speaker fees and honoraria from Philips. A. Travieso declared having received an unrestricted research training grant from Philips. J. Escaned is supported by the

Intensification of Research Activity project INT22/00088 from Spanish Instituto de Salud Carlos III. He also declares serving as speaker and advisory board of Philips. A. Jerónimo, D. Chipayo, and N. Gonzalo declared no conflicts of interest whatsoever.

REFERENCES

1. Riley RF, Henry TD, Mahmud E, et al. SCAI position statement on optimal percutaneous coronary interventional therapy for complex coronary artery disease. *Catheter Cardiovasc Interv.* 2020;96:346-362.
2. Khan AA, Murtaza G, Khalid MF, et al. Outcomes of rotational atherectomy versus orbital atherectomy for the treatment of heavily calcified coronary stenosis: A systematic review and meta-analysis. *Catheter Cardiovasc Interv.* 2021;98:884-892.
3. Escaned J, Collet C, Ryan N, et al. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. *Eur Heart J.* 2017; 38:3124-3134.
4. Chambers JW, Feldman RL, Himmelstein SI, et al. Pivotal trial to evaluate the safety and efficacy of the orbital atherectomy system in treating de novo, severely calcified coronary lesions (ORBIT II). *JACC Cardiovasc Interv.* 2014;7:510-518.
5. Lee M, Genereux P, Shlofmitz R, et al. Orbital atherectomy for treating de novo, severely calcified coronary lesions: 3-year results of the pivotal ORBIT II trial. *Cardiovasc Revasc Med.* 2017;18:261-264.

REC Interv Cardiol. 2023;5(4):311-322
https://doi.org/10.24875/RECICE.M22000317

Clinical case

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation

Impella-Clip: una estrategia segura y eficaz en el shock *secundario a insuficiencia mitral aguda*

Clara Ugueto-Rodrigo,* Alfonso Jurado-Román, Lucía Fernández-Gassó, Guillermo Galeote-García, and Raúl Moreno

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

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000318
https://doi.org/10.24875/RECICE.M22000319

CASE PRESENTATION

This is the case of a 61-year-old man with cardiovascular risk factors who presents with a 3-day history of intermittent oppressive pain in the middle of his chest. The electrocardiogram confirmed the presence of an inferior-posterior wall ST-segment elevation. The emergency coronary angiography revealed the acute occlusion of a dominant left circumflex artery (videos 1 and 2 of the supplementary data) that was revascularized with 2 drug-eluting stents in the proximal left circumflex artery (bifurcation with the first obtuse marginal artery) using the TAP technique (T and small protrusion) (figure 1 and video 3 of the supplementary data). No other significant epicardial lesions were found. During the procedure the patient became desaturated, developed progressive hypotension, and eventually required invasive mechanical ventilation and intra-aortic balloon pump implantation. The echocardiogram confirmed the presence of significant mitral regurgitation (MR) with a slightly depressed left ventricular ejection fraction (LVEF) and inferior-lateral and apical akinesis with

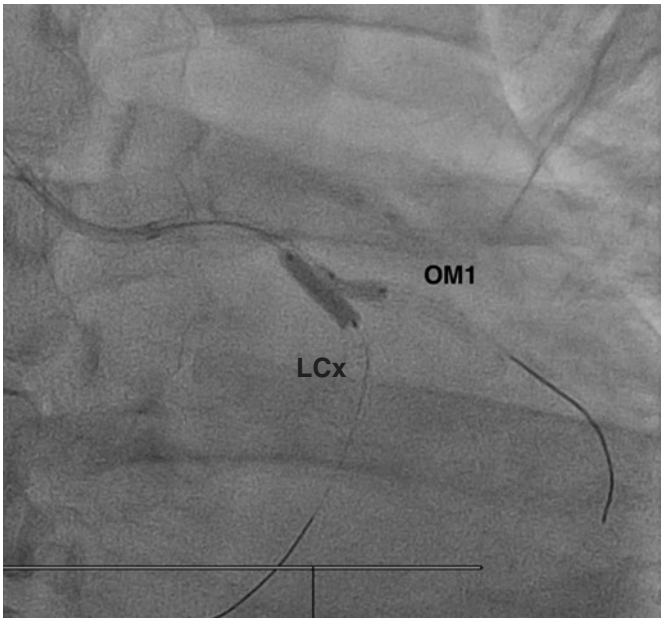


Figure 1. Revascularization using the TAP technique (T and small protrusion). LCx, left circumflex artery; OM1, first obtuse marginal artery.

* **Corresponding author.**
E-mail address: claraugueto@gmail.com (C. Ugueto-Rodrigo).
𝕏 @Hemodin_LaPaz

Online 19 October 2022.

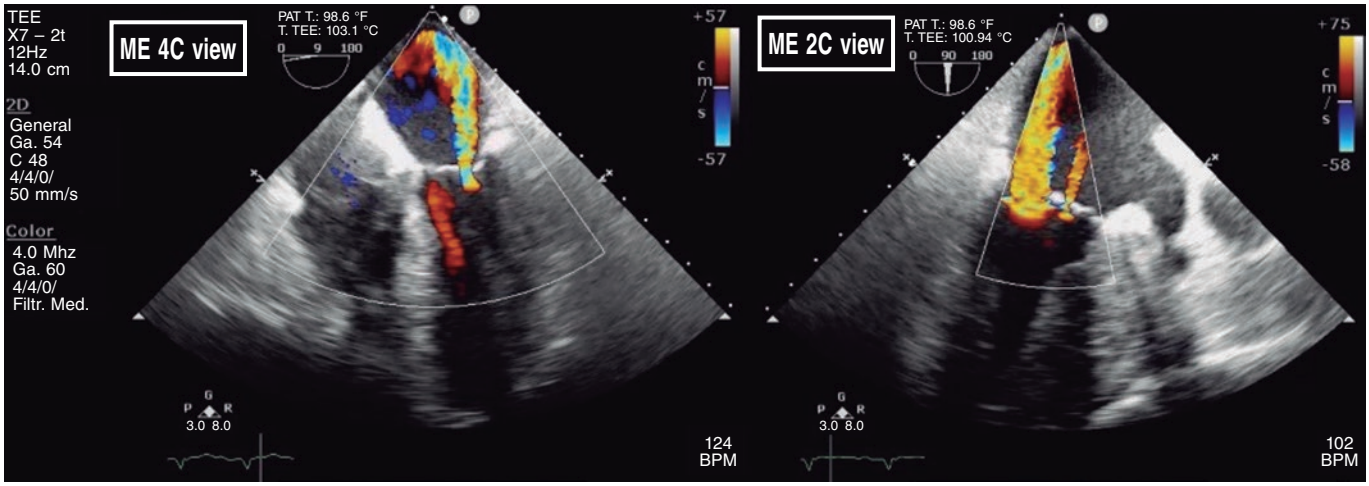


Figure 2. Transesophageal echocardiography showing severe central mitral regurgitation in A3-P3 with another jet in A2-P2.

Figure 3. Only access via right femoral artery.

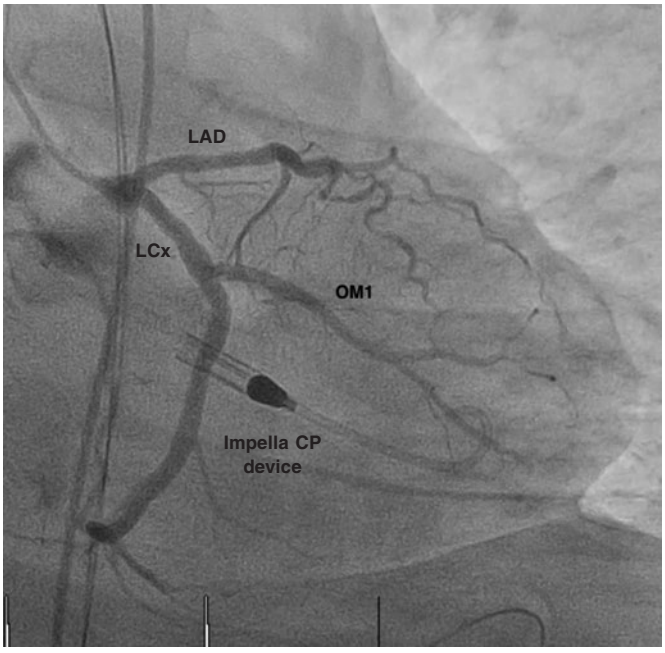


Figure 4. Impella CP device with previous patent stents. LAD, left anterior descending coronary artery; LCx, left circumflex artery; OM1, first obtuse marginal artery.

preserved right ventricular function. The transesophageal echocardiography confirmed the diagnosis of acute mitral regurgitation of ischemic etiology with a predominant jet at medial level, and no organ damage to the valve or the subvalvular apparatus (figure 2 and video 4 of the supplementary data). Within the next few hours, the patient developed refractory hypotension to vasoactive drugs and multi-organ failure. In the successive electrocardiograms performed the inferior wall ST-segment elevation was maintained. After studying disease progression, the intra-aortic balloon pump was exchanged for an Impella CP device (Abiomed; United States) via right femoral artery. A different coronary angiography was performed through the Impella introducer-sheath (figure 3) that discarded the presence of stent thrombosis (figure 4). Within the next few days, mechanical support was maintained with the Impella CP device at a rate of 2.5 L/min, and negative fluid balances were forced through continuous veno-venous hemodiafiltration that allowed extubation 72 hours later. Severe mitral regurgitation with a slightly improved LVEF still persisted on the control echocardiography, which stopped the removal of the Impella CP device. Also, the patient developed hemolysis with significant anemia (Hemoglobin levels of 7.8 g/dL) and thrombocytopenia, and required transfusion support. No significant bleeding event was reported. Since it was necessary to remove the device and LVEF had recently improved with a perspective of recovery of acute valvular heart disease, the implantation of an Impella 5.0 device was decided via right subclavian access. Ten days after days the acute event, do you think of a way to move on with treatment?

The case was published after obtaining the patient's verbal consent.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors contributed drafting or reviewing the case.

CONFLICTS OF INTEREST

R. Moreno is associate editor of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure the impartial handling of the manuscript has been followed. A. Jurado-Román is a member of the editorial team. The remaining authors declared no conflicts of interest whatsoever.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000317.

https://doi.org/10.24875/RECICE.M22000318

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation. How would I approach it?

Impella-Clip: una estrategia segura y eficaz en el shock *secundario a insuficiencia mitral aguda. ¿Cómo lo haría?*

Isaac Pascual[a,b,c,*]

[a] *Cardiología Intervencionista, Área del Corazón, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain*
[b] *Departamento de Medicina, Universidad de Oviedo, Oviedo, Asturias, Spain*
[c] *Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Asturias, Spain*

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000317
https://doi.org/10.24875/RECICE.M22000319

HOW WOULD I APPROACH IT?

In their case presentation, authors described an interesting case of acute severe mitral regurgitation of functional etiology due to inferior wall myocardial infarction progressing into cardiogenic shock.

Acute and subacute mitral regurgitation due to myocardial infarction is a clinical condition of grim prognosis that is relatively common in our routine clinical practice.[1]

These patients' sign of presentation can be rapidly progressive heart failure hours or days after the ischemic event with poor response to medical therapy. No wonder then that, on many occasions,[2,3] in the evolved infarction without reperfusion or delayed reperfusion setting, severe rapidly progressive courses towards cardiogenic shock can occur.

* **Corresponding author.**
E-mail address: ipascua@live.com (I. Pascual).

Online 19 October 2022.

The fundamental anatomical mechanism through which mitral regurgitation occurs can be posterior leaflet restriction often in its more medial or medial-central scallops (P3 or P2-P3) due to specific regional dysfunction of myocardial contractility due to infarction.[1]

As in the case presented here, these are often inferior or inferior-posterior wall myocardial infarctions due to the occlusions of very-well developed left circumflex arteries or very dominant right coronary arteries. These are high-surgical risk patients following their poor clinical and hemodynamic situation. Although, traditionally, the only possible procedure for these patients was mitral valve repair or replacement surgery, surgical results are associated with a high in-hospital mortality rate due to both these patients' unstable clinical situation and procedural complications.[1]

In this sense, transcatheter mitral valve repair with edge-to-edge approximation has proven as a safe and effective option even in the presence of cardiogenic shock.[1-3]

In this clinical setting, the first thing that should be taken into consideration is the patient's hemodynamic support with the device each center is most experienced at. Afterwards, transcatheter mitral valve repair can be considered to treat valvular heart disease as a first-line therapy in cases of favorable anatomy as it is a fast and effective solution with a low rate of complications and lower mortality rates reported compared to surgical and, obviously, conservative treatment.[1]

In a case like the one presented by the authors, the first I would do is to guarantee the patient's hemodynamic support. In this sense, devices like the Impella CP (Abiomed, United States) or a combination of extracorporeal membrane oxygenation and intra-aortic balloon pump could be good alternatives.

The next step would be to perform transcatheter mitral valve repair with the MitraClip device (Abbott vascular, United States). I would use the right femoral venous access with ultrasound-guided puncture and perform a transesophageal echocardiography-guided transseptal puncture (posterior and superior). The technical characteristics of the procedure in an acute setting are no different compared to those of a scheduled case. Due to the medial-central origin, width of the device, and length of the leaflet, in that area my strategy would be to use a MitraClip NTW device (small and wide) for the most commissural region (A3-P3) probably followed by a second similar MitraClip device (NTW) attached to the former towards the valve medial-central region.

In cases where the posterior leaflet has a larger size and there is a possibility of associated anterior leaflet pseudoprolapse, the use of a larger clip (XT or XTW) or a capture maneuver regardless of the leaflets would be necessary to facilitate device implantation and improve valve coaptation.

We should be extra cautious with patients like the one presented here due to the possibility of an unusual interference between the MitraClip release catheter and the Impella catheter when crossing the mitral valve to capture the leaflets.

It is of paramount importance to reduce hemodynamic support momentarily (in this case the blood flow supplied by the Impella device) to assess the transmitral gradient, the degree of residual mitral regurgitation after the first clip, and the final outcomes.

The case presented here is that of a particularly significant clinical condition due to its severity, emergency, and high-surgical risk.

Transcatheter mitral valve repair with edge-to-edge approximation can be considered a first-line therapy not only because it is not too aggressive, and also because it is safe, fast, and effective in patients with severe, acute, functional mitral regurgitation with heart failure due to myocardial infarction causing mitral posterior leaflet restriction.[1]

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

I. Pascual is a proctor of MitraClip for Abbott Vascular.

REFERENCES

1. Haberman D, Estévez-Loureiro R, Benito-Gonzalez T, et al. Conservative, surgical, and percutaneous treatment for mitral regurgitation shortly after acute myocardial infarction. *Eur Heart J.* 2022;43:641-650.
2. Jung RG, Simard T, Kovach C, et al. Transcatheter Mitral Valve Repair in Cardiogenic Shock and Mitral Regurgitation: A Patient-Level, Multicenter Analysis. *JACC Cardiovasc Interv.* 2021;11:1-11.
3. Tang GHL, Estevez-Loureiro R, Yu Y, et al. Survival Following Edge-to-Edge Transcatheter Mitral Valve Repair in Patients With Cardiogenic Shock: A Nationwide Analysis. *J Am Heart Assoc.* 2021;20:e019882.

https://doi.org/10.24875/RECICE.M22000319

Impella-Clip: a secure and effective strategy in cardiogenic shock due to acute severe mitral regurgitation. Case resolution

Impella-Clip: una estrategia segura y eficaz en el shock *secundario a insuficiencia mitral aguda. Resolución*

Clara Ugueto-Rodrigo,* Alfonso Jurado-Román, Lucía Fernández-Gassó, Guillermo Galeote-García, and Raúl Moreno

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

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000317
https://doi.org/10.24875/RECICE.M22000318

CASE RESOLUTION

Given the impossibility to remove the Impella 5.0 device (figure 1) and due to the high surgical risk involved (EuroSCORE II, 48,9%; Society of Thoracic Surgeons score (STS), 16%), percutaneous mitral valve repair was attempted with a MitraClip device (Abbott Laboratories, United States).

With support from an Impella 5.0 device at a rate of 2 L/min and under transesophageal echocardiography guidance the MitraClip NTW device was implanted at A3-P3 level (greater effective regurgitant orifice area), which resulted in a reduced regurgitant jet (videos 1 and 2 of the supplementary data), improved blood flow into the pulmonary veins, and a transmitral gradient of 4 mmHg. Result was reassessed by reducing hemodynamic support temporarily at 1 L/min. A grade III-IV central regurgitant jet was seen. A second MitraClip NT was implanted at A2-P2 level (videos 3 and 4 of the supplementary data). Difficulties during its positioning due to interference with the Impella 5.0 device were reported, which is why reversal maneuvers towards the atrium were performed. Finally, capture or grasping turned out effective, and the lack of residual mitral regurgitation was confirmed. However, although transmitral gradient increased up to 7 mmHg,

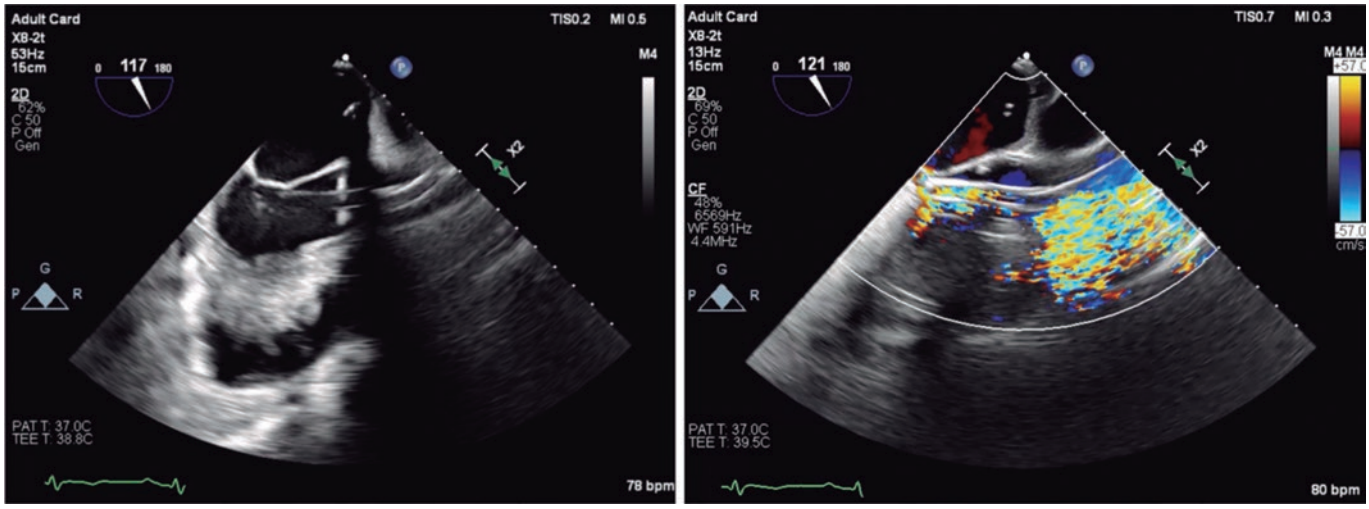


Figure 1. Normal position of the Impella device as seen on the transesophageal echocardiography.

* **Corresponding author.**
E-mail address: claraugueto@gmail.com (C. Ugueto-Rodrigo).
@Hemodin_LaPaz

Online 19 October 2022.

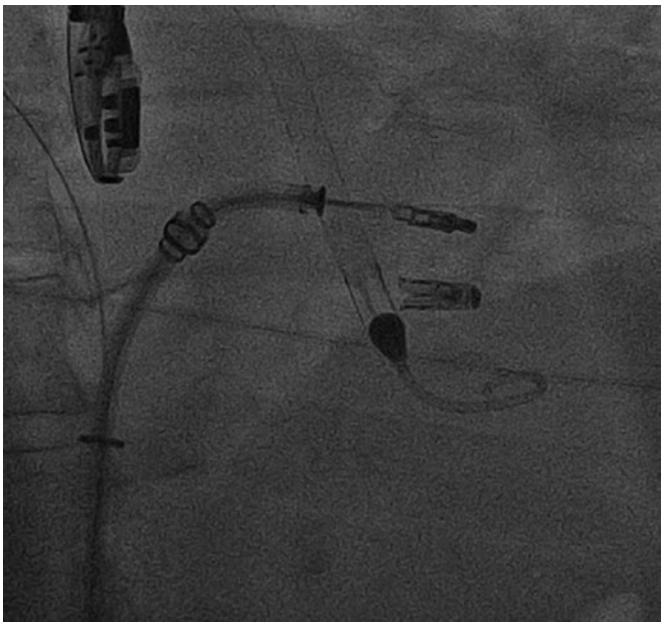


Figure 2. Final procedural outcomes.

after reducing hemodynamic support down to 0.5 L/min, the gradient dropped down to 5 mmHg. Since the presence of hemoglobin levels of 8.6 g/dL and heart rate of 90 bpm could make the gradient could go up slightly—overestimating the measurements—the second device was released with such gradient (figure 2). The patient was extubated and the Impella 5.0 device was removed 72 hours later with satisfactory disease progression.

Acute mitral regurgitation is one mechanical complication of infarction that leads to higher mortality rates (35% to 50%)[1] because it is associated with cardiogenic shock (CS) with increased retrograde pressure and volume. Circulatory support and vasoactive drugs necessary here. The Impella device actively unloads the left ventricle, increases cardiac output,[1] and is indicated in the acute phase.[2]

Traditional treatment has consisted of emergency heart valve replacement that is associated with significant perioperative mortality. Over the last few years, percutaneous mitral valve repair has proven beneficial in asymptomatic secondary mitral regurgitation despite optimal medical therapy.[2] However, data are scarce on acute mitral regurgitation with secondary cardiogenic shock,[1,3] which could be particularly beneficial in this setting.

This case describes how a combined strategy of Impella and MitraClip is both safe and effective. However, several technical considerations should be made at this point: *a)* the MitraClip device should be positioned carefully due to interference with the Impella device; *b)* hemodynamic support should be reduced to assess results since this support can overestimate the reduction of mitral regurgitation; and *c)* anemia and tachycardia are not rare, factors that could overestimate the residual gradient.

Long-term follow-up and more evidence are necessary to support this strategy. However, in the ischemic severe acute mitral regurgitation setting complicated with cardiogenic shock, complete percutaneous resolution (coronary revascularization, Impella and percutaneous mitral valve repair) could be the treatment of choice.

The case was published after obtaining the patient's verbal consent.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

All the authors contributed drafting or reviewing the case.

CONFLICTS OF INTEREST

R. Moreno is associate editor of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure the impartial handling of the manuscript has been followed. A. Jurado-Román is a member of the editorial team. The remaining authors declared no conflicts of interest whatsoever.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M22000317.

REFERENCES

1. Vandenbriele C, Balthazar T, Wilson J, et al. Left Impella-device as bridge from cardiogenic shock with acute, severe mitral regurgitation to MitraClip-procedure: a new option for critically ill patients. *Eur Heart J Acute Cardiovasc Care.* 2021;10:415-421.
2. McDonagh T, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42:3599-3726.
3. Estévez-Loureiro R, Shuvy M, Taramasso M, et al. Use of MitraClip for mitral valve repair in patients with acute mitral regurgitation following acute myocardial infarction: Effect of cardiogenic shock on outcomes (IREMMI Registry). *Catheter Cardiovasc Interv.* 2021;97:1259-1267.

https://doi.org/10.24875/RECICE.M22000324

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula

Hemoptisis masiva. Embolización selectiva de fístula de arteria bronquial a arteria pulmonar izquierda

Federico Liberman,[a,*] Nicolás Zaderenko,[a] Guillermo Pacheco,[a] Juan Pablo Casas,[b] and José Lugones[c]

[a] *Servicio de Cardiología, Unidad Cardiovascular, Sanatorio Allende, Córdoba, Argentina*
[b] *Servicio de Neumonología, Sanatorio Allende, Córdoba, Argentina*
[c] *Servicio de Diagnóstico por Imágenes, Sanatorio Allende, Córdoba, Argentina*

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000325
https://doi.org/10.24875/RECICE.M22000326

CASE PRESENTATION

Hemoptysis is the subglottal expectoration of blood from the tracheobronchial tree. Most cases of massive hemoptysis originate at the bronchial arteries (90%) and often become complicated due to systemic arterial blood pressure. The mechanism of action is the rupture of hypervascularized reticulum and vascular dilatation as a response to the substances released in the inflammatory process. This clinical entity has elevated morbidity and mortality rates. Early diagnosis and the timely administration of therapy are of paramount importance.

This is the case of a 73-year-old woman with a past medical history of breast cancer with ED presentation of early onset massive hemoptysis. She was admitted to the intensive care unit with a heart rate of 122 bpm, arterial blood pressure of 78/45 mmHg, and oxygen saturation of 82% with high-flow oxygen mask. Emergency orotracheal intubation and mechanical ventilation were decided. Given the patient's hemodynamic instability, vasopressor drug infusion was started at increasing doses until a mean arterial blood pressure of 60 mmHg was reached with noradrenalin at 0.3 µg/kg/min. Lab test results showed hemoglobin levels of 7.5 g/dL, hematocrit of 21%, PaO_2 of 62%, and hyperlactacidemia. A total of 2 bags of packed red blood cells were transfused, and the patient was transferred to the computed tomography scan room. The CT scan revealed the presence of a fistula from the left bronchial artery towards the upper branch of the left pulmonary artery with images consistent with alveolar hemorrhage compromising all lobes from both pulmonary fields (figure 1).

It also revealed the occupation of the left main bronchus and the lower and upper lobe branches with dense material suggestive of blood clots due to its high spontaneous density (figure 2). Given this clinical presentation and the features revealed by the CT scan, right bronchial selective intubation was decided. Afterwards, the patient was immediately transferred to the cath lab for endovascular embolization.

The patient gave her informed consent for publication purposes.

*** Corresponding author.**
E-mail address: libermanfederico@gmail.com (F. Liberman).
𝕏 @Fedeliberman; @NZaderenko

Online 10 March 2023.

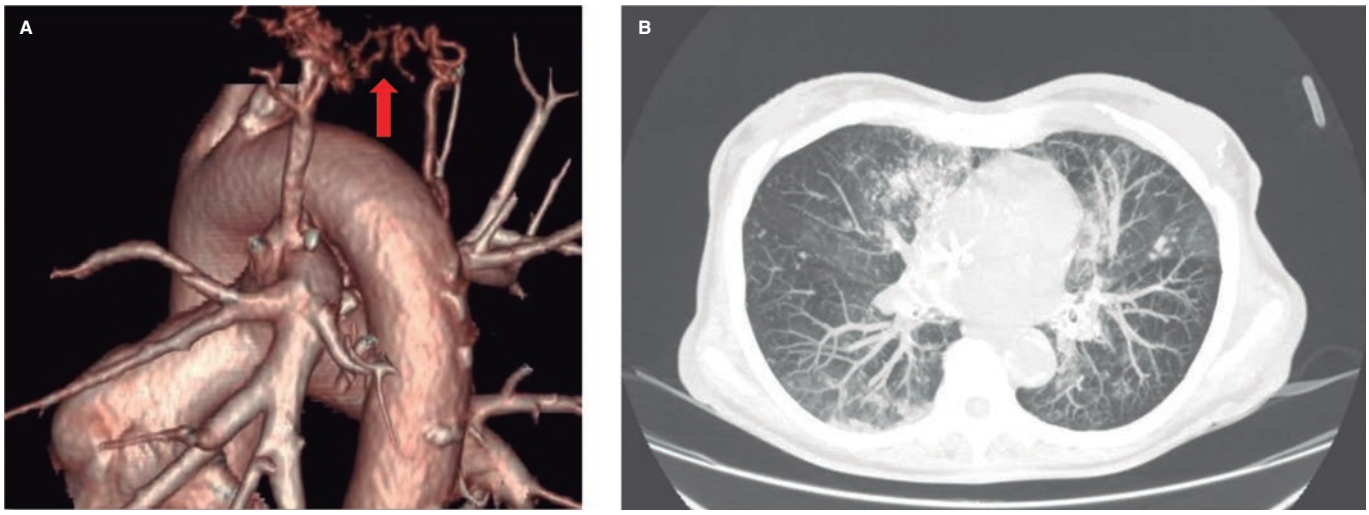


Figure 1. Computed tomography scan at admission. **A:** 3D reconstruction showing the arterio-arterial fistula from the pulmonary artery branch towards the bronchial artery. **B:** axial view showing an image consistent with bilateral alveolar bleeding.

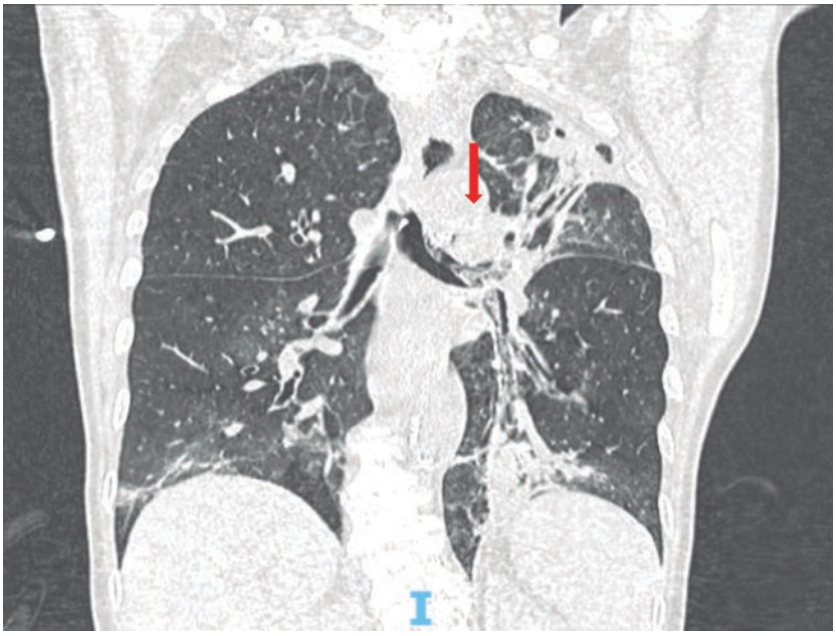


Figure 2. Computed tomography scan at admission. Coronal view showing the left main bronchus occupied by the blood clots.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

F. Liberman drafted and reviewed the manuscript. N. Zaderenko, J.P. Casas, and G. Pacheco treated the patient themselves, drafted and supervised the manuscript. J. Lugones also supervised the manuscript and provided the images.

CONFLICTS OF INTEREST

None reported.

https://doi.org/10.24875/RECICE.M22000325

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula. How would I approach it?

Hemoptisis masiva. Embolización selectiva de fístula de arteria bronquial a arteria pulmonar izquierda. ¿Cómo lo haría?

Javier Portales Fernández*

Cardiología Intervencionista, Hospital de Cáceres, Cáceres, Spain

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000324
https://doi.org/10.24875/RECICE.M22000326

HOW WOULD I APPROACH IT?

This is the case of a massive hemoptysis requiring orotracheal intubation where the origin of the hemorrhage can be clearly identified in a fistula from the left bronchial artery—with fistulous trajectory—to the left pulmonary artery upper branch.

In view of the situation, and once the patient has been stabilized with right selective intubation, discussion starts on how to save the lung from blood content.

Currently, interventional radiology in Spain is available in almost every PCI-capable center meaning that our participation as interventional cardiologists is not required anymore. However, thanks to the «infarction code» network, the geographic availability of cath labs is even greater compared to vascular interventional radiology suites, as it happened to us in our beginnings.

In this case, the source of bleeding has already been found, which means we can attempt the catheterization of the bronchial artery right away. Access via pulmonary artery is indicated for cases when the bronchial artery cannot be catheterized. In these cases, it'd be closed with coils as selectively as possible to prevent massive pulmonary infarction from happening.[1]

Cardiologists have a great variety of devices available to catheterize arteries originate at the aorta like the coronary or bronchial arteries. «Visceral» catheters like the COBRA one work great to catheterize this kind of ostia while highly «torqueable» and harmless hydrophilic catheters are used to study coronary ostia (figure 1).

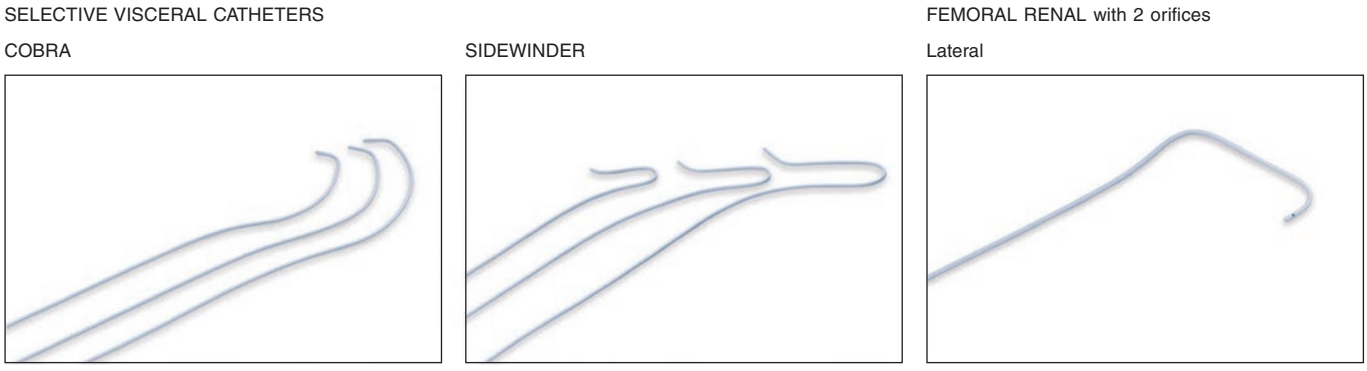


Figure 1. Visceral catheters used to study the branches of both the ascending and the descending aorta.

* **Corresponding author.**
E-mail address: portales70@hotmail.com (J. Portales Fernández).

Online 10 March 2023.

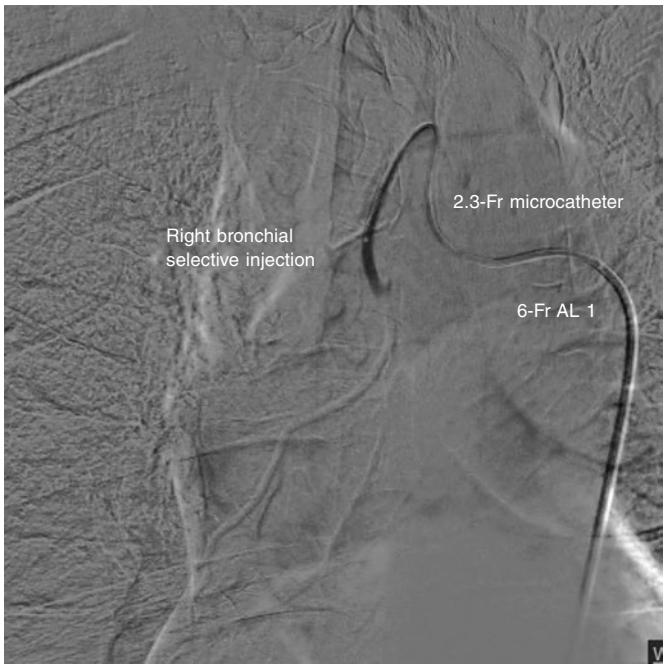


Figure 2. Selective injection into right bronchial artery. After catheterization with the Amplatz 1 guide catheter, a microcatheter is mounted over a 0.14 in guidewire.

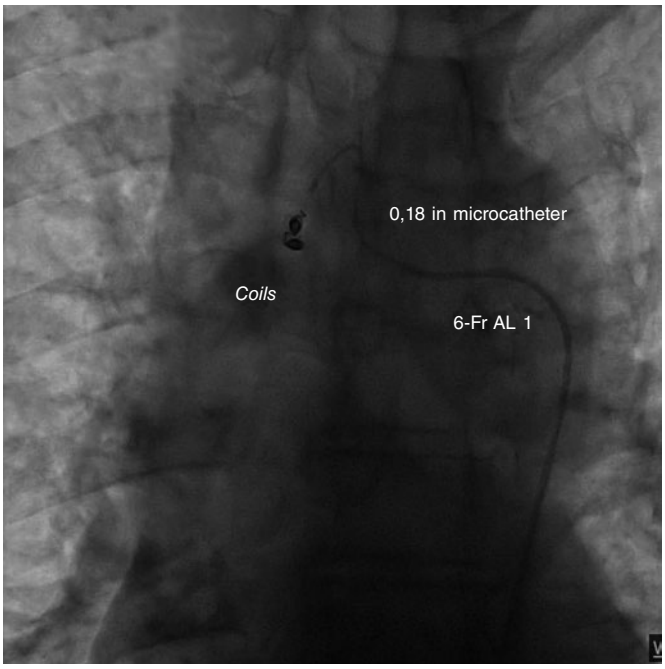


Figure 3. Embolization of the right bronchial artery with 0.18 in coils.

Since these catheters are often unavailable at the cath lab, the Amplatz guide catheter with apex curve can be used as if we were looking to perform a bypass, and even an EBU guide catheter to modify the curve with another guidewire through the straight end. Once the artery has been catheterized, although not selectively, passing a 0.14 in guidewire can be relatively easy to do to bring stability to the whole surgical kit. Using the radial or femoral access is something that's completely irrelevant. However, since location is in the thoracic aorta, the femoral access could be one we're most comfortable with in intubated patients (figure 2).

A 2.4-Fr microcatheter can be mounted over this guidewire for 0.18 in coils or even a 4-Fr catheter to inject embolization material by thoroughly selecting the target area as much as possible.

I would rather use 0.18 in coils as the method of choice to release them before ever reaching the fistulous trajectory. Afterwards, I'd check whether it has been properly sealed and no collaterals have been recruited prior to the fistulous trajectory (figure 3).

In no coils are available, I'd probably use embolization material like Spongostan gelatin sponge to create gel particles that can stop the bleeding when they can't get through. It is mixed from 2 syringes containing serum, contrast, and small «confetti» layers of Spongostan that are linked through a 3-way stopcock.[2] The content from one syringe is passed on to the next until it has the consistency of small pieces of gel. I would gently inject it through the microcatheter, and if the contrast agent still couldn't make it through the fistulous trajectory, I'd keep on injecting at low pressure. This can stop the bleeding and help achieve the effect obtained with the coils when we've ran out of them, and passage is still not under control. I would never use particles because they migrate through the fistulous trajectory and cause massive pulmonary infarction.

Finally, if the bleeding cannot be stopped, I would leave a balloon inflated to gain time to evacuate the patient to thoracic surgery or the interventional radiology suite.

The takeaway message is that we need to be prepared one way or another[3] to solve emergency complications that can be solved using interventional radiology techniques in places where an angiographer—for the lack of an experienced radiologist—is available.

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

J. Portales Fernández received fees for his collaboration for Medtronic, and Boston Scientific.

ACKNOWLEDGEMENTS

We wish to thank Dr. Sergio Moyano Calvente, interventional radiologist at Hospital Universitario de Cáceres, Cáceres, Spain for years of collaboration and mutual work.

REFERENCES

1. Tamashiro A, Miceli MH, Rando C, et al. Pulmonary artery access embolization in patients with massive hemoptysis in whom bronchial and/or nonbronchial systemic artery embolization is contraindicated. *Cardiovasc Intervent Radiol.* 2008;31:633e7.
2. Abadal JM. Spongostan preparation for Endovascular Embolization. Available at: https://youtu.be/zhq0hYQ8iGs. Accessed 30 Nov 2022.
3. Sopko DR, Smith TP. Bronchial Artery Embolization for Hemoptysis. *Semin Intervent Radiol.* 2011;28:48-62.

https://doi.org/10.24875/RECICE.M22000326

Massive hemoptysis. Selective embolization of bronchial artery-left pulmonary artery fistula. Case resolution

Hemoptisis masiva. Embolización selectiva de fístula de arteria bronquial a arteria pulmonar izquierda. Resolución

Federico Liberman,[a,*] Nicolás Zaderenko,[a] Guillermo Pacheco,[a] Juan Pablo Casas,[b] and José Lugones[c]

[a] *Servicio de Cardiología, Unidad Cardiovascular, Sanatorio Allende, Córdoba, Argentina*
[b] *Servicio de Neumonología, Sanatorio Allende, Córdoba, Argentina*
[c] *Servicio de Diagnóstico por Imágenes, Sanatorio Allende, Córdoba, Argentina*

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000324
https://doi.org/10.24875/RECICE.M22000325

CASE RESOLUTION

Emergency transfer of the patient to the cath lab was decided for pulmonary angiography and endovascular embolization. A 5-Fr femoral introducer sheath was used to insert a vertebral catheter with which a largely developed bronchial branch was selectively catheterized (emergency from the aortic arch) towards the pulmonary parenchyma creating a high-flow arterio-arterial fistula with a segmental arterial branch of the lung left upper lobe (video 1 of the supplementary data). Afterwards, a 2.4-Fr (proximal diameter)/1.9-Fr (distal diameter) Echelon 14 microcatheter was passed (Medtronic, United States) through which 2 6 mm × 20 mm Axium Prime 3D detachable coils (Medtronic, United States) were implanted from the distal to the middle third of the bronchial tree (figure 1). The target vessel was successfully embolized resulting in an overt decrease of the cardiac output at fistula level (video 2 of the supplementary data). Procedure was performed uneventfully. After it was completed the amount of vasopressor drugs (noradrenaline and vasopressin) administered was gradually reduced. Forty-eight hours later, the patient was extubated and weaned from mechanical ventilation. Seventy-two hours after the procedure, a follow-up coronary computed tomography angiography confirmed consolidation in the apical and posterior segments of left lower lobe and left perihilar region without evidence of contrast extravasation at the embolization site. Since the patients showed no signs of hemoptysis she was discharged from the hospital 6 days after admission.

Pulmonary circulation depends on pulmonary and bronchial arteries alike. While the pulmonary artery and its branches make up a low-pressure system that supplies the pulmonary parenchyma mainly, the circulation tha comes from the bronchial arteries has a relatively high pressure and supplies the endobronchial tree basically. It is responsible for only 2% of the lung overall vascular supply. In 90% of the cases of potentially life-threatening hemoptysis the origin of bleeding is the bronchial followed by the pulmonary arteries or an unidentified source of bleeding in the remaining 10% of the cases.[1] Regarding the main etiologies involved, the case series published to this date include bronchiectasis, tuberculosis, and pulmonary malignant neoplasms. Although its exact incidence rate is still unknown, systemic-pulmonary fistula is rare and has often been misrepresented as the cause of hemoptysis. In cases of massive hemoptysis, treatment

* **Corresponding author.**
E-mail address: libermanfederico@gmail.com (F. Liberman).
𝕏 @Fedeliberman; @NZaderenko

Online 10 March 2023.

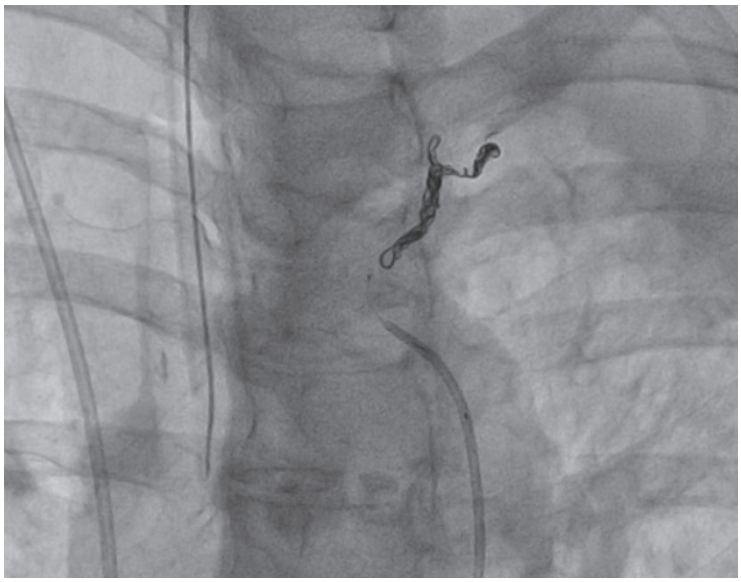


Figure 1. Angiography. Axium Prime 3D detachable coils (6 mm × 20 mm) implanted from the distal to the middle third of the bronchial tree.

depends on the underlying cause. Early treatment involves stabilizing the patient and, when available in the emergency setting, bronchoscopy can be useful. In suspicious or confirmed cases on the computed tomography scan of systemic-pulmonary fistula, arteriography and endovascular embolization are elective while surgery should be spared for selected cases.[2] In the metanalysis conducted by Zheng et al.[2] the embolization of the bronchial artery due to massive hemoptysis (21 studies, 2511 cases) had rates of minor and major complications of 10% and 2%, respectively. Compared to the surgical treatment of hemoptysis, the endovascular procedure had a lower rate of adverse events.[3] On the other hand, in these cases, conservative treatment is associated with mortality rates > 50%

The case presented here shows the severity and hemodynamic compromise due to massive hemoptysis following an extremely rare cause with effective endovascular resolution.

The patient gave her informed consent for publication purposes.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

F. Liberman drafted and reviewed the manuscript. N. Zaderenko, J.P. Casas, and G. Pacheco treated the patient themselves, drafted and supervised the manuscript. J. Lugones also supervised the manuscript and provided the images.

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.M22000326.

REFERENCES

1. Charya AV, Holden VK, Pickering EM. Management of life-threatening hemoptysis in the ICU. *J Thorac Dis.* 2021;13:5139-5158.
2. Zheng Z, Zhuang Z, Yang M, et al. Bronchial artery embolization for hemoptysis: A systematic review and meta-analysis. *J Interv Med.* 2021;4:172-180.
3. Ittrich H, Bockhorn M, Klose H, Simon M. The Diagnosis and Treatment of Hemoptysis. *Dtsch Arztebl Int.* 2017;114:371-381.

REC Interv Cardiol. 2023;5(4):323-324
https://doi.org/10.24875/RECICE.M23000378

New TAVI technique for difficult valve crossing

Nueva técnica para cruce valvular complicado en TAVI

José M. de la Torre-Hernández,* Gabriela Veiga Fernández, Sergio Barrera, Fermín Sainz Laso, Dae-Hyun Lee, and Tamara García Camarero

Servicio de Cardiología, Hospital Universitario Marqués de Valdecilla, Instituto de Investigación Sanitaria IDIVAL, Santander, Spain

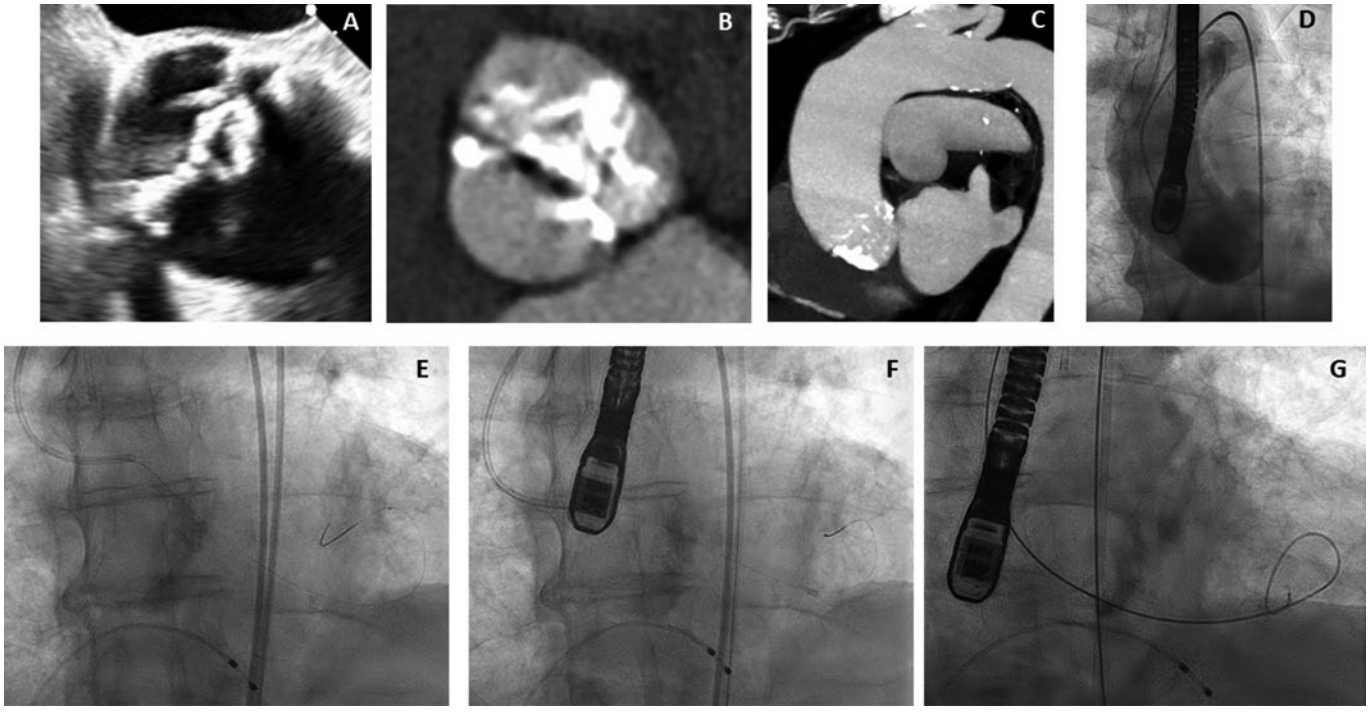


Figure 1.

This is the case of an 83-year-old man with symptomatic, severe aortic valve stenosis referred for transcatheter aortic valve implantation (TAVI). The echocardiogram revealed the presence of a severely calcified stenotic aortic valve (0.6 cm^2) with bicuspid anatomy (figure 1A). The computed tomography scan revealed an Agatston calcium score of 17 727 (figure 1B), a 30 mm aortic annulus diameter, and dilated aortic root and aortic angulation > 70º (figure 1C). Aortography was performed (figure 1D).

Crossing the aortic valve with a guidewire for 60 min using catheters of various curves/sizes and several types of guidewires (with or without J-shaped tip, whether hydrophilic or not) was attempted by 2 highly skilled operators. Strategy, then, changed and a XB4 6F left coronary guide catheter (Cordis, United States) was used to manipulate a 0.014 inch hydrophilic Pilot 50 intracoronary guidewire (Abbott, United States) that easily crossed the aortic valve (figure 1E). A 6-Fr guide catheter extension system (Deeper, IHT-Cordynamic, Spain) was mounted on the wire and advanced to the left ventricular apex (figure 1F). Afterwards, the intracoronary guidewire was replaced by a 0.035 inch extra-stiff guidewire by removing both the guide and extension catheter systems (figure 1G). This original new approach took just 5 min.

The impossibility of crossing the aortic valve with a guidewire is rare. In our case the difficulty was due to a severely stenotic valve with massive calcification, bicuspid morphology, horizontal aorta, and dilatation of both the aortic root and the annulus.

* **Corresponding author.**
E-mail addresses: josemariadela.torre@scsalud.es; chematorre60@gmail.com (J.M. de la Torre-Hernández).

Received 16 February 2023. Accepted 24 March 2023. Online 4 May 2023.

This case is a truly original and novel technique, simple and safe, to achieve the guidewire crossing of a very stenotic aortic valve with a complex anatomy. This technique illustrates the cross-over use of coronary and structural interventional tools to solve complex problems.

Consent was obtained from the patient for the publication of this case.

FUNDING

None reported.

AUTHORS' CONTRIBUTIONS

All authors contributed to data collection, drafting, review, and approval of the manuscript.

CONFLICTS OF INTEREST

J. M. de la Torre-Hernández is editor-in-chief of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The other authors do not declare any conflict.

REC Interv Cardiol. 2023;5(4):325-326
https://doi.org/10.24875/RECICE.M23000383

Unsuspected residual coronary guidewire fragment

Fragmento de guía coronaria insospechado

Felipe Hernández Hernández*

Unidad Integral de Cardiología (UICAR), Hospital La Luz Quironsalud, Madrid, Spain

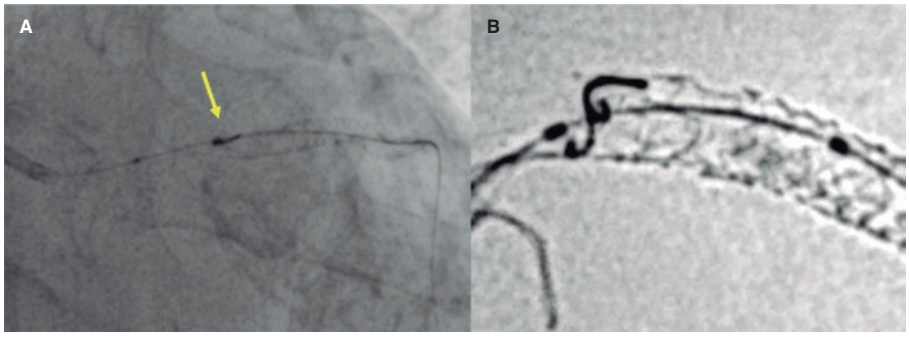


Figure 1.

This is the case of a 74-year-old woman treated with 2 overlapping stents in the proximal-to-middle segment of the left anterior descending coronary artery due to severe symptomatic disease. A Sion guidewire (Asahi Intecc, Japan) was recrossed towards the left circumflex artery to finish with postdilatation of the overlapping zone between the proximal left anterior descending coronary artery and left main coronary artery. While the recrossed guidewire was being removed, the distal loop tangled up with the stent at left circumflex artery ostial level and it couldn't be removed (figure 1A, yellow arrow). A low-profile balloon was advanced over the guidewire that was eventually removed. Still, a small radiopaque distal fragment got trapped in the stent of the left main coronary artery (figure 1B) (Clearstent, Siemens Healthcare, Germany) suspicious of residual material in the coronary sinus not visible through conventional fluoroscopy. The result was assessed on an optical coherence tomography that revealed the presence of guidewire fragments in the left main coronary artery. In-stent postdilatation was repeated with a noncompliant balloon at high pressures (video 1 of the supplementary data). The optical coherence tomography confirmed the crushing of the guidewire fragment on the stent struts (figure 2A, white arrow), and an extremely thin guidewire fragment entering the guide catheter (figure 2B, white arrow, and videos 2-4 of the supplementary data). The procedure was completed, and the patient was discharged uneventfully.

At 6-month follow-up, an echocardiogram showed a linear hyperechoic image in the ascending aorta (figure 2C, yellow arrows). A computed tomography scan revealed the presence of residual metal guidewire fragments protruding from the left main coronary artery and moving towards the aorta (figure 2D, asterisk). A conservative approach was decided since the patient remained asymptomatic and without inducible ischemia. No clinical events have ever been reported at 2-year follow-up (on dual antiplatelet therapy).

The patient gave her written informed consent for publishing purposes.

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

None reported.

* **Corresponding author.**
E-mail address: felipeivus@hotmail.com (F. Hernández Hernández).
𝕏 @pipecardio

Received 25 January 2023. Accepted 29 March 2023. Online 8 June 2023.

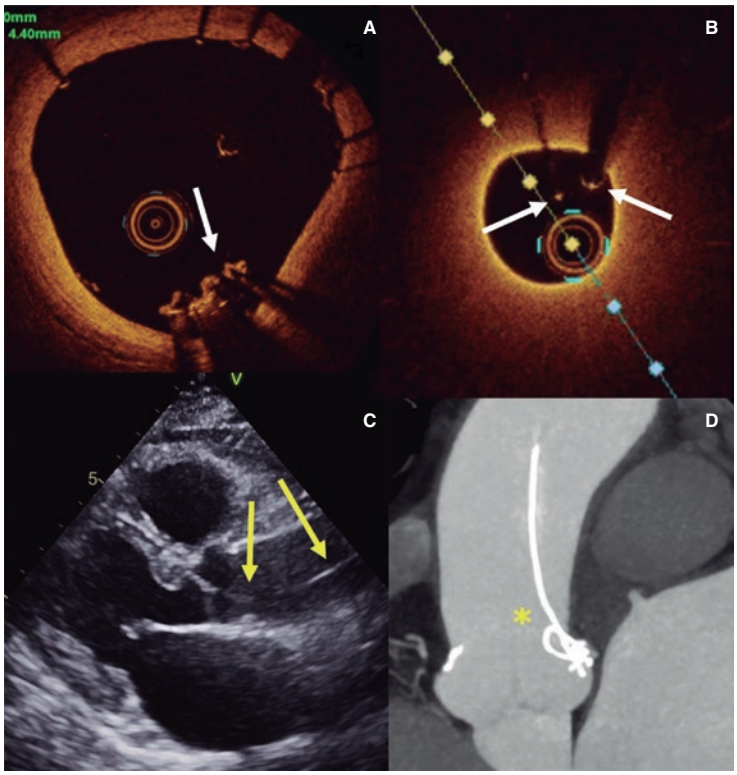


Figure 2.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M23000383.

REC Interv Cardiol. 2023;5(4):327-328
https://doi.org/10.24875/RECICE.M23000385

The mystery of the Dragon's tail solved by 3D reconstruction

El misterio de la cola de dragón resuelto por la reconstrucción 3D

Sandra Santos-Martínez,* Miguel Leiva-Gordillo, Ricardo García-Belenguer, Paula Tejedor-Viñuela, and Pedro Morillas-Blasco

Servicio de Cardiología, Hospital General Universitario de Elche, Elche, Alicante, Spain

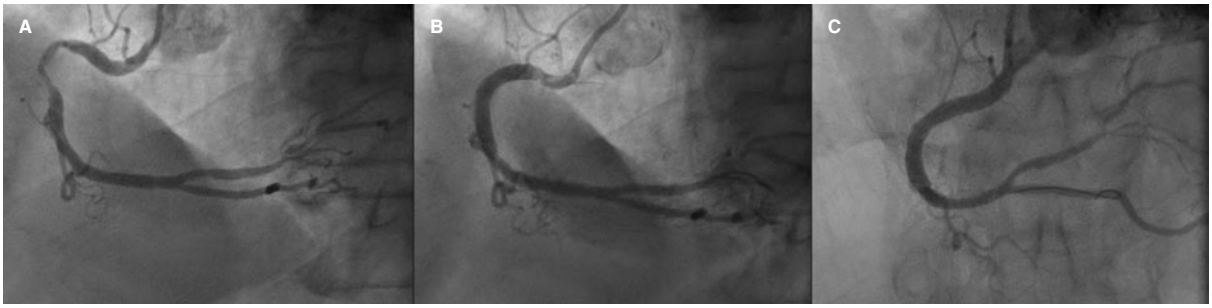


Figure 1.

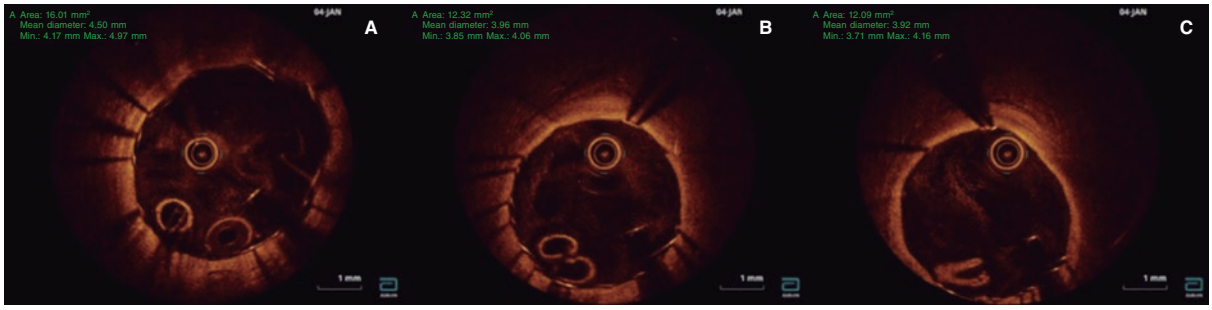


Figure 2.

This is the case of a 78-year-old man with hypertension and dyslipidemia admitted due to unstable angina. The coronary angiography confirmed the presence of a chronic occlusion at middle left anterior descending coronary artery level and significant stenosis of the middle right coronary artery with a shepherd's crook morphology of the proximal segment (figure 1A). Angioplasty was performed using an AL-1 catheter and advancing a SION Blue guidewire (Asahi Intecc, Japan). A 4.5 mm × 30 mm zotarolimus-eluting stent was directly implanted. The follow-up angiography revealed the presence of an image consistent with dissection of the artery proximal segment (figure 1B). Afterwards, an intracoronary image was acquired using optical coherence tomography (OCT) (DragonFly OPTIS, Abbott Vascular, United States) that confirmed the presence of a iatrogenic type B dissection presumably due to catheter impaction against the vessel wall. It was treated by implanting a 5.0 mm × 12 mm zotarolimus-eluting stent that overlapped with the previous one. The new OCT performed confirmed its proper expansion and the sealing of dissection. However, a double circle image was seen in several frames (figure 2A,B) gradually coming together until they eventually meet each other (figure 2C). Thanks to the 3D reconstruction of the image, it was revealed that the catheter was folded over itself (figure 3, arrow). The likely mechanism to obtain this image is the difficulty found when trying to advance the OCT catheter due to the double curve created by the withdrawal of the AL-1 catheter (to try to assess the angioplasty result) added to the shepherd's crook morphology of the artery (zigzag course).

The patient gave his written informed consent for publication purposes.

* **Corresponding author.**
E-mail address: sandrasantosmartinez@gmail.com (S. Santos-Martínez).
𝕏 @drassantos @mLeiva_ @PaulaTejedorV @pedromorillas68.

Received 19 February 2023. Accepted 10 April 2023. Online 22 May 2023.

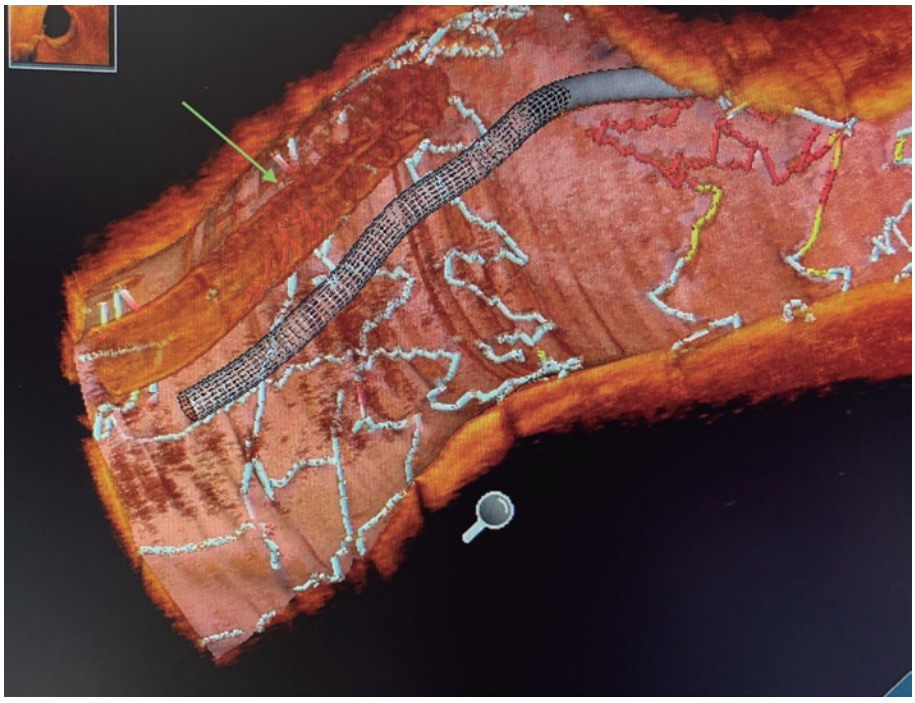


Figure 3.

FUNDING

None whatsoever.

AUTHORS' CONTRIBUTIONS

S. Santos-Martínez, and P. Tejedor-Viñuela drafted the manuscript and completed its critical review. M. Leiva-Gordillo performed the final processing of the images. R. García-Belenger, and P. Morillas-Blasco reviewed the manuscript and approved its final version for publication. All the authors approved such version.

CONFLICTS OF INTEREST

None reported.

REC Interv Cardiol. 2023;5(4):329
https://doi.org/10.24875/RECICE.M23000396

Letter to the Editor

Doctor, I want a TAVI! Should patients choose the type of aortic valve procedure they want?

¡Doctor, póngame un TAVI! ¿Pueden los pacientes elegir el tipo de intervención sobre la válvula aórtica?

Manuel Martínez-Sellés[a,b,c,d,*]

[a] *Servicio de Cardiología, Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[b] *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Spain*
[c] *Facultad de Ciencias Biomédicas y de la Salud, Universidad Europea, Madrid, Spain*
[d] *Facultad de Medicina, Universidad Complutense, Madrid, Spain*

SEE RELATED CONTENT:
https://doi.org/10.24875/RECICE.M22000340

To the Editor,

Vázquez Rodríguez et al.[1] elegantly demonstrate that transcatheter aortic valve implantation (TAVI) is cost-effective even in low-surgical risk patients. This cost-effectiveness adds to the excellent data regarding survival reported in real-life settings in Spain even in cohorts of very old patients with frequent comorbidities.[2] Former data also confirm the cost-effectiveness of this technique,[3-5] as well as its favorable outcomes,[6] thus making it a viable option for low-risk patients as well.[7]

Therefore, in the management of symptomatic severe aortic stenosis where both surgical aortic valve replacement (SAVR) and TAVI are feasible options, and once the patient has been properly informed and given his/her written informed consent, he/she should be able to choose TAVI even if the heart team recommends SAVR. We should remember that 2 different domains exist regarding decision-making: the professional or objective domain that determines whether treatment is proportionate (and benefits can be expected), and the one pertaining to the patient, also called subjective domain, that determines whether the procedure is a common one (that is, not perceived as an unbearable aggression) (figure 1). Denying the decision-making capacity of a properly informed patient is unethical, and as noted by Vázquez Rodríguez et al.,[1] cannot be justified from a financial standpoint either.

		Objective assessment: Proportionate	Objective assessment: Disproportionate
Subjective assessment	Common SAVR	SAVR or TAVI based on expert technical criteria	Do not offer unfeasible procedures
	Unusual SAVR	TAVI	

Figure 1. Two different decision-making domains: the professional or objective domain that determines whether treatment is proportionate, and the patient's—subjective—who determines whether it is a common procedure. SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

FUNDING

None whatsoever.

CONFLICTS OF INTEREST

None reported.

REFERENCES

1. Vázquez Rodríguez J, Pinar Bermúdez E, Luis Zamorano J, et al. Cost-effectiveness of SAPIEN 3 transcatheter aortic valve implantation in low surgical mortality risk patients in Spain. *REC Interv Cardiol.* 2023;5:38-45.
2. Vicent L, Fernández-Cordón C, Nombela-Franco L, et al. Baseline ECG and Prognosis After Transcatheter Aortic Valve Implantation: The Role of Interatrial Block. *J Am Heart Assoc.* 2020;9:e017624.
3. Pinar E, García de Lara J, Hurtado J, et al. Cost-effectiveness analysis of the SAPIEN 3 transcatheter aortic valve implant in patients with symptomatic severe aortic stenosis. *Rev Esp Cardiol.* 2022;75:325-333.
4. Chotnoppharatphatthara P, Yoodee V, Taesotikul S, Yadee J, Permsuwan U. Transcatheter aortic valve implantation in patients with severe symptomatic aortic valve stenosis: systematic review of cost-effectiveness analysis. *Eur J Health Econ.* 2023;24:359-376.
5. Zhou JY, Liew D, Duffy SJ, Walton A, Htun N, Stub D. Cost-effectiveness of transcatheter versus surgical aortic valve replacement in low-risk patients with severe aortic stenosis. *Heart Lung Circ.* 2021;30:547-554.
6. UK TAVI Trial Investigators; Toff WD, Hildick-Smith D, Kovac J, et al. Effect of transcatheter aortic valve implantation vs surgical aortic valve replacement on all-cause mortality in patients with aortic stenosis: a randomized clinical trial. *JAMA.* 2022;327:1875-1887.
7. Lim GB. Suitability of TAVI in low-risk patients. *Nat Rev Cardiol.* 2023;20:284.

*** Corresponding author.**
E-mail address: mmselles@secardiologia.es (M. Martínez-Sellés).

Online 29 June 2023.