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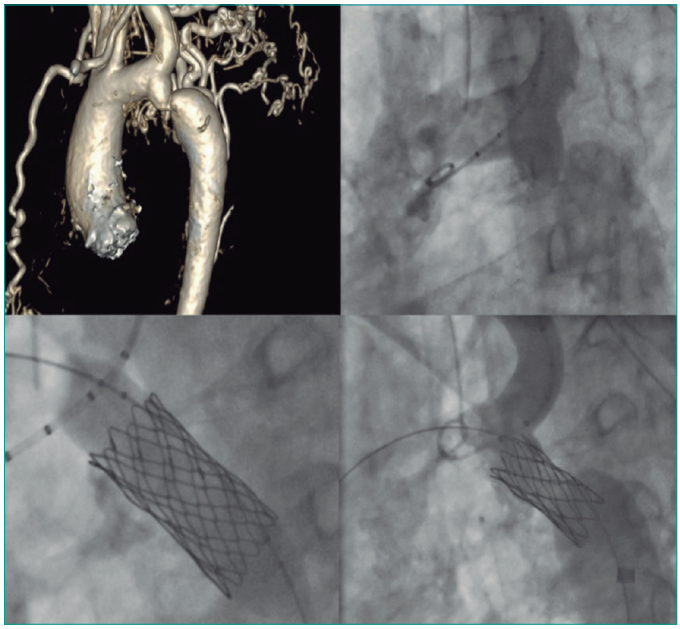

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CONTENTS

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Editorial

TAVI in centers without on-site cardiac surgery. Need or dare?

TAVI en centros sin cirugía cardiaca in situ. ¿Necesidad o temeridad?

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Since its incorporation into routine clinical practice more than 20 years ago, transcatheter aortic valve implantation (TAVI) has progressively gained acceptance within the cardiology community, driven by a successful and comprehensive clinical program that began with early reports in inoperable[1] and high-risk patients,[2] around 2010.

From the earliest studies, patient eligibility for TAVI was determined by a multidisciplinary committee of cardiologists and surgeons— which came to be known as the heart team—and procedures were performed exclusively at centers with on-site cardiac surgery. Similarly, all subsequent clinical practice guidelines on the management of TAVI have assigned the highest level of recommendation to performing the procedure in centers with a heart team and on-site cardiac surgery, a requirement that has persisted through the most recent European clinical practice guidelines.[3]

On the other hand, the marked increase in the number of procedures is making it difficult for hospitals with on-site cardiac surgery to meet this growing demand, thereby considerably prolonging waiting times—an especially sensitive issue given the high mortality rate of patients in this situation, which may exceed 15%.[4] Therefore, it may be time to ask the following question: is the presence of a cardiac surgery department at the center still a prerequisite for establishing a TAVI program?

In an article published in *REC: Interventional Cardiology*, Rocha de Almeida et al.[5] present their experience with 300 patients undergoing TAVI at a center without on-site cardiac surgery. Despite the absence of on-site cardiac surgery, what is striking at first glance is that this is a regional referral center with an interventional team experienced in performing the procedure at high-volume centers. Thus, this represents an initial experience for the center, but not for its operators.

In this series of 300 TAVI procedures performed over approximately 4 years, outcomes were comparable to those of high-volume centers; despite an advanced mean age (82 years), a mean Society of Thoracic Surgeons (STS) score of 3.8, and 17% of patients being categorized as high risk (STS score > 8), the 30-day mortality rate (primary endpoint) was 3.7% and the in-hospital mortality rate, 2%, with no conversions to surgery, annular rupture, coronary obstruction, or prosthetic embolization, and only 2 cases of percutaneous pericardiocentesis were required due to guidewire perforation.[5]

In fact, compared with the Portuguese registry,[6] the 30-day mortality rate was numerically lower (3.7% vs 4.8%; *P* = not significant [NS]), as was the stroke rate (2.7% vs 4.6%; *P* = NS), with similar rates of bailout cardiac surgery (0 vs 0.4%), comparable vascular complications (8% vs 6.8%; *P* = NS), and an identical rate of permanent pacemaker implantation (20% vs 19%).

Similar experiences have been reported in the literature from other countries, with varying sample sizes and generally retrospective designs (table 1). The earliest published experience of TAVI without on-site cardiac surgery was reported by Eggebrecht et al.[7,9] using data from the German registry and comparing the outcomes at centers with a "visiting" surgeon with those obtained at centers with on-site cardiac surgery, without any differences being reported in the 30-day mortality rate (6.2% vs 8.3%; *P* = NS) and with very low rates of bailout surgery (2.2% vs 1.6%). This experience has been replicated in other countries, such as Austria,[8] with similar mortality rates in centers with and without on-site cardiac surgery (6.9% vs 6.2%; *P* = NS), and Spain,[10] with a comparable 30-day mortality rate (6.1%) and a very low rate of bailout surgery (0.3%). In more recent registries including lower-risk patients, such as the Israeli experience,[11] the 30-day mortality rate can be as low as < 1%.

As optimistic as these registries may appear when initiating a TAVI program without on-site cardiac surgery, the importance of care organization for this purpose must not be overlooked. High-volume centers with on-site cardiac surgery have the advantage of hospital-wide adaptation to this type of procedure, as well as training of all involved specialties, including cardiology, cardiac surgery, anesthesia, and intensive care. The authors highlight two critically important aspects: when they initiated the program, they already had extensive experience in TAVI, and the center served as a regional cardiology referral institution. Assuming that a TAVI program without on-site surgery can be initiated without all necessary safeguards would simply place patients at risk.

A notable feature of contemporary practice is that refinement of procedural steps, improvements in materials, enhanced team training, and supervision by experienced operators during program initiation have resulted in excellent TAVI and very low complication rates,[12] particularly in patients with low STS scores. Furthermore, performing this procedure at centers without on-site surgery has different implications in high-risk patients with limited surgical bailout options than in low-risk patients, in whom bailout surgery remains feasible, although infrequent and usually

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Table 1. Studies on TAVI in centers with and without on-site cardiac surgery

Study	Country	Patients		Vascular complications		30-day mortality rate		Bailout surgery	
		In centers without on-site cardiac surgery (n)	In centers with on-site cardiac surgery (n)	In centers without on-site cardiac surgery (%)	In centers with on-site cardiac surgery (%)	In centers without on-site cardiac surgery (%)	In centers with on-site cardiac surgery (%)	In centers without on-site cardiac surgery (%)	In centers with on-site cardiac surgery (%)
Eggebrecht et al.[7]	Germany	178	1754	18.5	22.2	6.2	8.3	2.2	1.5
Egger et al.[8]	Austria	290	290	9.3	4.8	6.9	6.2	—	—
Eggebrecht et al.[9]	Germany	550	550	—	—	1.8*	2.9*	—	—
Roa Garrido et al.[10]	Spain	384	—	—	—	6.1	—	0.3	—
Barashi et al.[11]	Israel	149	—	0.67	—	0.67	—	0	—

* In-hospital mortality.

associated with unfavorable outcomes.[12] Therefore, careful patient selection appears mandatory, with the participation of a heart team capable of determining eligibilty for TAVI at centers without on-site surgery and auditing outcomes.

Further insight may be provided by the new prospective Italian registry TAVI at Home,[13] which will include a total of 200 patients undergoing TAVI at centers without on-site surgery under strict inclusion and exclusion criteria (> 75 years, high or prohibitive risk, non-bicuspid valves, and no degenerated surgical valves) always under the scrutiny of a heart team including cardiac surgeons, clinical cardiologists, interventional cardiologists, imaging specialists, and anesthesiologists.

Moreover, in Italy, the randomized TRACS trial is underway, comparing TAVI performed at centers with vs without on-site cardiac surgery,[14] with a planned enrollment of 566 patients and inclusion and exclusion criteria very similar to those of the TAVI at Home registry.

In conclusion, and in response to the question posed in this editorial, we firmly believe that performing TAVI at centers without on-site cardiac surgery is, without question, a necessary step. Accordingly, strict requirements and systematic outcome auditing are essential to ensure that this necessity does not translate into undue risk.

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CONFLICTS OF INTEREST

None declared.

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Editorial

Interventional management of congenital heart disease: integrating perspectives for a shared future

Intervencionismo en cardiopatías congénitas: suma de miradas para un futuro compartido

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The comprehensive management of patients with congenital heart disease is one of the major challenges in contemporary cardiology. In its early stages, the management of these patients was based primarily on diagnosis and palliative care. Afterwards, the goal shifted to ensuring survival, and, currently, the challenge is for patients to reach adulthood with good quality of life, minimizing morbidity associated with their congenital heart condition and prior procedures, while ensuring structured follow-up.

The major shift came from 2 parallel revolutions: advances in diagnostic capability and structural heart procedures. Due to developments in echocardiography, magnetic resonance imaging, and computed tomography, early and precise diagnosis is now possible—even in utero—allowing clinicians to properly inform families about the diagnosis and prognosis of these conditions. At the same time, surgical advances and, notably, significant progress made in percutaneous coronary interventions have transformed the natural course of this disease.

Cardiac catheterization, initially conceived as a diagnostic tool, soon acquired a decisive therapeutic role. In 1953, Rubio Álvarez et al.[1] performed the first balloon valvulotomy. A decade later, Rashkind and Miller[2] described atrial septostomy. These milestones marked the beginning of percutaneous coronary intervention, first as a palliative therapy and later as an established therapeutic option. Currently, many patients avoid surgery, lengths of stay are shorter, recovery is faster, and percutaneous coronary intervention has become a well-established, safe, and effective alternative.[3]

Percutaneous procedures are now the first-line therapy for obstructive lesions (valvular stenosis, aortic coarctation, etc.) and closure of septal defects and ducts (patent ductus arteriosus). Moreover, these procedures often serve as essential adjuncts in the management of complex congenital heart disease, including in patients with single-ventricle physiology who have undergone cavopulmonary diversion techniques.

In Spain, hemodynamic activity in congenital heart disease is distributed across 3 different types of cath lab based on the profile of the patients: pediatric labs (primarily for patients < 18 years), adult labs (primarily for patients ≥ 18 years), and mixed labs (no age distinction), which in some cases differ by working teams. Diagnostic catheterization remains the most frequently performed procedure, especially in adult cath labs accounting for 65% of cases.[4]

With increasing survival, a growing number of patients with congenital heart disease reach adulthood, creating the need for repeated diagnostic and therapeutic catheterizations, which are often prolonged and technically complex. Optimal management requires integrating a deep understanding of congenital heart disease pathophysiology with expertise in vascular complications typical of adulthood.

The complexity of many scenarios—both biventricular (eg, tetralogy of Fallot, pulmonary atresia with ventricular septal defect, or transposition of the great arteries repaired with atrial or arterial switch) and single-ventricle anatomies (various forms of cavopulmonary diversion)—requires more than just technology: it demands true collaboration among teams. Cumulative experience demonstrates that the combined expertise of pediatric and adult interventional cardiologists generates irreplaceable added value. The pediatric interventional cardiologist contributes knowledge on congenital physiology, long-term disease progression, and complications associated with palliative or corrective procedures performed throughout life, whereas the adult interventional cardiologist contributes experience with device technology and vascular access issues typical of older patients.

Although this synergy benefits most clinical scenarios, it is especially relevant in the following:

- Closure of complex defects: sinus venosus atrial septal defects (associated with anomalous pulmonary venous drainage), ventricular septal defects, persistent ductus arteriosus in adults with pulmonary hypertension or calcification, and dehiscence of surgical conduits (mainly in patients with atrial switch procedures for transposition of the great arteries).

- Treatment of obstructive lesions: aortic coarctation (especially in patients with prior childhood procedures); stenosis of surgically placed conduits (atrial switch procedures for transposition of the great arteries or right ventricle–to–pulmonary artery conduits); or treatment of branch pulmonary arteries with angioplasty with or without stenting.

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- Pulmonary valve procedures: this is a rapidly expanding field in which the incorporation of multiple techniques now allows treatment of dilated right ventricular outflow tracts resulting from childhood surgical procedures, with excellent results comparable to surgery but with reduced procedural morbidity.[5] Therefore, techniques involving stenting in dilated outflow tracts allow subsequent placement of balloon-expandable valves with excellent outcomes. However, the major forthcoming advance is the consolidation of self-expandable valves, which simplify valve implantation. In these situations, the experience of adult interventional cardiologists with self-expandable valves in other settings, such as aortic valve procedures, is highly valuable.

- Evaluation of single-ventricle physiology: it requires repeated cardiac catheterizations from the earliest stages of life. The pediatric interventional cardiologist contributes not only essential insight into the underlying pathophysiology but also expertise in managing complications associated with single-ventricle physiology and the palliative procedures needed to help patients reach adulthood in the best possible functional condition. Consequently, these patients often undergo interventions for stenosis of palliative conduits or branch pulmonary arteries, closure of systemic–pulmonary collaterals, or optimization of Fontan circulation through creation or closure of fenestrations.[6]

- Coronary anomalies and complications: the adult interventional cardiologist plays a crucial role, as experience in areas such as atherosclerotic disease is invaluable in addressing and treating coronary anomalies percutaneously.

In our setting, the joint work model established since 2015 between pediatric and adult teams illustrates this philosophy. It is not just about sharing a cath lab but generating shared spaces for discussion and decision-making through multidisciplinary clinical sessions to standardize criteria and enable individualized strategy planning. A recent example reflecting the benefits of this collaborative model is a Fontan optimization case involving stenting and collateral closure. The patient was a 41-year-old woman with complex congenital heart disease and single-ventricle physiology—characterized by atrioventricular concordance with ventriculoarterial discordance, complete transposition of the great arteries, a large ventricular septal defect, pulmonary stenosis, and right ventricular hypoplasia—who had undergone multiple surgical procedures (Blalock–Taussig shunt at 13 months, systemic–pulmonary shunt at 2.5 years, bidirectional Glenn at 9 years, and extracardiac Fontan at 17 years). She exhibited reduced functional capacity and Fontan-associated hepatopathy. Cardiac catheterization confirmed a severely calcified Fontan conduit with significant stenosis at its insertion into the right pulmonary artery. Balloon sizing was performed, followed by implantation of a covered stent postdilated with a 20-mm balloon, achieving a good result. A marked stenosis at the Glenn-to–right pulmonary artery anastomosis was confirmed via right internal jugular vein, and a 34 mm bare-metal stent was implanted (figure 1A,B). The aortography performed via arterial access revealed the presence of large aortopulmonary collaterals supplying the 2 upper lung lobes, which were successfully occluded. The first one, toward the right and left upper lobes, was closed using an Amplatzer Vascular Plug 4 (Abbott Cardiovascular, United States) and coils; the second, toward the right upper lobe, was also closed with an Amplatzer Vascular Plug 4 and coils (figure 1C,F). This case illustrates the synergy between pediatric and adult interventional cardiologists in completing treatment.

The increasing number of adults with congenital heart disease has led to more frequent, longer, and technically demanding procedures, requiring combined expertise in congenital heart disease and adult vascular complications. The joint cath-lab model for congenital heart disease should be promoted to facilitate individualized case discussion and procedural planning, both of which are essential for therapeutic success. Cross-disciplinary training and communication among teams are critical to establishing a modern, collaborative approach to interventional care in congenital heart disease. The European clinical practice guidelines on the management of adult congenital heart disease emphasize the importance of a structured transition and the need for multidisciplinary heart teams.[7] Furthermore, studies show that long-term outcomes improve significantly in centers with combined pediatric and adult experience.[5]

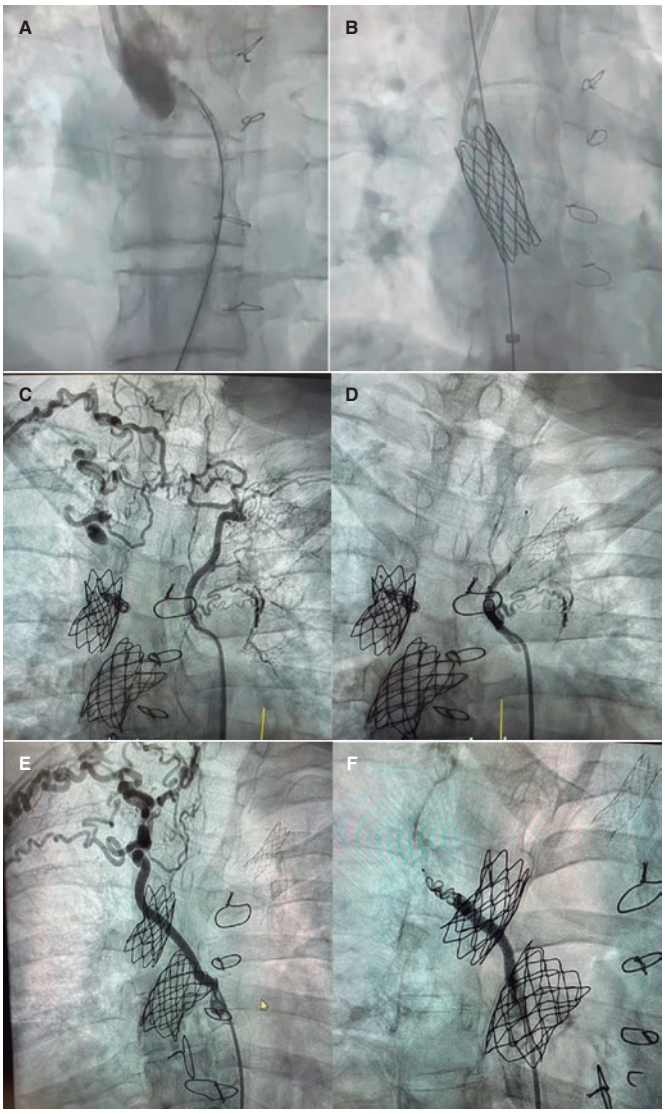

Figure 1. Fontan optimization. **A:** stenosis at the Glenn–right pulmonary artery anastomosis. **B:** bare-metal stent implanted in the stenosis. **C:** large aortopulmonary collateral supplying the right and left upper lung lobes. **D:** occlusion of this collateral. **E:** large aortopulmonary collateral supplying the right upper lobe. **F:** occlusion of the collateral.

The field of congenital heart disease reminds us that progress does not come from isolated disciplines, but from shared effort. The current challenge is no longer simply to extend life, but to ensure its quality. Therefore, integration of pediatric and adult cardiology in the interventional management of congenital heart disease is no longer optional, but essential.

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ETHICAL CONSIDERATIONS

Informed consent was obtained from the patient described in the case, including approval for publication.

CONFLICTS OF INTEREST

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Original article

Transcatheter aortic valve implantation without immediate cardiac surgery backup. A single-center retrospective analysis

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ABSTRACT

Introduction and objectives: Transcatheter aortic valve implantation (TAVI) is traditionally performed with on-site cardiac surgery (CS) backup. However, procedural advances enabled TAVI to be performed safely without immediate CS backup. This study describes our single-center experience with TAVI performed in a center without on-site CS backup.
Methods: We conducted a retrospective analysis of the first 300 patients undergoing TAVI without on-site CS backup between 2020 and 2024. The primary endpoint was 30-day mortality. Secondary endpoints included procedural and in-hospital mortality, stroke, emergency cardiac surgery (ECS), vascular complications, major hemorrhage, and pacemaker implantation. Outcomes were compared with those from the Portuguese national TAVI registry.
Results: The cohort mean age was 82 ± 5 years (54% women). The median STS risk score was 3.8 [IQR, 2.3–6.6], with 17% high-risk patients (STS > 8). Most procedures were elective (83%). Transfemoral access was used in 99% of cases, and self-expandable valves were implanted in 95%. The 30-day mortality rate was 3.7% (n = 11), while stroke occurred in 2.7% (n = 8). The procedural survival rate was 99% (n = 298). No cases of ECS occurred (n = 0), coronary obstruction, TAVI-in-TAVI deployment as a bailout, or valve embolization were reported. Pericardial tamponade occurred in 0.7% of cases (n = 2). Major hemorrhage and vascular complications occurred in 8%, and pacemaker implantation in 20%. The 1-year mortality rate was 12%, with 4% attributed to cardiovascular causes; among survivors, and 91% reported symptomatic improvement. There were no significant differences in outcomes vs the results from the TAVI national registry.
Conclusions: TAVI was safely and effectively performed without on-site CS, including emergency and complex cases. The non-ECS rate and outcomes comparable to national benchmarks support the feasibility of TAVI in selected non-CS centers. In this context, expanding TAVI access may reduce waiting times and improve the management of severe aortic stenosis while maintaining high procedural quality.

Keywords: Transcatheter aortic valve implantation. TAVI. Severe aortic stenosis. Cardiac surgery backup.

Implante percutáneo de válvula aórtica sin apoyo de cirugía cardiaca inmediata. Análisis retrospectivo de un centro

RESUMEN

Introducción y objetivos: El implante percutáneo de válvula aórtica (TAVI) se realiza tradicionalmente con el apoyo de cirugía cardiaca mínimamente invasiva (CCMI) en el mismo centro. Sin embargo, los avances en los procedimientos han permitido realizar TAVI de forma segura sin cirugía cardiaca inmediata. Este estudio describe la experiencia de nuestro centro en el TAVI sin CCMI.
Métodos: Análisis retrospectivo de los primeros 300 pacientes a quienes se realizó TAVI sin CCMI entre 2020 y 2024. El objetivo principal fue la mortalidad a los 30 días. Los objetivos secundarios fueron la mortalidad intraprocedimiento y la mortalidad hospitalaria, el accidente cerebrovascular, la cirugía cardiaca de urgencia (CCU), las complicaciones vasculares, la hemorragia grave y el implante de marcapasos. Los resultados se compararon con el registro nacional portugués de TAVI.

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Resultados: La edad media de la cohorte fue de 82 ± 5 años y el 54% eran mujeres. La mediana de la puntuación de riesgo STS fue de 3,8 [IQR: 2,3-6,6], con el 17% de pacientes de alto riesgo (STS > 8). La mayoría de las intervenciones fueron electivas (83%). Se utilizó el acceso transfemoral en el 99% de los casos y se implantaron válvulas autoexpandibles en el 95% de ellos. La tasa de mortalidad a los 30 días fue del 3,7 % (n = 11). Se produjeron accidentes cerebrovasculares en el 2,7% (n = 8). La tasa de supervivencia al procedimiento fue del 99% (n = 298). No se precisó CCU en ningún paciente y no hubo casos de obstrucción coronaria, necesidad de TAVI en TAVI como medida de rescate ni embolización valvular. Dos pacientes presentaron taponamiento pericárdico (0,7%). Se produjeron hemorragias graves y complicaciones vasculares en el 8% de los pacientes, y se implantó marcapasos en el 20%. Al año, la tasa de mortalidad fue del 12%, el 4% por causas cardiovasculares. El 91% de los supervivientes presentaron una mejora de los síntomas. No hubo diferencias significativas en los resultados en comparación con los del registro nacional de TAVI.
Conclusiones: El TAVI se realizó de forma segura y eficaz sin CCMI, incluso en casos urgentes y complejos. La no necesidad de CCU y los resultados comparables a los referentes nacionales respaldan la viabilidad del TAVI en centros seleccionados sin cirugía cardiaca. Ampliar el acceso al TAVI en este contexto puede reducir los tiempos de espera y mejorar la atención de la estenosis aórtica grave, al tiempo que se mantiene una alta calidad del procedimiento.

Palabras clave: Implante percutáneo de válvula aórtica. TAVI. Estenosis aórtica grave. Cirugía cardiaca mínimamente invasiva.

Abbreviations

AS: aortic stenosis. **CS:** cardiac surgery. **ECS:** emergency cardiac surgery. **TAVI:** transcatheter aortic valve implantation.

INTRODUCTION

Aortic stenosis (AS) is the most common primary valvular heart disease requiring intervention.[1] Its prevalence is estimated at 3–5% in individuals older than 75 years,[2,3] and it is expected to increase due to longer life expectancy, growing awareness, and improved diagnostic accuracy.[4] The mortality rate of untreated severe symptomatic AS reaches 10-20% within the first year and 45% at 4 years.[2,5]

Transcatheter aortic valve implantation (TAVI) is a well-established, less invasive alternative to surgical aortic valve replacement for patients with severe symptomatic AS.[1,6] Initially reserved for high-risk patients, TAVI indications have expanded to intermediate-risk and older lower-risk patients.[1,6] Improvements in device technology, procedural techniques, and operator expertise have led to fewer complications and enhanced overall safety.[3] The increasing prevalence of AS and the expansion of TAVI indications highlight the need to increase procedural capacity to meet current and future clinical demands and ensure timely access to treatment.[7]

Current clinical practice guidelines recommend that TAVI must be performed exclusively at centers with on-site cardiac surgery (CS) backup,[1,6] as surgical backup provides a safety net in complications requiring emergency cardiac surgery (ECS).[8] Nonetheless, the rate of ECS has significantly decreased to 0.5-1% of TAVI,[9] and the outcomes of ECS remain poor,[9] with a 54% survival rate at the index event and only 22% at 1 year,[10] raising concerns about the actual benefits of mandatory surgical backup.

TAVI availability remains variable, with regional disparities due to the centralized distribution of CS centers.[4,11] As a result, access is often limited in regions without tertiary CS centers, leading to prolonged waiting periods associated with a worse prognosis.[3] TAVI waiting list mortality rate reaches 18%, highlighting the need for timely intervention.[12] Expanding TAVI to centers without on-site CS will improve access, increase procedures, reduce health care inequalities, and alleviate surgical centers, allowing them to focus on higher-risk procedures.[3,13] The limited number of eligible centers constrains the national procedural volume, preventing the health system's ability to meet the population's growing TAVI needs.[4,14]

This study aims to describe our experience with TAVI in a center without on-site CS and compare outcomes to the national benchmark of centers with surgical backup.

METHODS

Study population

We conducted a retrospective, single-center cohort study including the first 300 consecutive patients who underwent TAVI at our center, *Hospital Espírito Santo de Évora* (Portugal), between 2020 and 2024. This study was conducted in a hospital without an on-site CS department. Patients were identified through the institutional structural heart procedure registry. The study was approved by the center ethics committee, informed consent was obtained from all participants, and the study was conducted in full compliance with the Declaration of Helsinki.

Data collection

Clinical, echocardiographic, laboratory, and procedural data were obtained from electronic health records, including imaging modalities, procedural documentation, and discharge summaries. Baseline characteristics included demographic, clinical, and echocardiographic parameters, and procedural information such as access route and valve type.

Endpoints

The primary endpoint was the 30-day all-cause mortality rate. The secondary endpoints were need for ECS, in-hospital mortality, stroke, 1-year all-cause mortality rate, 1-year cardiac death, vascular complications, major hemorrhage, and permanent pacemaker implantation. Outcomes were defined according to the Valve Academic Research Consortium-3 (VARC-3) criteria.[15] ECS was defined as any unplanned cardiac surgical conversion to open surgery required to manage a life-threatening complication occurring during or shortly after the procedure, performed before the patient leaves the procedural environment.

In addition, outcomes were compared with the most recent Portuguese national TAVI registry,[16] which exclusively includes centers with on-site CS, to provide a benchmark for procedural safety and efficacy profile.

Follow-up

Follow-up was performed through clinic visits at 3 and 12 months, complemented by telephone contact and review of electronic health records when in-person visits were not possible. Symptomatic improvement was evaluated based on changes in New York Heart Association (NYHA) functional class.

Statistical analysis

Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data were expressed as mean ± standard deviation (SD) and compared using the Student *t* test. Non-normally distributed variables were expressed as the median and interquartile range (IQR) and compared using the Mann–Whitney U test. Statistical significance was set at a 2-tailed *P*-value < .05. All statistical analyses were performed using Stata version 18.0 (StataCorp, United States).

RESULTS

Baseline characteristics

The first consecutive 300 patients undergoing TAVI between 2020 and 2024 were included. The cohort mean age was 82 ± 5 years (62–101), and 54% (n = 161) were women. The median Society of Thoracic Surgery (STS) risk score was 3.8 [IQR, 2.3–6.6], with 17% (n = 51) classified as high-risk (STS > 8). Prior hospitalization for symptomatic AS occurred in 21% (n = 64). Seven patients (2%) had undergone previous surgical aortic valve replacement and were treated with the valve-in-valve procedure. Low-flow low-gradient severe AS was observed in 10% (n = 31) and bicuspid aortic valve in 6% (n = 18). The baseline characteristics of the included patients are summarized in table 1 and table 2. The Portuguese National TAVI registry included 2346 patients. Compared with our cohort, the national registry included more patients with NYHA FC > II (68% vs 51%; *P* < .01) and COPD (22% vs 12%; *P* < .01), whereas our center had a higher prevalence of chronic kidney disease (50% vs 38%; *P* < .01). The baseline characteristics of the Portuguese National TAVI Registry and a comparison with our cohort are shown in table 3.

Procedural characteristics

Most of our procedures were elective (83%; n = 249), while 17% (n = 51) were performed urgently following unplanned hospital admission for symptomatic severe AS. Cardiogenic shock was found in 5% (n = 15), and 4% (n = 12) required ventilatory support (table 3). Transfemoral access was used in 99% of cases (n = 298); the remaining 2 were performed via transcarotid and through an aortofemoral bypass graft route, both with surgical exposure by the vascular surgery team. Self-expandable valves were used in 95% of cases (n = 286), predominantly the Evolut family (Medtronic, United States) in 91%, n = 259, followed by Navitor (Abbott, United States) in 7% (n = 20) and Acurate (Boston Scientific, United States) in 2% (n = 6). The balloon-expandable valve Myval (Meril, India) was used in 5% (n = 14) (table 4).

Table 1. Baseline characteristics and comorbidities

Baseline characteristics	Values
Age, years	82 ± 5 [62-101]
Female sex, % (n)	54 (161)
STS score, %	3.75; IQR [2.29-6.55]
Low risk (STS < 4), % (n)	52 (156)
Intermediate risk (STS 4-8) %, (n)	31 (93)
High risk (STS > 8) % (n)	17 (51)
EuroSCORE, %	2.23 IQR [2.29-6.55]
Prior hospitalization due to AS, % (n)	21 (64)
Hypertension, % (n)	86 (258)
Diabetes mellitus, % (n)	35 (104)
Dyslipidemia, % (n)	71 (214)
eGFR < 60 mL/min/1.73m²	50 (50)
AF/flutter, % (n)	22 (65)
Pacemaker, % (n)	15 (46)
CAD, % (n)	21 (63)
Transthoracic echocardiogram	
Mean transaortic gradient (mmHg)	48 ± 14
Peak transaortic velocity (m/s)	4.3 ± 0.7
AVA (cm²)	0.74 ± 0.2
LVEF (%)	57 ± 12
LVEF < 40%, % (n)	12 (36)
LF/LG AS, % (n)	10 (31)
SPAP (mmHg)	38 ± 14
Significant aortic regurgitation, % (n)*	24 (71)
Significant mitral regurgitation, % (n)*	27 (83)
CCTA	
Aortic annulus perimeter, mm	74 ± 9
Aortic annulus area, cm²	4.3 ± 0.9
Aortic annulus diameter derived from perimeter, mm	23.3 ± 3.3
Aortic valve calcium score, UA	2912 ± 1572
Femoral artery min diameter, mm	7.1 ± 1.3
Bicuspid aortic valve, % (n)	6 (18)

Data is expressed as number (n) and standard deviation [ST]. Baseline characteristics, prevalence, and comorbidities, including transthoracic echocardiography and coronary computed tomography angiography (CCTA) findings from the total population.
AF, atrial fibrillation; AS, aortic stenosis; AVA, aortic valve area; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; eGFR, estimated glomerular filtration rate; LF/LG, low-flow low-gradient; LVEF, left ventricular ejection fraction; SAVR, surgical aortic valve replacement; SPAP, systolic pulmonary arterial pressure; STS, Society of Thoracic Surgeons.
* Significant valvular heart disease was defined as > grade 2.

Table 2. Baseline characteristics comparison between our cohort and the Portuguese TAVI registry

Baseline characteristics	Our center (n = 300)	National registry (n = 2346)	*P* value
Age, years	82 ± 5	81 ± 7	.6
Female sex, %	54	53	.8
STS risk score, % [IQR]	3.8 [2.3-6.6]	4.7 [3.0-7.1]	.7
EuroSCORE II risk, %	2.3 [1.6-4.0]	4.3 [2.5-7.1]	.3
NYHA class > 2, %	51	68	< .01
DM, %	35	33	.5
COPD, %	12	22	< .01
GRF < 60 mL/kg/m², %	50	38	< .01
AF, %	22	25	.3
PCI, %	14	23	< .01
Stroke, %	8	12	.06
TTE			
Mean gradient (mmHg)	48 ± 14	49 ± 16	.8
AVA (cm²)	0.72 ± 0.20	0.64 ± 0.20	.7
LVEF < 50, %	21	28	.08

Baseline characteristics comparison between our cohort and the National TAVI registry.[16]
AF, atrial fibrillation; AVA, aortic valve area; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; GFR, glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; TTE, transthoracic echocardiography.

Procedural and 1-month outcomes

The primary endpoint, 30-day mortality rate, was 3.7% (n = 11), while in-hospital mortality was 2% (n = 6). Survival at the end of the procedure was achieved in 99% of patients (n = 298). No patient required ECS. Two patients (0.7%) underwent transcathether pericardiocentesis for cardiac tamponade, one due to a self-contained left ventricular guidewire perforation that did not require ECS, and the other of undetermined cause, which persisted and ultimately required delayed exploratory cardiac surgery, resulting in postoperative death. No cases of aortic valvular annulus rupture, coronary obstruction, TAVI-in-TAVI deployment, or valve embolization occurred. Stroke occurred in 2.7% (n = 8), 1.6% of which (n = 5) were disabling, while major bleeding and vascular complications were each observed in 8%. Pacemaker implantation was required in 20% (n = 61) (table 4). A detailed description of procedural and early causes of death is shown in table S1.

Follow-up outcomes

The 1-year all-cause mortality rate was 12% (n = 36), and cardiac death, 4% (n = 12). A detailed description of the causes of death is provided in table S1. Readmission occurred in 17% (n = 51), including 32 cardiovascular and 19 non-cardiovascular events. A detailed description of the causes of readmission is provided in table S1. Among surviving patients with available data, 91% reported symptomatic improvement, assessed by the NYHA functional class (table 4).

Table 3. Clinical context and procedural characteristics

Clinical context	Values
Elective procedure, % (n)	83 (248)
Admitted prior to procedure, % (n)	17 (52)
Days until TAVI (if admitted), (days)	12 ± 8
Cardiogenic shock, % (n)	5 (15)
Invasive mechanical ventilation, % (n)	1.7 (5)
Non-invasive mechanical ventilation, % (n)	2.7 (8)
Significant coronary artery disease, % (n)	11 (33)
Pre-TAVI PCI, % (n)	7 (21)
Serum creatinine (mg/dL)	1.05 [0.86-1.41]
Hemoglobin (g/dL)	12.2 ± 1.9
NT-proBNP (pg/mL)	1865 [292-4250]
Evaluation time (days)	15 [3-54]
Waiting time (days)	59 [22-122]
Patient origin	
Our hospital area, % (n)	62 (185)
Our area of influence, % (n)	17 (53)
Outside our area of influence, % (n)	21 (63)
Procedural characteristics	
Femoral access, % (n)	99 (299)
Secondary access	
Radial, % (n)	10 (29)
Femoral, % (n)	90 (271)
Pre-dilation, % (n)	58 (175)
Valve type	
Self-expandable valves, % (n)	95 (286)
Evolut, % (n)	91 (260/286)
Acurate, % (n)	2 (6/286)
Navitor, % (n)	7 (20/286)
Balloon-expandable valves, % (n)	5 (14)
Myval, % (n)	100 (14/14)
Valve size (mm)	27.5 ± 3.0
Post-dilation, % (n)	38 (113)
Fluoroscopy time (min)	26 [21-33]
Contrast volume (mL)	216 [173-263]

Clinical context characteristics of the population and procedural characteristics. Data is expressed as percentage and number (n) unless otherwise indicated. LAD, left anterior descending coronary artery; LCx, left circumflex artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; TAVI, transcatheter aortic valve implantation.

Table 4. Procedural and follow-up outcomes

Procedural outcomes	Values
Procedural death, % (n)	0.7 (2)
In hospital death, % (n)	2 (6)
Stroke, % (n)	2.7 (8)
Emergency cardiac surgery, % (n)	0 (0)
Major bleeding, % (n)	8 (25)
Vascular complication, % (n)	8 (24)
Acute kidney injury, % (n)	6 (18)
Tamponade, % (n)	0.7 (2)
Length of ICU stay (days)	2 [2-3]
Length of stay (days)	3 [2-6]
In elective patients (days)	3 [2-5]
Follow-up outcomes	
1 month	
30-day mortality, % (n)	3.7 (11)
Permanent pacemaker implantation, % (n)	20 (61)
1 year	
1-year mortality, % (n)	12.4 (27/217)
Cardiac death, % (n)	4 (8/203)
Hospital readmission, % (n)	17 (51/300)
Symptomatic improvement, % (n)	91 (246/269)

Procedural and follow-up outcomes by VARC-3 Criteria.[15] Data with %, (n) are expressed as percentages and number. The variables with (days) are expressed as number of days and IQR. Major bleeding is defined as VARC-3 type 2-3: overt bleeding requiring medical intervention, hospitalization, or transfusion ≥ 1 unit of blood. Emergency cardiac surgery is any unplanned cardiac surgery needed to manage life-threatening complications during or shortly after the procedure, performed before the patient leaves the procedural setting. Vascular complications are arterial or venous injury, dissection, stenosis, ischemia, thrombosis, pseudoaneurysm, hematoma, distal embolization, or closure device failure related to access sites requiring intervention or resulting in clinical sequelae. Acute kidney injury is defined according to KDIGO criteria as an increase in serum creatinine ≥ 0.3 mg/dL within 48 hours or ≥ 1.5 times baseline within 7 days.

National TAVI registry comparison

Compared with the Portuguese TAVI national registry results available[16] (table 5), our center demonstrated a non-statistically significant lower 30-day mortality rate (3.7% vs 4.8%; OR, 0.8; 95%CI, 0.44–1.47; P = .5) and similar 1-year mortality rates (12% vs 11%; OR, 1.0; 95%CI, 0.76–1.47; P = .8) (figure 1). The rate of ECS was equivalent in both groups (0% vs 0.4%; P = .5), as were the rates of vascular complications (8% vs 6.8%; P = .4) and major bleeding (8.3% vs 13.3%; P = .2). Our stroke rate was numerically lower (2.7% vs 4.6%; P = .1), as was the rate of acute kidney injury (6% vs 4.2%; P = .5). Pacemaker implantation rates were similar (20% vs 19%; P = .7) (figure 2). However, 1-year hospitalization was more frequent in our cohort (17% vs 9.6%; P = .03).

DISCUSSION

This single-center study is the first national experience of TAVI in a non-on-site CS backup center. Our results suggest that this model

Table 5. Outcomes comparison between our center and the national registry

Outcome measure, % (n)	Our center (n = 300)	National registry (n = 2346)	Odds ratio 95%CI	*P*
30-day mortality	3.7 (11)	4.8 (110/2297)	0.8 [0.4-1.4]	.79
1-year mortality	12 (36)	11 (194/1706)	1.1 [0.6-1.5]	.86
Tamponade	0.7 (2)	1.0 (8/775)	0.6 [0.2-2]	.73
Coronary obstruction	0 (0)	1.8 (14/772)	NE	.09
Emergency cardiac surgery	0 (0)	0.4 (4/954)	0.8 [0.2-6.8]	.35
TAVI-in-TAVI	0 (0)	1.1 (8/725)	NE	.09
Vascular complication	8 (24)	7 (120/1766)	1.2 [0.9-1.6]	.43
Major hemorrhage	8 (25)	13 (273/2054)	0.6 [0.4-0.9]	.02
Stroke	2.7 (8)	4.6 (88/1893)	0.6 [0.3-1.2]	.14
AKI	6 (18)	4.2 (79/1892)	1.5 [0.9-2.1]	.46
Pacemaker implantation	20 (60)	19.0 (374/1964)	1.1 [0.9-1.3]	.69
Hospital readmission	17 (51)	10 (98/1017)	1.9 [1.3-2.8]	.03

Procedural and clinical outcomes comparison between our cohort and the TAVI National Registry.[16] Data is expressed as percentages. Acute kidney injury (AKI) is defined according to KDIGO criteria as an increase in serum creatinine ≥ 0.3 mg/dL within 48 hours or ≥ 1.5 times baseline levels within 7 days. 95%CI, 95% confidence interval; NE, not estimable; TAVI, transcatheter aortic valve implantation.

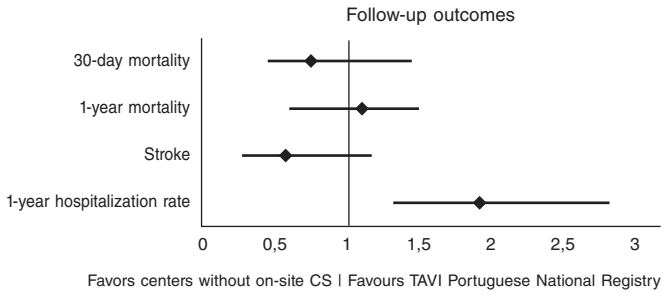

Figure 1. Forest plot comparing the odds ratios (OR) of primary endpoints between our center without on-site cardiac surgery (CS) backup and the national Portuguese TAVI registry[16] (all centers with on-site CS backup).

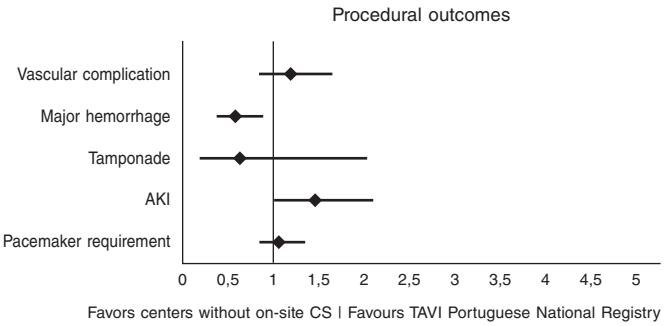

Figure 2. Forest plot of procedural outcomes comparing our center without on-site CS backup with the national Portuguese TAVI registry[16] (centers with on-site CS backup).

is feasible and safe, with outcomes comparable to those reported by national and international series, including centers with surgical backup. Our outcomes were similar across key endpoints vs the National Portuguese TAVI registry,[16] which includes only centers with surgical backup. Although no patients from our series required ECS, and 1 patient underwent delayed surgical intervention due to persistent pericardial effusion, the procedure was unsuccessful. This observation is consistent with other reports indicating that outcomes of emergency conversion after TAVI are generally poor, even in centers with surgical backup.[8,10]

TAVI safety and efficacy profile have improved significantly through careful procedural planning, the involvement of a multidisciplinary heart team (including cardiac surgery), and growing operator experience supported by technological advances. As a result, the need for immediate surgical backup has become increasingly less relevant. Although the complications that require surgical intervention remain rare, they are associated with high morbidity and mortality despite surgical management. Within this context, our results support the feasibility and suggest the non-inferiority of performing TAVI without on-site CS, reinforcing its applicability across various clinical scenarios, including younger individuals and those with multivalvular or coronary artery disease.

Our program reflects the contemporary TAVI landscape, including a heterogeneous and high-risk population with a significant proportion of emergency and unstable cases, including hospitalized patients and those in cardiogenic shock. In addition, we treated patients with complex anatomical and clinical characteristics such as valve-in-valve procedures, bicuspid aortic valves, reduced LVEF, and pulmonary hypertension. This all-comers profile mirrors the real-world spectrum that structured TAVI programs must address today, extending beyond elective transfemoral procedures for native AS.

Of note, our median waiting time for the procedure was short (59 days [IQR, 22-122]), and 20% of patients were referred from outside our direct hospital catchment area. This suggests that our center has become a regional reference for TAVI despite the lack of on-site CS, which reflects both the accessibility of our program and the trust placed in our heart team's expertise. Importantly, many of these patients were referred because traditional TAVI centers could not meet procedural demand promptly, highlighting our role in addressing unmet clinical needs within the region.

Our findings align closely with results from countries where TAVI is performed without on-site CS, including Spain,[11] Germany,[17] and Austria.[18] In Spain, the multicenter registry reported a conversion rate to open-heart surgery of 0.3% in centers without on-site CS backup.[11] The German AQUA registry, which included more than 17 000 patients, found no significant differences in outcomes between centers with and without CS, with a 30-day mortality rate of 3.8% in hospitals with visiting CS vs 4.2% in those with CS backup, with emergency surgery rates of 0.3% and 0.7%, respectively[17]. Similarly, a study from Austria has shown favorable outcomes in centers without on-site surgery, with no significant differences in in-hospital mortality or surgical conversion rates.[18] Our outcomes are consistent with these findings, with a 30-day mortality rate of 3.7% and no cases of ECS. Consistent with previous experiences from other countries, our results demonstrate equivalent and non-inferior results compared with centers that have on-site surgical backup.

Importantly, our study reflects a more recent era, with procedures performed in lower-risk patients, using the latest-generation devices, by more experienced operators, and following more precise preoperative planning with advanced CT imaging modalities. In addition, unlike earlier studies where visiting surgeons were present, our center performed all procedures without on-site surgical support, demonstrating the feasibility of a fully independent model. This study provides contemporary real-world evidence that TAVI can be safely and effectively performed in selected patients in centers without on-site CS backup, supporting broader access while maintaining quality standards.

Our study carries important policy implications. In the context of rising TAVI demand and resource constraints in high-volume surgical centers, decentralizing care to centers without on-site CS backup may enhance access without compromising patient outcomes. Our data supports the expansion of TAVI programs under carefully controlled conditions: standardized protocols, well-trained interventional teams, strong referral networks, and access to surgical support within a structured regional pathway. Regulatory agencies may consider revisiting existing requirements for on-site surgery, fostering a model where expertise guides the safe implementation of structural heart procedures while ensuring timely access to defined surgical centers for protocoled backup in case of delayed surgical needs.

These findings highlight the safety and viability of expanding TAVI programs to selected centers without surgical backup. With rigorous patient selection, experienced operators, and standardized procedural pathways, excellent outcomes can be achieved without immediate surgical support. Our experience supports a more inclusive structural heart care model that delivers timely and effective therapy to a broader patient population without compromising safety or efficacy.

Limitations

While these results are encouraging, several limitations must be acknowledged. First, this was a single-center, retrospective study, and although data collection was comprehensive, the potential for unmeasured confounding remains. Second, long-term follow-up beyond 1 year was unavailable, limiting conclusions on valve durability and late complications. Third, patient selection and procedural planning were guided by a highly experienced heart team, which may not be generalizable to all centers without surgical backup. Finally, although the baseline characteristics of our cohort and those of the Portuguese national registry (table 3) appear to be broadly comparable, result comparisons should be interpreted with caution, as no statistical adjustment was performed, the analysis was retrospective, and patients in the registry generally had a less favorable clinical profile.

CONCLUSIONS

Our study demonstrates that TAVI can be safely and effectively performed in centers without on-site CS backup, even in a heterogeneous, all-comers population. Outcomes appear broadly comparable and support the non-inferiority of this approach relative to centers with on-site CS. The risk of ECS was very low, and its incremental benefit may be limited, while CS centers remain few and frequently overburdened. These findings suggest that, with careful case planning and growing operator experience, expanding TAVI programs to selected non-CS centers is a safe and feasible strategy to address the growing demand and improve access for patients with severe AS. Randomized controlled trials are needed to confirm these results and guide broader implementation.

DATA AVAILABILITY

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This study was approved by *Hospital Espírito Santo de Évora* ethics committee, ULSAC. All procedures were performed in full compliance with the ethical standards of the center research committee and with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study. This study was conducted in full compliance with the SAGER guidelines. Sex and gender considerations were addressed appropriately, and any potential sex- or gender-related differences were assessed and reported where relevant.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

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

AUTHORS' CONTRIBUTIONS

A. Rocha de Almeida: conceptualization, methodology, data curation, formal analysis, investigation, original draft writing and review and editing of the final draft. R. Fernandes, Â. Bento, D. Neves, D. Brás, G. Mendes were in charge of original draft writing and review and editing of the final draft. R. Rocha, M. Paralta Figueiredo and R. Viana were in charge of data curation, reviewed and edited the final draft. R. Louro and Á. Laranjeira Santos were in charge of review and editing of the final draft. L. Patrício was in charge of conceptualization, supervision, review and editing of the final draft and validation. All authors read and approved the final draft.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- TAVI programs are recommended to be established in centers with on-site CS, as some complications may require emergency surgery.
- However, the rate of post-TACI ECS is consistently low, and the added clinical benefit of having immediate surgical backup is limited in contemporary practice.

WHAT DOES THIS STUDY ADD?

- This is the first national study to assess TAVI outcomes in a center without immediate on-site CS backup.
- Among 300 consecutive patients, 30-day mortality rate was comparable to national and international cohorts, and the need for ECS was 0% (n = 0).
- These findings support the safety and feasibility of performing TAVI in selected centers without on-site CS backup.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000549.

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Original article

How does major bleeding influence decision-making in patients eligible for transfemoral TAVI? A single-center experience

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ABSTRACT

Introduction and objectives: To evaluate the impact of bleeding on the risk-benefit balance of coronary revascularization prior to transfemoral transcatheter aortic valve implantation (TF-TAVI).
Methods: We conducted a retrospective analysis of the patients who underwent TF-TAVI at our center between 2008 and 2018 to evalute the management of coronary artery disease (percutaneous revascularization vs no revascularization). Subsequently, the rate of major bleeding —defined according to the Bleeding Academic Research Consortium (BARC) criteria (type 3-5)— and major adverse cardiovascular events (MACE) was compared between the 2 groups over a mean 60-month follow-up period.
Results: A total of 379 patients were included. The overall rate of major bleeding was 21.4%, higher in revascularized patients but without reaching statistical significance. The rate of major bleeding between coronary angiography and TF-TAVI implantation was 5.5% and significantly higher in revascularized patients (12.0% vs 3.5%; P = .07). During the hospitalization for TF-TAVI and throughout follow-up, the rate of major bleeding was 6.1% and 9.6%, respectively, with no significant inter-group differences. There were no significant differences either in the 5-year rate of MACE.
Conclusions: In our patient cohort, pre-TF-TAVI preoperative coronary revascularization was associated with an initially higher bleeding risk; however, no statistically significant differences were observed in major bleeding or MACE at the 5-year follow-up. These findings support the need to generate high-quality clinical evidence to demonstrate the net clinical benefit of coronary revascularization in this context.

Keywords: Transcatheter aortic valve implantation. Coronary revascularization. Bleeding.

¿Cómo influye un sangrado mayor en la toma de decisiones en pacientes candidatos a TAVI transfemoral? Experiencia de un centro

RESUMEN

Introducción y objetivos: Valorar el impacto del sangrado en la relación riesgo-beneficio de la revascularización coronaria previa al implante percutáneo de válvula aórtica por vía transfemoral (TAVI-TF).
Métodos: Se realizó un análisis retrospectivo de los pacientes tratados con TAVI-TF en nuestro centro entre los años 2008 y 2018, y se identificó la actuación sobre su enfermedad coronaria (revascularización percutánea frente a no revascularización). Posteriormente, se comparó entre ambos grupos la incidencia de sangrado mayor, definido por los criterios del *Bleeding Academic Research Consortium* (BARC) (tipos 3-5), y de eventos cardiovasculares adversos mayores (MACE) isquémicos durante un seguimiento medio de 60 meses.

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Resultados: Se incluyeron 379 pacientes. La incidencia total de sangrado mayor fue del 21,4%, más alta en los pacientes con revascularización, pero sin alcanzar la significación estadística. La incidencia global de sangrado mayor entre la coronariografía diagnóstica y el TAVI fue del 5,5%, y resultó significativamente más alta en los pacientes revascularizados (12,0% frente a 3,5%; p = 0,07). Durante el ingreso para el TAVI-TF y el seguimiento posterior de 60 meses, la incidencia global de sangrado mayor fue del 6,1% y del 9,6%, respectivamente, sin diferencias significativas entre ambos grupos. Tampoco hubo diferencias en la incidencia de MACE a los 5 años de seguimiento.
Conclusiones: En nuestra cohorte de pacientes, la revascularización coronaria previa al TAVI-TF conlleva un aumento inicial del riesgo de sangrado, sin diferencias estadísticamente significativas en sangrado mayor ni en MACE en el seguimiento a 5 años. Estos hallazgos apoyan la necesidad de generar una evidencia clínica de calidad que demuestre un beneficio clínico neto de la revascularización en este contexto.

Palabras clave: Implante percutáneo de válvula aórtica. Revascularización coronaria. Sangrados.

Abbreviations

MACE: major adverse cardiovascular events. **TF-TAVI:** transfemoral transcatheter aortic valve implantation.

INTRODUCTION

Currently, transfemoral transcatheter aortic valve implantation (TF-TAVI) is the treatment of choice for most patients with severe aortic stenosis, particularly those with high surgical risk or advanced age.[1] Several clinical trials have demonstrated comparable clinical outcomes between TF-TAVI and surgical aortic valve replacement.[2-4] Major and minor bleeding remain one of the most frequent procedural complications and are associated with higher morbidity and mortality rates.[5] Although, in recent years, improvements in materials (reduction in caliber required for valve implantation) and increasing operator experience have substantially reduced perioperative bleeding rates, such rates remain significantly high. One of the main risk factors for bleeding is the requirement for perioperative dual antiplatelet therapy,[6] most widely necessary when coronary revascularization is performed along with TAVI.

In addition, the high prevalence of coronary artery disease in patients undergoing TF-TAVI, reported in up to 80% of cases in published series, along with current clinical practice guideline recommendations to revascularize all ≥ 70% proximal coronary stenoses, results in a high rate of revascularization.[1]

Our group recently published data showing that systematic, complete revascularization in patients undergoing TF-TAVI does not provide prognostic benefit in terms of mortality or major adverse cardiovascular events (MACE) (a composite of death, myocardial infarction, stroke, and heart failure-related hospitalization.)[7] Given the high rate of bleeding events in these patients, it is of substantial clinical interest to evaluate whether revascularization may confer an increased bleeding risk and assess its clinical impact.[6]

METHODS

We conducted a retrospective study based on the historical cohort of patients who underwent TF-TAVI at our center from 2008 through 2018. Study information was drawn from the local database (Géminis) and supplemented by electronic health record review to document follow-up events. The study was approved by the Clinical Research Ethics Committee of A Coruña-Ferrol (Spain). The primary endpoint of the study was to compare the rate of major bleeding—defined according to the Bleeding Academic Research Consortium (BARC) criteria (types 3–5)—occurring after diagnostic coronary angiography, during the index hospitalization for TAVI, and during follow-up. Additional endpoints included the rate of MACE and the composite endpoint of MACE plus major bleeding over the same period of time, comparing patients who underwent percutaneous coronary revascularization with those managed conservatively.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation, and qualitative variables as proportions. We used the Student *t* test and analysis of variance (ANOVA) with first-order polynomial contrast for continuous variables. For categorical variables, we used the chi-square test for linear trend or Fisher's exact test as appropriate.

We conducted survival analyses using the Cox proportional hazards model to determine whether an association existed between coronary revascularization and patient prognosis in terms of mortality, MACE, major bleeding (BARC 3–5), and a composite of MACE and major bleeding. Results were expressed as age- and sex-adjusted survival curves.

Statistical analysis was performed with SPSS 26.0 (IBM, United States) and R version 4.1.3 (R Foundation for Statistical Computing, Austria). Statistical significance was set at $P < .05$ for all comparisons.

RESULTS

A total of 379 patients who underwent TF-TAVI between 2008 and 2018 were included. Four patients were lost to follow-up, leaving 375 patients for the statistical analysis. Table 1 illustrates the patients' baseline characteristics, with a mean age of 83.1 years and predominance of the female sex and intermediate surgical risk (Society of Thoracic Surgeons score, 4.3%). Although most baseline characteristics were well balanced between patients with and without revascularization, the latter had a slightly higher surgical risk (4.5% vs 3.5%) and a higher proportion of women (61.3% vs 47.8%).

Regarding symptoms, most patients were in New York Heart Association functional class III (74.7%). Among revascularized patients, 25.0% (23 patients) reported angina symptoms vs only 15.7% (41 patients)

from the nonrevascularized group. Regarding anticoagulant therapy, 29.2% (83 patients) from the nonrevascularized group were on vitamin K antagonists and 3.9% (11 patients) on direct oral anticoagulants. These rates were slightly lower among revascularized patients, with 23.1% (21 patients) on vitamin K antagonists and 3.3% (3 patients) on direct oral anticoagulants (table 1).

Table 1. Baseline characteristics of the patients

Variable	Nonrevascularized	Revascularized	Total	*P*
Age, years	84 (5.5)	82 (6.7)	83.1 (5.9)	.015
Female sex	176 (61.3%)	44 (47.8%)	220 (58.0%)	.022
Diabetes	83 (28.9%)	36 (39.1%)	119 (31.4%)	.066
Hypertension	219 (76.3%)	73 (79.3%)	292 (77.0%)	.546
Hypercholesterolemia	165 (57.5%)	65 (70.7%)	230 (60.6%)	.025
Body mass index	29.6 (5.2)	28.3 (5.5)	29.3 (5.3)	.032
Baseline hemoglobin (mg/dL)	12.1 (1.6)	11.8 (1.8)	12.1 (1.7)	.160
Creatinine clearance (mL/min)	55.7 (20.9)	53.6 (21.4)	55.2 (21.0)	.420
STS score	4.5% (2.5)	3.5% (3.8)	4.3% (2.9)	.002
EuroSCORE I	13.3% (7.8)	8.6% (5.2)	12.2% (7.5)	.001
EuroSCORE II	4.4% (3.4)	2.6% (1.9)	4.0% (3.2)	.001
Baseline LVEF	59.7% (13.2)	56.9% (13.5)	59.0% (13.3)	.083
Baseline Max PG (mmHg)	80.6 (25.0)	79.1 (22.2)	80.3 (24.4)	.602
Baseline Mean PG (mmHg)	47.1 (15.4)	47.2 (14.0)	47.1 (15.0)	.952
Baseline aortic regurgitation				.384
Grade 0	69 (24.2%)	23 (25.6%)	92 (24.3%)	
Grade 1	151 (53.0%)	54 (60.0%)	205 (54.0%)	
Grade 2	46 (16.1%)	11 (12.2%)	57 (15.0%)	
Grade 3	15 (5.3%)	1 (1.1%)	16 (4.2%)	
Grade 4	4 (1.4%)	1 (1.1%)	5 (1.3%)	
Angina symptoms	45 (15.7%)	23 (25.0%)	68 (17.9%)	.043
NYHA class				.278
0	1 (0.3%)	1 (1.1%)	2 (0.5%)	
1	41 (14.3%)	19 (20.7%)	60 (15.8%)	
3	221 (77.0%)	62 (67.4%)	283 (74.7%)	
4	24 (8.4%)	10 (10.9%)	34 (8.9%)	
Prior AMI	32 (11.3%)	21 (23.1%)	53 (14.0%)	.005
Prior CABG	18 (6.3%)	6 (6.6%)	24 (6.3%)	.931
Prior PCI	24 (8.5%)	75 (82.4%)	99 (26.1%)	.001
Stroke	26 (9.2%)	8 (8.9%)	34 (9.0%)	.932
Liver disease	8 (2.8%)	1 (1.1%)	9 (2.4%)	.351
COPD	39 (13.7%)	7 (7.7%)	46 (12.1%)	.126
Peripheral arterial disease	9 (3.1%)	5 (5.4%)	14 (3.7%)	.309
VKA therapy	83 (29.2%)	21 (23.1%)	104 (27.4%)	.254
DOAC therapy	11 (3.9%)	3 (3.3%)	14 (3.7%)	.801

AMI, myocardial infarction; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulants; LVEF, left ventricular ejection fraction; Max PG, maximum pressure gradient; Mean PG, mean pressure gradient; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; VKA, vitamin K antagonist.

Percutaneous revascularization and bleeding

Of the patients undergoing TF-TAVI, 92 (24.3%) underwent coronary revascularization, which in our center was always performed before valve replacement, with a median interval of 88 days (46–162) between revascularization and TAVI. Consequently, most revascularized patients were on dual antiplatelet therapy when they underwent TAVI. The decision to revascularize was made in a multidisciplinary meeting according to contemporary clinical practice guidelines (2008–2018). The prevailing strategy was to revascularize most coronary lesions, and the clinical criterion remained unchanged throughout the study period.

Clinical outcomes during follow-up are shown in table 2. There were no statistically significant differences in the time elapsed between diagnostic catheterization and TAVI between the 2 groups (median of 118 days for revascularized patients and 123 days for the nonrevascularized ones; P = .835). Figure 1 illustrates that the overall rate of major bleeding was 21.4% (81/375), with a rate of 28.3% (26/92) for revascularized patients and 19.0% (55/283) for the nonrevascularized ones, without reaching statistical significance (P = .074).

Table S1 illustrates the bleeding events classified by BARC criteria according to revascularization status during follow-up. The overall rate of major bleeding (BARC 3–5) between coronary angiography and TF-TAVI was 5.5% (21/375) and was significantly higher among revascularized patients (12.0% vs 3.5%; P = .007). During the index hospitalization for TF-TAVI, the overall rate of major bleeding was 6.1% (23/375), with no statistically significant differences between the 2 groups (8.7% vs 5.3%; P = .31). During post-TAVI follow-up, the overall rate of major bleeding was 9.6% (36/375), with no significant differences between the groups either (7.6% vs 10.2%; P = .545) (figure 1).

After a mean follow-up of 60 months, 55.1% (209/379) of patients experienced MACE: 55.7% in the nonrevascularized group (160 patients), and 53.2% in the revascularized group (49 patients). There were no statistically significant differences (P = .082) (figure 2). The overall mortality rate at 60 months was 42.2% (161/378): 43.7% in nonrevascularized patients (125 patients), and 39.0% in revascularized ones (36 patients). Again, no significant differences were reported (P = .380) (figure 3).

The revascularized group exhibited higher rates of myocardial infarction (11.5% vs 2.8%; P = .001) and repeat revascularization (6.5% vs 1.0%; P = .003).

After a mean 60-month follow-up, the composite endpoint (MACE or major bleeding) occurred in 62.0% (235 patients) of the total sample, without significant differences across the groups (66.3% nonrevascularized vs 60.6% revascularized; P = .139) (figure 4).

Table 2. Clinical outcomes during follow-up according to revascularization status

Clinical outcome	Nonrevascularized n (%)	Revascularized n (%)	Total, n (%)	*P*
Major bleeding (BARC 3-5)	55 (19.0%)	26 (28.3%)	81 (21.4%)	.074
MACE at 60 months	160 (55.7%)	49 (53.2%)	209 (55.1%)	.082
Pre-TAVI MACE	58 (20.4%)	25 (27.2%)	83 (22.1%)	NS
Mortality at 60 months	125 (43.7%)	36 (39.0%)	161 (42.2%)	NS
AMI at 60 months	8 (2.8%)	10 (11.5%)	18 (4.8%)	.001
Revascularization at 60 months	3 (1.0%)	6 (6.5%)	9 (2.4%)	.003
Composite endpoint	174 (60.6%)	61 (66.3%)	235 (62.0%)	.139

AMI, myocardial infarction; BARC, Bleeding Academic Research Consortium; MACE, major adverse cardiovascular events; NS, not significant; TAVI, transcatheter aortic valve implantation.

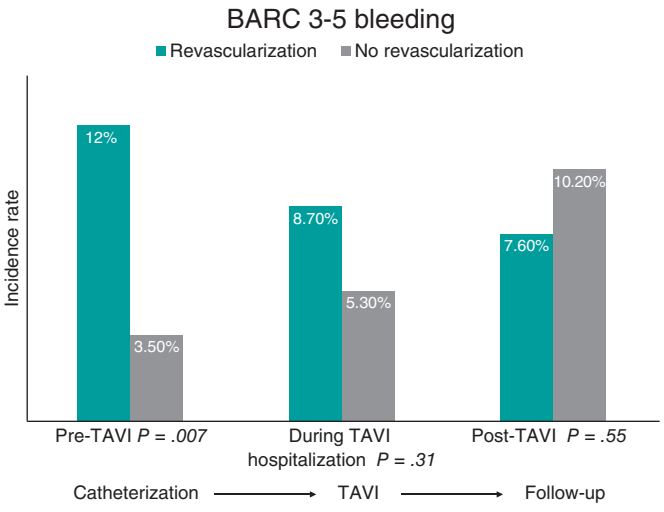


Figure 1. Central illustration. Overall rate of major bleeding across follow-up periods. BARC, Bleeding Academic Research Consortium; TAVI, transcatheter aortic valve implantation.

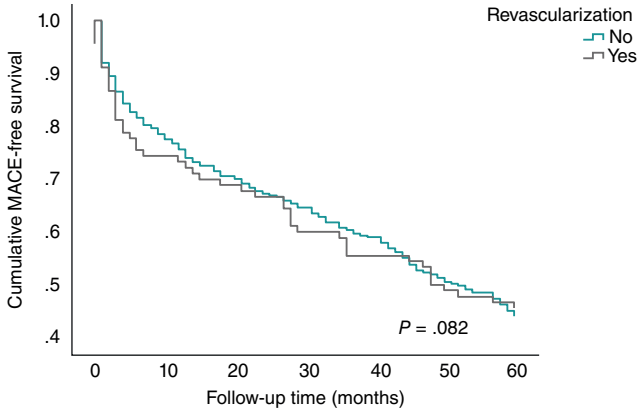
DISCUSSION

There is currently no definitive clinical evidence on the optimal management of coronary artery disease in patients scheduled for TAVI. Clinical guidelines recommend percutaneous revascularization in all patients undergoing TF-TAVI with percent diameter stenoses ≥ 70% in the target vessel proximal segments, with a Class IIa recommendation. However, to this date, only 2 randomized clinical trials have assessed the benefit of pre-TAVI revascularization, with conflicting results.[8,9]

Major bleeding remains one of the most frequent and prognostically relevant complications after TF-TAVI. In fact, in the PARTNER 2 trial conducted with intermediate-risk patients, major bleeding was reported in up to 15.2% of patients 1 year after TAVI.[3] Despite this, evidence on the impact of pre-TAVI coronary revascularization on bleeding risk is scarce.

In the ACTIVATION trial,[8] a total of 235 patients scheduled for TF-TAVI who had significant coronary artery disease were randomized to undergo percutaneous revascularization (n = 119) or receive optimal medical therapy (n = 116). Outcomes in the 2 groups were evaluated according to a composite primary endpoint of all-cause mortality and hospitalization. At 1 year, noninferiority of the strategy of adding percutaneous revascularization to TF-TAVI could not be demonstrated in patients who did not undergo revascularization; however, higher bleeding rates were observed in the intervention group.

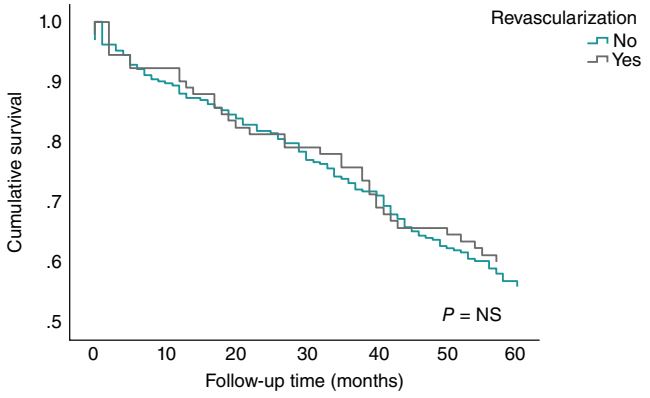
The results of the NOTION-3 trial[9] have been recently published. In this study, 452 patients scheduled to undergo TF-TAVI with



Number at risk according to revascularization status

No	286	224	201	184	167	145	115
Yes	91	68	63	55	51	46	42

Figure 2. Kaplan–Meier curve for MACE-free survival by revascularization status.



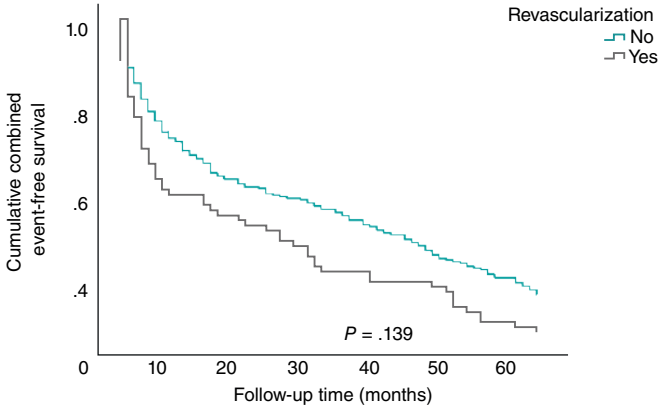
Number at risk according to revascularization status

No	286	256	240	222	202	176	123
Yes	91	83	75	71	64	59	42

Figure 3. Kaplan–Meier curve for overall survival by revascularization status.

significant coronary artery disease were randomized to receive either an invasive or a conservative strategy. In this case, the decision to revascularize was guided by the severity of stenosis as assessed by fractional flow reserve. Outcomes were evaluated according to a composite primary endpoint of all-cause mortality, myocardial infarction, and emergency revascularization. At 2 years, patients who had been revascularized showed a significant reduction in the risk of MACE compared with the conservative strategy (26.0% vs 36.0%), driven primarily by a higher rate of unplanned revascularization and without an effect on mortality. However, this risk reduction was accompanied by a higher rate of bleeding events (28.0% vs 20.0%). A major limitation of this trial is its open-label design and the fact that it did not exclude patients with angina, which may have contributed to the increased rate of unplanned revascularization.

In our study, there were no statistically significant differences in MACE or major bleeding at 60 months between revascularized and nonrevascularized patients. However, a higher rate of major bleeding occurred among the former during the time elapsed between diagnostic coronary angiography and TAVI, which is



Number at risk according to revascularization status

No	286	202	179	165	148	130	102
Yes	91	56	50	41	39	34	31

Figure 4. Kaplan–Meier curve for combined event–free survival (ischemic or hemorrhagic) by revascularization status.

consistent with former studies demonstrating higher bleeding rates in patients on dual antiplatelet therapy.[8,9] Furthermore, this group exhibited higher rates of myocardial infarction and subsequent revascularization. Although these findings were expected, they should be interpreted with caution because, despite statistically significant differences, the small number of events limits statistical power to draw definitive conclusions. A reasonable strategy may be selective revascularization aimed at symptom control, particularly in patients with angina.

Our study has several important limitations. The most significant one is that it is a single-center, observational, nonrandomized, retrospective analysis, which results in multiple sources of selection bias. First, a biological selection bias exists because the study includes patients who self-selected by surviving to a mean age of 83 years with sufficient biological status to be considered eligible for TF-TAVI. Second, a clinical selection bias is present regarding which patients were selected for TAVI, as the retrospective design makes it impossible to standardize the criteria originally used to determine candidacy. Finally, our cohort only includes patients in whom the procedure was ultimately performed—not those who initially underwent evaluation for TAVI—which means that some patients who underwent diagnostic cardiac catheterization (with or without revascularization) may not have proceeded to TAVI and are therefore not included. The proportion of such patients and the reasons for not completing the procedure are unknown. Although the causes may be diverse, given the procedural risks of coronary interventions and the frequent presence of complex coronary artery disease in this population, it is plausible that some candidates did not undergo TAVI because of revascularization-related complications; however, this cannot be demonstrated with our data and remains speculative. Moreover, this is a single-center study with a limited sample size, which may restrict the external validity of the findings and the statistical power to detect inter-group differences.

CONCLUSIONS

In our cohort, pre-TF-TAVI systematic coronary revascularization was associated with an increased early risk of major bleeding, specifically between diagnostic catheterization and valve implantation. There were no statistically significant differences in long-term

major bleeding, MACE, or the composite endpoint between revascularized and nonrevascularized patients. These findings, together with recent evidence indicating that revascularization of stable coronary disease does not clearly improve prognosis,[10] reinforce the need for high-quality clinical evidence to define the clinical impact of pre-TAVI systematic coronary revascularization.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

The study was approved by the Clinical Research Ethics Committee of A Coruña-Ferrol. Informed consent was not required due to the retrospective design of the study and use of a preexisting clinical database. SAGER guidelines were followed to minimize potential sex-related bias.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

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

AUTHORS' CONTRIBUTIONS

C. Vidau Getán contributed to data collection and manuscript drafting. D. López Vázquez was the main reviewer and contributed to refinement of statistical analysis. X. Flores Ríos conceived the study and conducted the initial statistical analysis. M. González Montes and G. González Barbeito participated in data collection. The remaining coauthors reviewed the final version of the manuscript. All authors gave their final approval.

CONFLICTS OF INTEREST

None declared.

WHAT IS KNOWN ABOUT THE TOPIC?

- Clinical practice guidelines recommend percutaneous revascularization in TAVI candidates with percent diameter stenoses ≥ 70% in the target vessel proximal segments.
- No high-quality evidence demonstrates a clinical benefit of systematic pre-TAVI coronary revascularization.
- Two clinical trials have been conducted in this patient population, with inconsistent results regarding the benefits observed in terms of ischemic events, and with a higher rate of bleeding events in revascularized patients.

WHAT DOES THIS STUDY ADD?

- Revascularized patients showed higher rates of early major bleeding (between diagnostic catheterization and TAVI), without significant long-term differences in ischemic or hemorrhagic events.
- Results support the need for robust evidence to clarify the clinical impact of systematic pre-TAVI coronary revascularization.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at: https://doi.org/10.24875/RECICE.M25000548.

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Original article

Optical coherence tomography for the diagnosis and management of stent thrombosis

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ABSTRACT

Introduction and objectives: Stent thrombosis (ST) is a rare but potentially fatal complication of percutaneous coronary interventions. With its high spatial resolution, optical coherence tomography (OCT) allows identification of underlying mechanical causes of stent thrombosis that may be overlooked by conventional angiography.
Methods: We conducted a prospective, single-center registry that consecutively included patients with a definitive diagnosis of ST who underwent OCT at the acute presentation. The presence of underlying mechanical abnormalities was assessed, and their likelihood as the primary cause of ST was determined. In-hospital and follow-up prognosis was evaluated.
Results: A total of 105 patients were included in the final analysis. Mechanical abnormalities were identified by the OCT in 87% of cases and deemed the most probable cause of ST in 77.1%. Findings varied significantly by timing of stent thrombosis: in acute cases, no mechanical abnormality was most common (41.8%); in subacute cases, stent underexpansion predominated (47.8%); in late cases, malapposition was most frequent (30.8%); and in very late cases, neoatherosclerosis was the leading cause (52%). However, no significant differences were found in relation to the type of stent involved. In all cases, treatment was tailored to correct the detected abnormality, with a new stent being implanted in 52% of patients. There were no OCT-related complications.
Conclusions: OCT is a safe and valuable tool in the assessment of ST as it allows the identification of distinct causative mechanisms according to timing of ST and helps optimize the management of patients experiencing this rare but serious complication.

Keywords: Optical coherence tomography. Stent thrombosis. Intracoronary imaging.

Tomografía de coherencia óptica en el diagnóstico y el tratamiento de la trombosis del *stent*

RESUMEN

Introducción y objetivos: La trombosis del *stent* (TS) es una complicación infrecuente del intervencionismo coronario, pero potencialmente letal. Su fisiopatología es multifactorial y en algunos casos no está bien esclarecida. La tomografía de coherencia óptica (OCT) ofrece una alta resolución espacial y permite identificar causas mecánicas subyacentes relacionadas con la TS que escapan a la angiografía convencional.
Métodos: Registro prospectivo unicéntrico que incluyó consecutivamente pacientes con diagnóstico de TS definitiva a los que se realizó OCT en el momento agudo. Se evaluó la presencia de anomalías mecánicas subyacentes y se estableció si podían considerarse la causa más probable de la TS. Se evaluaron el pronóstico intrahospitalario y la evolución clínica durante el seguimiento.
Resultados: Se incluyeron 105 pacientes. Se identificaron anomalías mecánicas por OCT en el 87% de los casos, y finalmente se establecieron como causa más probable de la TS en el 77,1%. Los hallazgos difirieron de manera significativa en función de la temporalidad de las TS: en las agudas, lo más frecuente fue no encontrar ninguna anomalía mecánica (41,8%); en las subagudas, predominó la infraexpansión del *stent* (47,8%); en las tardías, la mala aposición (30,8%), y en las muy tardías, la neoateroesclerosis (52%). En cambio, no se encontraron diferencias en los hallazgos de OCT en función del tipo de *stent* trombosado. En todos los casos se realizó un tratamiento dirigido a corregir la anomalía detectada, con implante de nuevo *stent* en el 52% de los pacientes. No se detectaron complicaciones relacionadas con la técnica de OCT.

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Conclusiones: La OCT es una herramienta segura y útil en el estudio de la TS. Permite identificar mecanismos causales específicos en función de la temporalidad y optimizar el tratamiento de los pacientes que sufren esta rara, pero grave, complicación.

Palabras clave: Tomografía de coherencia óptica. Trombosis del *stent*. Imagen intracoronaria.

Abbreviations

OCT: optical coherence tomography. **ST:** stent thrombosis.

INTRODUCTION

Technological advances in coronary intervention, particularly the development of new-generation drug-eluting stents, have transformed the treatment of ischemic heart disease by effectively reducing restenosis and improving clinical outcomes for the patients.[1] Nonetheless, stent thrombosis (ST) remains a rare but devastating complication, with an associated mortality rate of up to 40%.[2] Its pathophysiological mechanisms are complex and multifactorial, involving patient-related factors, implantation technique, stent type, and the natural progression of the disease.[3]

Traditionally, coronary angiography has been the tool of choice for assessing potential complications after stent implantation. However, its inability to adequately visualize the interaction between the stent and the vessel wall limits its diagnostic utility. In this context, optical coherence tomography (OCT), owing to its excellent spatial resolution, enables in vivo identification of underlying mechanical abnormalities that may be responsible for or contribute to ST.

The primary endpoint of this study was to evaluate the role of OCT in characterizing the mechanisms involved in ST, analyzing its feasibility, safety profile, therapeutic implications, and potential to optimize revascularization strategies in this complex clinical setting. Preliminary findings from this study were reported previously,[4] and the final results are presented herein.

METHODS

Study population

We conducted a prospective, single-center registry that consecutively included patients with a diagnosis of definite ST, as defined by Academic Research Consortium criteria, from October 2013 through December 2022 at *Hospital Universitario de La Princesa* (Madrid, Spain). Throughout this period, stents were implanted in 6881 patients. Patients with severe hemodynamic instability or lesions inaccessible with the OCT catheter were excluded.

We applied a systematic protocol that included OCT acquisition before and after treatment. If antegrade flow was not restored after crossing the lesion with the guidewire, thrombus aspiration was recommended; furthermore, when TIMI grade 0–1 flow persisted, inflation of a balloon < 2 mm in diameter at low pressure was recommended to avoid distortion of the underlying lesion. The final treatment strategy for ST was left to the operator's discretion.

ST was classified based on the interval since implantation as acute (< 24 h), subacute (24 h to 30 d), late (30 d to 1 y), or very late (> 1 y). Stents were categorized as bare-metal, first-generation drug-eluting, new-generation drug-eluting, or bioresorbable stents.

We performed prospective clinical follow-up to assess in-hospital mortality and, after discharge, a composite of cardiac death, recurrent myocardial infarction, recurrent ST, or repeat culprit vessel revascularization.

The study protocol was approved by *Hospital Universitario de La Princesa* Ethics Committee, and all patients gave their prior written informed consent before being included in the study.

OCT acquisition and analysis

OCT systems available at the time (Dragonfly, St. Jude Medical, and OPTIS AptiVue, Abbott) were used. Images were acquired with a nonocclusive technique and a contrast volume of 15 mL at a rate of 5 mL/s for the left coronary system and 12 mL at a rate of 4 mL/s for the right coronary artery. The analyzed segment included the stent and 10 mm adjacent to its edges. Poor-quality studies due to insufficient flushing or artefacts were excluded. Additionally, we performed a cross-sectional morphometric analysis, including minimum lumen area, minimum and maximum stent area, reference areas and diameters, stent expansion index (minimum stent area / mean reference area ×100), thrombus burden (length and area), and malapposition (axial distance from the strut surface to the lumen border greater than the strut thickness [significant if > 200 µm]).[5] Struts directly exposed to the vessel lumen were classified as uncovered. Neoatherosclerosis was defined as neointimal changes including lipidic, fibro-lipidic, or calcified tissue. Plaque rupture was assessed too. The presence of edge dissection (separation of vascular tissue extending into the media, ≥ 2 mm in length and > 60°)[6] or stent edge disease (ruptured lipid plaque adjacent to the stent edge, due to incomplete coverage or disease progression)[7,8] was evaluated.

Primary endpoint: mechanical abnormalities and dominant finding

We analyzed the presence of mechanical abnormalities and identified a dominant finding for each case. When multiple abnormalities coexisted, we defined the dominant finding as the one prevailing in the area with the greatest thrombus burden.[9] Potentially causative mechanical abnormalities included edge dissection, underexpansion, severe malapposition, edge disease progression, neoatherosclerosis, and uncovered struts (for late and very late ST). Furthermore, we recorded the absence of mechanical abnormalities. The dominant finding was, then, assessed as the potential main cause of ST, after excluding other possible causes, such as inadequate antiplatelet therapy or prothrombotic clinical conditions. Predictors of neoatherosclerosis and plaque rupture in very late ST were also studied.

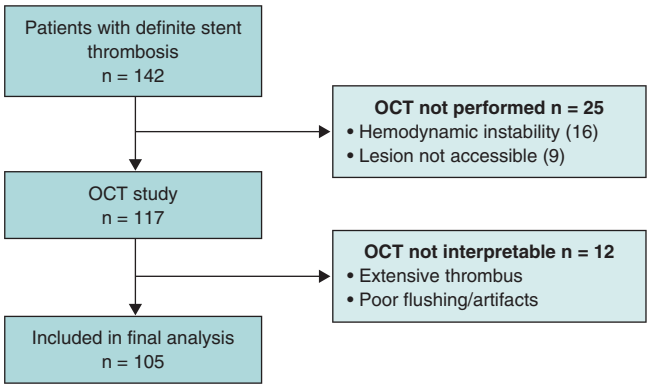

Figure 1. Flowchart of patient inclusion in the study. OCT, optical coherence tomography.

Statistical analysis

Statistical analysis was performed using R software. Continuous variables were expressed as mean (SD) or median (interquartile range, P25–P75) and compared using the Student *t* test or Wilcoxon test. For comparisons across more than 2 groups, ANOVA or Kruskal–Wallis tests were used. Categorical variables were compared using the chi-square test or Fisher's exact test. Logistic regression models were applied to identify possible predictors of in-hospital mortality, and Cox regression models were used for post discharge events. Survival analyses were performed with Kaplan–Meier curves and log-rank tests. Statistical significance was defined as $P < .05$.

RESULTS

Clinical and angiographic characteristics

A total of 142 patients with a diagnosis of definite ST were registered, 105 of whom were included in the final analysis (figure 1). A total of 17 cases of acute ST (16%), 23 cases of subacute ST (22%), 13 cases of late ST (12%), and 52 cases of very late ST (50%) were reported. The baseline patient characteristics based on the ST timing (acute/subacute vs late/very late) are shown in table 1. The most common presentation was ST-segment elevation myocardial infarction (81.9%), and the most frequently affected vessel was the left anterior descending coronary artery (42%). Most thrombosed devices were new-generation drug-eluting stents (53.3%), followed by bare-metal stents (28.6%), first-generation drug-eluting stents (13.3%), and bioresorbable scaffolds (4.8%). Bare-metal stents were significantly more common in late/very late ST, whereas new-generation drug-eluting stents and bioresorbable scaffolds were more common in acute/subacute ST. For ST treatment, drug-eluting stents and drug-coated balloons were used significantly more often in late and very late ST, whereas glycoprotein IIb/IIIa inhibitors and balloon optimization were more frequently employed in acute and subacute ST.

OCT analysis

No complications related to the OCT technique were observed. Morphometric and stent–vessel wall interaction data are shown in table 2. A total of 24 834 cross-sections were evaluated, of which 1453 (5.8%) could not be analyzed because of abundant residual thrombus.

Table 1. Baseline, angiographic, and procedural characteristics of the study population

Variables	Overall n = 105 (%)	Acute/ subacute ST n = 40 (%)	Late/very late ST n = 65 (%)	*P*
Age, years	65.8 ± 11.8	49	82	–
Male sex	89 (84.8)	30 (76.9)	59 (89.4)	.150
Risk factors				
Smoking	47 (44.8)	16 (41)	31 (47)	.697
Hypertension	68 (64.8)	25 (64.1)	43 (65.1)	1.0
Dyslipidemia	69 (65.7)	19 (48.7)	50 (75.7)	.009
Diabetes mellitus	28 (26.7)	10 (25.6)	18 (27.8)	1.0
Previous treatment				< .001
Dual antiplatelet therapy	45 (40.9)	32 (80)	13 (20)	
Single antiplatelet therapy	53 (50.5)	7 (18)	46 (69.7)	–
None	5 (3.8)	0	5 (7.6)	–
Clinical presentation				< .001
STEMI	83 (81.9)	34 (85)	49 (75.3)	
Killip-Kimball class IV	14 (13.3)	5 (12.8)	9 (13.6)	–
Stents analyzed	105	40	65	< .001
Bare-metal stent	30 (28.6)	6 (15.4)	24 (36.4)	–
First-generation DES	14 (13.3)	1 (2.6)	13 (19.7)	–
New-generation DES	56 (53.3)	29 (72.5)	27 (41.5)	–
Bioresorbable scaffold	5 (4.8)	4 (10.3)	1 (1.5)	–
Type of treatment				< 0.001
Conservative	6 (5.7)	2 (5.3)	2 (3.1)	–
Standard balloon (SC/NC)	24 (22.9)	13 (34.2)	11 (16.9)	–
Drug-coated balloon	4 (3.8)	0	4 (6.1)	–
Drug-eluting stent	52 (49.5)	12 (30)	40 (61.5)	–
Bioresorbable stent	3 (2.9)	0	3 (4.6)	–
NC balloon + GP IIb/IIIa inhibitor	12 (11.4)	10 (26.3)	2 (3.1)	–

DES, drug-eluting stent; NC, non-compliant; SC, semi-compliant; ST, stent thrombosis; STEMI: ST-segment elevation myocardial infarction.

There were no differences in underexpansion rates based on the type of thrombosis, and only a minimum stent area < 4.5 mm^2 was observed in subacute ST. The number of uncovered struts decreased significantly over time (although 30% of stents still exhibited uncovered struts at the 1-year follow-up), as did thrombus burden and malapposition (figure 2). Additionally, we analyzed these findings by stent type (table 3), showing that uncovered or malapposed struts were more frequent in drug-eluting stents than in bare-metal stents.

Table 2. Morphometric analysis and stent–vessel wall interaction according to type of stent thrombosis

Variables	Acute ST (n = 17)	Subacute ST (n = 23)	Late ST (n = 13)	Very late ST (n = 52)	*P*
Thrombus					
Fr with thrombus per stent, %	68.8 ± 24	61.7 ± 21	37.1 ± 27.9	42.6 ± 24.3	< .001
Maximum thrombus area, mm^2	4.38 ± 1.72	3.12 ± 1.82	2.5 ± 1.6	2.0 ± 1.4	< .001
Maximum length, mm	22.9 ± 30	15.35 ± 19	8.4 ± 5.8	7.9 ± 4.7	< .001
Malapposition					
Fr with malapposition per stent, %	13.3 ± 14	9.3 ± 9	11.4 ± 11.5	2.3 ± 5.9	< .001
Maximum area, mm^2	0.48 ± 0.54	0.61 ± 0.7	1.29 ± 1.5	0.42 ± 1.21	< .001
Maximum strut length, mm	3.11 ± 3.99	1.92 ± 2.12	2.26 ± 2.3	0.6 ± 1.31	< .001
Stents with at least 1 Fr with malapposition, %	13 (76.5)	17 (73.9)	10 (76.9)	10 (19.2)	< .001
Coverage					
Fr with uncovered struts, %	88.2 ± 27.5	77.9 ± 30.6	21.3 ± 28.5	3.37 ± 11.42	< .001
Maximum length of uncovered struts, mm	19.3 ± 11.6	16.1 ± 8.5	5.1 ± 8.6	1.6 ± 5.3	< .001
Stents with at least 1 uncovered Fr, %	17 (100)	22 (95.6)	10 (76.9)	15 (28.8)	< .001
Neoatherosclerosis					
Fr with neoatherosclerosis per stent, n	0	0	3.1 ± 2.9	41.1 ± 47.8	< .001
Stents with at least 1 Fr with neoatherosclerosis, n	0	0	3 (23)	78	< .001
Expansion					
Mean reference area, mm^2	7.74 ± 2.15	5.76 ± 2.41	7.46 ± 2.29	6.19 ± 2.09	.012
Minimum stent area, mm^2	6.98 ± 2.06	4.35 ± 1.53	6.09 ± 2.03	5.6 ± 1.89	< .001
Expansion index, %	91.78 ± 21	86.9 ± 42.6	84 ± 19.9	95.21 ± 32.4	0.48
Expansion index < 80%, n (%)	6 (35.3)	12 (52.1)	5 (38.5)	17 (33.3)	0.1

Fr, frames; ST, stent thrombosis.

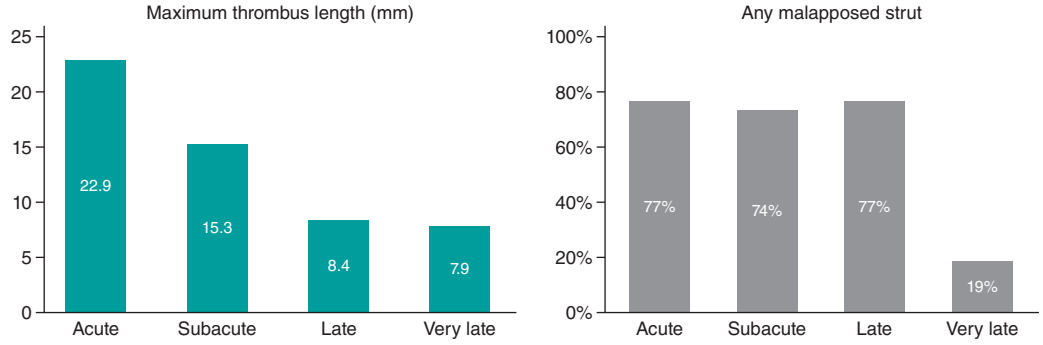

Figure 2. Morphometric findings over time.

Primary endpoint

Underlying mechanical abnormalities were identified in 91 of 105 patients (86.7%). Of these, 10 patients also had documented nonadherence to antiplatelet therapy in the days preceding ST; therefore, a mechanical abnormality was considered the most likely single cause in 81 patients (77.1%). The global distribution of dominant findings is shown in figure 3, and representative examples of ST cases in figure 4.

The dominant finding varied significantly by ST timing ($P < .001$) (table 4). In acute ST, the most frequent result was no identifiable abnormality (41.2%), and the dominant finding was stent-edge dissection (23.5%); in subacute ST, it was underexpansion (47.8%); in late ST, malapposition; and in very late ST, neoatherosclerosis (52%). However, there were no significant differences by stent type ($P = .07$): in bare-metal and first-generation drug-eluting stents, the most common abnormality was neoatherosclerosis (46.7% and 35.7%, respectively), whereas in new-generation drug-eluting

Table 3. Morphometric analysis according to stent type

Variables	Bare-metal stent (n = 30)	First-generation DES (n = 14)	New-generation DES (n = 56)	Bioresorbable scaffold (n = 5)	*P*
No. of Fr with uncovered struts	29.4 ± 64	27.8 ± 87	130.6 ± 128.6	121.8 ± 89.4	< .001
Stents with at least 1 uncovered strut, %	10 (33)	6 (42)	42 (75)	5 (100)	< .001
No. of frames with thrombus per stent	82.3 ± 44	100.9 ± 51	134.4 ± 83.2	73.4 ± 59.7	.022
Stents with at least 1 malapposed strut, %	6 (20)	5 (35.7)	36 (64.3)	3 (60)	< .001
Stents with expansion < 80%, %	20.7	0.5	44.6	0.4	.104
Stents with neoatherosclerosis, %	17 (56.7)	7 (50)	16 (28.6)	0	.013

DES, drug-eluting stent; Fr, frames.

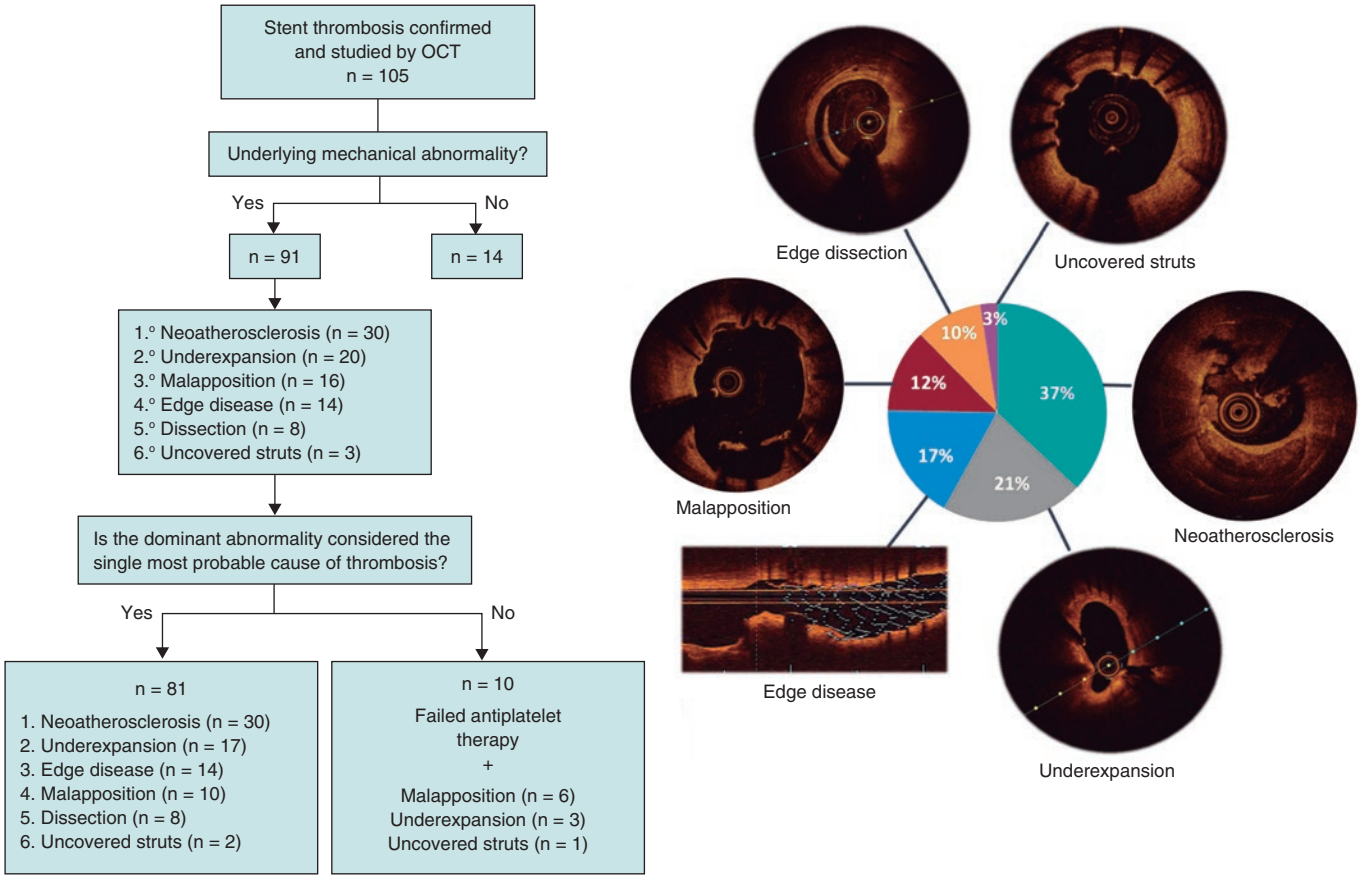

Figure 3. Central illustration. Assignment of the dominant finding and most likely cause of stent thrombosis. OCT, optical coherence tomography.

stents, underexpansion predominated (26.8%). In very late ST, neoatherosclerosis was the most common finding in both bare-metal and drug-eluting stents (56.7% vs 50%; *P* = .45), regardless of whether thrombosis occurred within 5 years or later after stent implantation. Five cases of bioresorbable scaffold thrombosis were recorded whose specific findings have already been reported previously.[10]

Neoatherosclerosis and plaque rupture

Neoatherosclerosis was identified in 40 patients, regardless of whether it was the dominant finding. There were no differences in baseline characteristics between patients with and without neoatherosclerosis, although those with neoatherosclerosis had larger minimum stent areas, smaller minimum lumen areas, and fewer uncovered and malapposed struts (table S1). Minimum lumen area was the only factor associated with a higher risk of neoatherosclerosis (odds ratio [OR], 0.39; 95% confidence interval [CI], 0.16–0.75; *P* = .013).

Plaque rupture was reported in 16 patients with neoatherosclerosis. There were no differences in baseline characteristics or in the composition of neoatherosclerosis between patients with and without plaque rupture (table S2). Despite the limited sample size, minimum lumen area was identified as a protective factor against

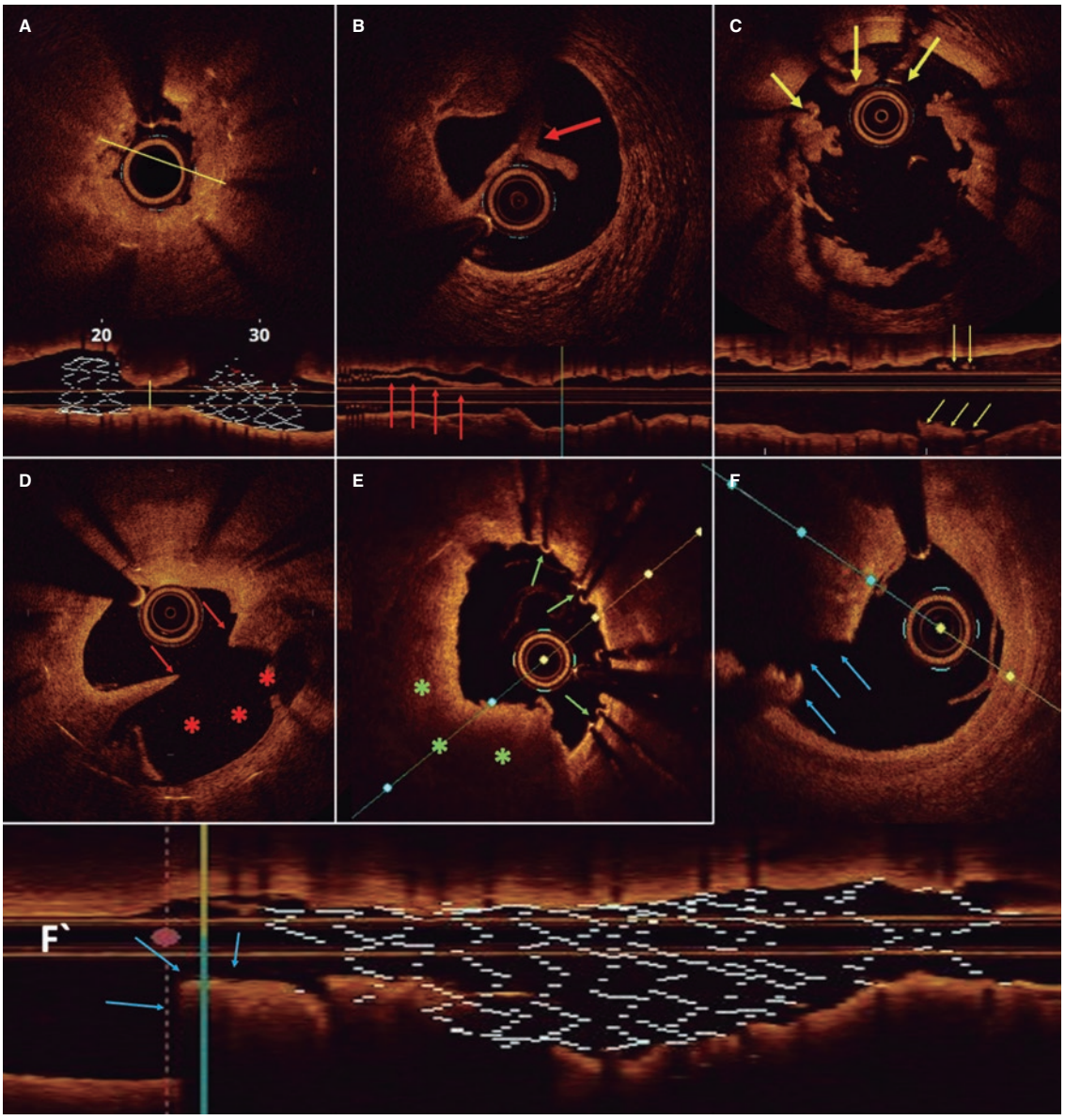

Figure 4. Representative optical coherence tomography findings. **A:** longitudinal and cross-sectional views of a stent with marked underexpansion (the line indicates minimum diameter). **B:** stent-edge dissection. Arrow indicates separated tissue flap from the vessel wall. **C:** malapposition. Arrows indicate struts associated with thrombus that are not in contact with the vessel wall. **D:** neoatherosclerosis with plaque rupture. Arrows indicate intimal discontinuity, and asterisks show the evacuated plaque cavity. **E:** uncovered struts (arrows). **F** and **F':** cross-sectional and longitudinal views of a stent with distal edge disease and plaque rupture (arrows).

plaque rupture (OR, 0.22; 95%CI, 0.04–0.7; $P = .035$). The presence of neovessels or calcium inside the stent was not associated with plaque rupture, nor was stent type.

Clinical follow-up

The in-hospital mortality rate for the overall cohort was 9.2%, with no significant differences being reported between patients who did and did not undergo OCT (8.5% vs 11%; $P = .7$). The main predictors of mortality were chronic kidney disease (OR, 9.56; 95%CI, 2.28–41.14; $P = .002$) and Killip-Kimball class III/IV status (OR, 14.8; 95%CI, 3.38–79.6; $P = .001$).

A total of 28 composite endpoints were recorded at the follow-up (median, 2143 days [15–2906]). Event-free survival rates at 1 and 5 years were 83.3% and 73.1%, respectively. There were 13 deaths at the follow-up. Estimated survival rates were 96% and 86.7% at 1 and 5 years, respectively (figure S1).

DISCUSSION

ST remains a serious complication with a high mortality rate.[11] Understanding its pathophysiology is essential for improving prevention, diagnosis, and eventually treatment.[12] In this context, OCT provides crucial real-time information, allowing for much more precise diagnosis and individualized treatment.

This study represents the largest national series of ST cases evaluated with OCT. The main findings are 1) the use of OCT in the

Table 4. Dominant findings according to timing of stent thrombosis and stent type

Dominant finding	Acute ST (n = 17)	Subacute ST (n = 23)	Late ST (n = 13)	Very late ST (n = 52)
Edge dissection	4 (23.5)	4 (17.4)	0	0
Underexpansion	2 (11.8)	11 (47.8)	1 (7.7)	6 (11.5)
Malapposition	3 (17.6)	3 (13.0)	4 (30.8)	6 (11.5)
Neoatherosclerosis	0	0	3 (23.1)	27 (52.0)
No finding	7 (41.8)	3 (13.0)	1 (7.7)	3 (5.7)
Edge disease	1 (5.9)	2 (8.7)	2 (15.4)	9 (17.3)
Uncovered struts	0	0	2 (15.4)	1 (2.0)
Dominant finding	**Bare-metal stent (n = 30)**	**First-generation DES (n = 14)**	**New-generation DES (n = 56)**	**Bioresorbable scaffold (n = 5)**
Edge dissection	2 (6.7)	0	5 (8.9)	1 (20.0)
Underexpansion	2 (6.7)	2 (14.2)	15 (26.8)	1 (20.0)
Malapposition	5 (16.7)	3 (21.4)	8 (14.3)	0
Neoatherosclerosis	14 (46.7)	5 (35.7)	11 (19.6)	0
No finding	1 (3.3)	2 (14.3)	9 (16.1)	2 (40.0)
Edge disease	6 (20.0)	1 (7.1)	6 (10.7)	1 (20.0)
Uncovered struts	0	1 (7.1)	2 (3.6)	0

DES, drug-eluting stent; ST, stent thrombosis.

acute phase of ST is safe and feasible in experienced centers; 2) OCT identified mechanical abnormalities in 86.7% of ST cases; 3) the dominant finding varied according to the timing of ST (in acute ST, no mechanical abnormality was most common, while underexpansion predominated in subacute ST, malapposition in late ST, and neoatherosclerosis in very late ST); 4) OCT enabled treatment guidance based on the dominant finding and might reduce the need for additional stenting; and 5) in-hospital mortality rate was low (9.2%), with Killip-Kimball class IV and chronic kidney disease being the main predictors.

An adequate-quality OCT study was achieved in 74% of patients, which is a rate considerably higher than that reported by the main European registries.[9,13] Although thrombus can limit visibility, image quality can be improved with thrombus aspiration or the use of catheter extension systems. Unlike other studies in which OCT was performed in a procedure separate from the index ST, our study conducted OCT during the acute event, representing a key methodological strength.

OCT demonstrated a remarkable ability to detect mechanical abnormalities (86.7%). In this setting, the information provided by angiography is insufficient. In the PESTO trial,[13] angiography identified the cause of ST in only 12% of cases, whereas OCT did so in more than 90% of the cases. The CLI-OPCI trial[14] was the first to demonstrate that OCT provides information on immediate stent outcomes not appreciable on angiography, prompting additional interventions in up to one-third of patients.

Although some findings are consistent with the PRESTIGE study,[9] our analysis provides relevant nuances. In particular, in acute ST, most cases showed no evident mechanical abnormalities (unlike our preliminary results, in which malapposition predominated). This finding reinforces the role of antithrombotic treatment and prothrombotic states as key factors, supported by the greater thrombus burden observed in early vs late ST. Unlike previous studies, our results emphasize the utility of OCT not only in identifying mechanical causes but also in avoiding unnecessary interventions, thereby underscoring the importance of optimal medical therapy. In addition, in our study, uncovered struts were not considered a cause of acute or subacute ST, based on the assumption that no stent is covered by neointima within the first 30 days.

The association between acute malapposition and ST remains controversial.[15-17] A possible explanation is that although malapposition is almost ubiquitous after stent implantation,[18,19] its relationship with thrombosis is difficult to establish because of the low probability of a later event.

Underexpansion, however, is established as one of the most important predictors of ST. In the CLI-OPCI study,[20] a minimum lumen area > 4.5 mm^2 was identified as a threshold for discriminating events during follow-up. This cutoff value is not achievable in small vessels and does not apply to left main lesions. Relative expansion[6,21] may thus be a more appropriate measure, although its superiority over absolute expansion in predicting events has not yet been established.

In late ST, malapposition was the most common finding. Most cases of nonsevere acute malapposition resolve during follow-up, although up to 30% may persist.[18] One study[22] reported substantially lower rates of malapposition (8%) than those observed in previous large registries,[9,13] likely because the index implantation was image-guided; this also supported that 75% of cases represented acquired malapposition.

Neoatherosclerosis was detected in most late and very late ST, irrespective of stent type, unlike other studies in which it predominated in drug-eluting stents. This may be explained by the longer interval between implantation and thrombosis in bare-metal stents, which is consistent with the observation that follow-up duration is the most important predictor of neoatherosclerosis.[23] The use of

OCT avoided unnecessary new stenting in 48% of patients, a higher rate compared with other ST series without image guidance[24] and even higher than in the PRESTIGE registry.[9]

Limitations

The present study has several limitations: 1) the absence of a control group precludes predictive evaluation of certain findings such as malapposition, and superiority of OCT over non–intracoronary image-guided interventions cannot be definitively established; 2) no core laboratory was used for OCT analysis, which may limit external reproducibility; 3) selection bias exists due to exclusion of the most severe patients and those with complex anatomy, which may account for favorable outcomes and could influence the prevalence of some mechanisms; 4) ST is a multifactorial process, and the dominant finding cannot be considered the definitive cause; 5) the presence of thrombus hampers evaluation of underlying structures; 6) the index stent implantation was not image-guided, preventing differentiation between acute and acquired malapposition; and 7) serial OCT studies were not performed in many patients, which means that correction of the detected abnormality could not be assessed.

CONCLUSIONS

OCT is a safe, feasible, and highly useful tool for the treatment of ST. It allows identification of the most likely cause of the event in most cases—which varies according to the timing of thrombosis—and enables individualized treatment by addressing the underlying abnormality.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This study was approved by *Hospital Universitario de La Princesa* Ethics Committee. All procedures conformed to the ethical principles of the Declaration of Helsinki. This study followed the SAGER guidelines. Written informed consent for publication was obtained and archived.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

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

AUTHORS' CONTRIBUTIONS

All authors contributed equally to the conception, design, and analysis of the study, as well as to drafting and revising the manuscript. Furthermore, all authors approved the final version and are responsible for its content.

CONFLICTS OF INTEREST

F. Alfonso is Associate Editor of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The remaining authors declared no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- ST is a rare but clinically significant complication, characterized by high mortality, recurrence, and a complex, multifactorial pathophysiology. A thorough understanding of its underlying mechanisms is essential to guide appropriate preventive and therapeutic strategies.

WHAT DOES THIS STUDY ADD?

- This study is the largest national series of consecutive ST cases evaluated with OCT and demonstrates the ability of this imaging modality to detect underlying mechanical abnormalities potentially involved in the pathogenesis of this serious complication.
- Mechanical abnormalities associated with ST vary significantly according to timing of presentation.
- Improving stent implantation technique could reduce the rate of ST by addressing causes such as malapposition and underexpansion.
- The use of OCT during ST treatment allows procedures to be guided and optimized.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000540.

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Original article

VerifyNow in acute coronary syndrome: design of the EPIC17-VERONICA trial to optimize platelet inhibition

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ABSTRACT

Introduction and objectives: De-escalation from prasugrel and ticagrelor to clopidogrel in patients undergoing percutaneous coronary intervention after acute coronary syndrome (ACS) is a strategy aimed at reducing bleeding. This study evaluates whether VerifyNow (Werfen, Spain)–guided de-escalation, based on platelet aggregation measurement, provides a therapeutic benefit in ACS management.
Methods: This ongoing multicenter, prospective, randomized 1:1 trial will enroll 634 patients with ACS who underwent revascularization with a sirolimus-eluting stent and were discharged on dual antiplatelet therapy with ticagrelor or prasugrel. Only those patients with a very low platelet reactivity level (platelet reactivity units ≤ 30) based on VerifyNow 1 month after discharge will be included. The primary endpoint is a composite of cardiovascular death, nonfatal acute myocardial infarction, nonfatal stroke, and bleeding at 1-year follow-up.
Results: The EPIC17-VERONICA study (NCT04654052) will reveal the efficacy profile of the de-escalation strategy, based on the VerifyNow platelet aggregation test, and determine the role of this device in the selection of patients who are eligible to benefit from this strategy.
Conclusions: This study will determine whether platelet function testing provide clinical benefit in the management of patients with ACS.

Keywords: Acute coronary syndrome. Antiplatelet therapy. Platelet function test. Bleeding.

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Ensayo VerifyNow para optimizar la inhibición plaquetaria en el síndrome coronario agudo: diseño del estudio EPIC17-VERONICA

RESUMEN

Introducción y objetivos: La desescalada desde prasugrel y ticagrelor a clopidogrel en pacientes tras intervencionismo coronario percutáneo por síndrome coronario agudo (SCA) constituye una de las estrategias para intentar disminuir las hemorragias. El objetivo de este estudio es averiguar si dicha desescalada guiada por la prueba de agregación plaquetaria VerifyNow (Werfen, España) tiene un efecto beneficioso en el tratamiento del SCA.
Métodos: Estudio multicéntrico, prospectivo y aleatorizado 1:1, en curso. Se incluirán 634 pacientes con SCA y revascularización con *stent* de sirolimus que sean dados de alta con doble terapia antiagregante con ticagrelor o prasugrel. Solo se incluirán aquellos con un nivel de reactividad plaquetaria muy bajo (unidades de reactividad plaquetaria ≤ 30) basado en VerifyNow al mes del alta. El objetivo primario es un combinado de muerte por causa cardiovascular, infarto agudo de miocardio no fatal, accidente cerebrovascular no fatal y sangrado en un seguimiento a 1 año.
Resultados: El estudio EPIC17-VERONICA (NCT04654052) permitirá averiguar la eficacia de la estrategia de desescalada basada en la prueba de agregación plaquetaria VerifyNow, además de conocer el papel de este dispositivo en la selección de los pacientes candidatos a beneficiarse de esta estrategia.
Conclusiones: Este estudio determinará si las pruebas de función plaquetaria aportan beneficio en el tratamiento tras el SCA.

Palabras clave: Síndrome coronario agudo. Terapia antiagregante. Prueba de función plaquetaria. Sangrado.

Abbreviations

ACS: acute coronary syndrome. **PCI:** percutaneous coronary intervention. **PRU:** platelet reactivity units.

INTRODUCTION

Following percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS), a 12-month regimen of dual antiplatelet therapy with a $P2Y_{12}$ receptor inhibitor and acetylsalicylic acid is recommended, regardless of the type of stent implanted, except when contraindicated.[1] Although prasugrel and ticagrelor are preferred over clopidogrel in this setting, there is ongoing debate regarding the potency and duration of dual antiplatelet therapy. This controversy stems from the fact that most patients concurrently face 2 opposing and potentially fatal risks—ischemic and hemorrhagic—which must be carefully balanced on an individual basis.

The introduction of stents with reduced thrombogenicity, together with evidence that thrombotic risk is highest during the first few months after PCI while hemorrhagic risk remains relatively constant throughout time, has led to research efforts focused on minimizing bleeding complications. These strategies include shortening dual antiplatelet therapy, using $P2Y_{12}$ inhibitors as monotherapy, and implementing de-escalation strategies.[2,3]

De-escalation consists of switching from prasugrel or ticagrelor to clopidogrel and can be guided (using genetic or platelet function testing) or unguided. Because this strategy may increase ischemic events, it is not recommended within the first month after PCI.[1]

In the TOPIC trial,[4] the unguided de-escalation strategy initiated 1 month after ACS significantly reduced hemorrhagic events (Bleeding Academic Research Consortium [BARC] grade ≥ 2 bleeding events) at 1 year without increasing the ischemic ones. In the TROPICAL-ACS trial,[5] the platelet function testing–guided de-escalation from prasugrel to clopidogrel 2 weeks after revascularization was noninferior to standard therapy, showing a trend toward fewer hemorrhages at 12 months and a similar rate of thrombotic events.[1,2,6] In the TALOS-AMI trial,[7] 12-month event rates were lower, primarily because of fewer hemorrhagic events among patients who underwent unguided de-escalation 1 month after ACS. Table 1 summarizes these studies.

After the positive results of the TOPIC trial, the *VerifyNow to optimise platelet inhibition in coronary acute syndrome* (EPIC17-VERONICA) trial (ClinicalTrials.gov: NCT04654052) aims to further refine this strategy by only applying de-escalation to patients with excessive antiplatelet effects from prasugrel or ticagrelor after the first month who are at theoretical risk of hemorrhage based on the VerifyNow platelet aggregation test (Werfen, Spain). Thus, patients demonstrating an adequate pharmacologic response will continue prasugrel or ticagrelor therapy for 1 year, whereas those with very low platelet reactivity after a 1-month regimen of dual antiplatelet therapy with these agents constitute the target population of this study.

METHODS

Design

We are conducting a multicenter, prospective, randomized clinical trial at 16 Spanish centers. Based on the results of the platelet aggregation test for $P2Y_{12}$ inhibition (platelet reactivity units [PRU]) using the VerifyNow system, patients with very low platelet reactivity (PRU ≤ 30) are randomized in a 1:1 ratio to either continue treatment with ticagrelor or prasugrel, or to de-escalate to clopidogrel. Patients with PRU > 30 are not randomized. The study flowchart is shown in figure 1.

The study is being conducted in full compliance with the principles outlined in the Declaration of Helsinki and has been approved by the central ethics committee (*Comité del Bierzo*, León, Spain) and endorsed by the ethics committees of all participant centers. The appendix lists the participant centers and principal investigators.

Table 1. De-escalation clinical trials in patients with acute coronary syndrome

	TOPIC (2017)[4]	TROPICAL-ACS (2018)[5]	TALOS-AMI (2021)[12]
Population	n = 645	n = 2610	n = 2697
Design	Open-label, single-center, randomized, superiority trial	Open-label, multicenter, randomized, noninferiority trial	Open-label, multicenter, randomized, noninferiority trial
Strategy	Standard therapy vs unguided de-escalation	Standard therapy vs platelet function testing–guided therapy (Multiplate device)	Standard therapy vs unguided de-escalation
Control group	Continued dual antiplatelet therapy with acetylsalicylic acid and ticagrelor or prasugrel	Continued dual antiplatelet therapy with acetylsalicylic acid and prasugrel	Continued dual antiplatelet therapy with acetylsalicylic acid and ticagrelor
Experimental group	De-escalation to acetylsalicylic acid and clopidogrel	1-week regimen of prasugrel, followed by 1-week regimen of clopidogrel and either prasugrel or clopidogrel from day 14 onward, according to platelet function testing results	De-escalation to acetylsalicylic acid and clopidogrel
Time from revascularization to de-escalation	1 month	2 weeks	1 month
Follow-up	1 year	1 year	1 year
Primary endpoint	Cardiac death, emergency revascularization, stroke, or BARC ≥ 2 bleeding events	Cardiac death, myocardial infarction, stroke, or BARC ≥ 2 bleeding events	Cardiac death, myocardial infarction, stroke, or BARC ≥ 2 bleeding events
Results	13.4% in experimental group vs 26.3% in control group (HR, 0.48; 95%CI, 0.34–0.68; $P < .01$)	7.3% in experimental group vs 9.0% in control group (HR, 0.81; 95%CI, 0.62–1.06; $P = .0004$)	4.6% in experimental group vs 8.2% in control group (HR, 0.55; 95%CI, 0.42–0.76; $P < .0001$)

95%CI, 95% confidence interval; BARC, Bleeding Academic Research Consortium; HR, hazard ratio.

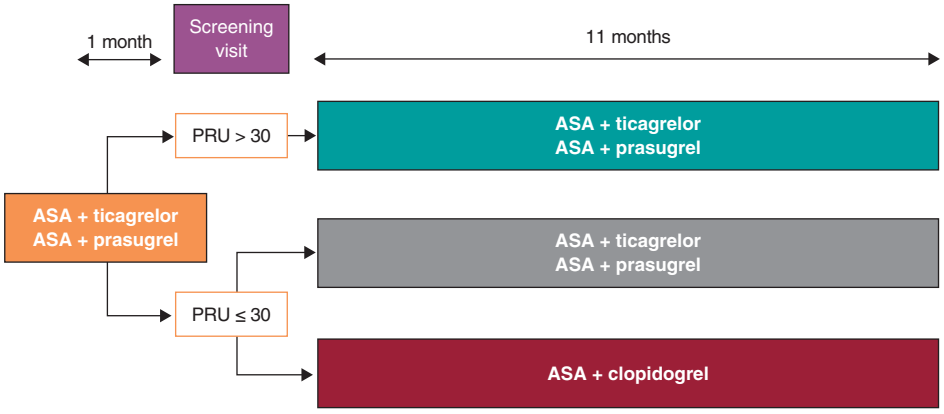

Figure 1. Study flowchart. AAS, acetylsalicylic acid; PRU, platelet reactivity units.

The study sponsor (*Fundación para la Educación en Procedimientos de Intervencionismo en Cardiología* [EPIC]) is fully responsible, together with the principal investigators, for data management and confidentiality.

Population

Inclusion and exclusion criteria

Table 2 summarizes the inclusion and exclusion criteria. Briefly, all patients with ACS undergoing PCI with a sirolimus-eluting stent and a bioresorbable polymer during hospitalization and discharged on dual antiplatelet therapy with acetylsalicylic acid and ticagrelor or prasugrel are eligible for inclusion.

Written informed consent must be obtained before the platelet aggregation tes is performed.

Study protocol and randomization

Eligible patients are scheduled for $P2Y_{12}$ receptor inhibition testing with the VerifyNow system between 30 and 40 days after hospital discharge. Measurements are obtained at least 6 hours after the administration of the last $P2Y_{12}$ inhibitor dose. Patients with PRU ≤ 30 (very low platelet reactivity) are randomized in a 1:1 ratio using an electronic system to either continue their current treatment or de-escalate to clopidogrel, 75 mg once daily. De-escalation is preceded by a loading dose of 600 mg administered 24 hours after the last dose of ticagrelor or 75 mg 24 hours after the last dose of prasugrel, in accordance with the 2017 European Society of Cardiology clinical practice guidelines.[8]

Table 2. Inclusion and exclusion criteria

Inclusion criteria
Patients > 18 years
Patients with acute coronary syndrome undergoing percutaneous revascularization with a sirolimus-eluting stent with a bioresorbable polymer and discharged on dual antiplatelet therapy with acetylsalicylic acid and ticagrelor or prasugrel
Signed informed consent
Exclusion criteria
History of intracranial hemorrhage
Contraindication to acetylsalicylic acid, clopidogrel, prasugrel, or ticagrelor
Major ischemic or bleeding events during the first month of antiplatelet therapy
Thrombocytopenia < 50 000/μL
Permanent oral anticoagulation
Pregnancy or breastfeeding
Inability to complete the 1-year follow-up
Life expectancy < 24 months

The remaining patients with PRU > 30 are not randomized, and their dual antiplatelet therapy remains unchanged from discharge.

Clinical follow-up

Patients in the 2 randomized groups undergo telephone follow-up to monitor clinical events at 2, 5, 8, and 11 months after enrollment, corresponding to 3, 6, 9, and 12 months after hospital discharge.

For patients with PRU > 30 on the 1-month VerifyNow platelet aggregation test who are not randomized, only baseline characteristics are recorded, and no further follow-up is conducted.

Protocol of the VerifyNow platelet aggregation test

The VerifyNow system determines platelet activity by measuring in vitro aggregation in a blood sample exposed to specific agonists. This optical detection instrument (figure 2), which operates on a turbidimetric principle, uses single-use cartridges. In this study, PRUTest-specific kits are employed. (Werfen, Spain) to assess platelet aggregation while on $P2Y_{12}$ receptor inhibitor therapy (ticagrelor, prasugrel, and clopidogrel). Each PRUTest kit contains lyophilized microbeads coated with fibrinogen, platelet activators, and a buffered solution. The test is based on the ability of activated platelets to bind fibrinogen-coated microbeads. Light transmission increases as activated platelets bind to and aggregate with the fibrinogen-coated microspheres. The kit measures this change in the optical signal and reports the results in PRU units (figure 3).

An antiplatelet effect of the drug is considered present with PRU ≤ 180 (figure 4). Only patients with PRU ≤ 30 are randomized, as these are considered to have very low platelet reactivity while on antiplatelet therapy.

Endpoints

The primary endpoint of the study is to compare the efficacy of de-escalation from ticagrelor or prasugrel to clopidogrel in patients undergoing PCI in the ACS setting, using the VerifyNow platelet aggregation test vs standard dual antiplatelet therapy at the 1-year follow-up. The rate of net adverse cardiovascular events is the primary endpoint of the study, defined as a composite of cardiac death, nonfatal myocardial infarction, nonfatal stroke, and hemorrhage (defined as Bleeding Academic Research Consortium [BARC] grade ≥ 2 bleeding events). The BARC scale is shown in table S1.

Figure 2. VerifyNow system. Reproduced with permission from Werfen.

Furthermore, the study aims to compare several secondary endpoints (table 3), such as the occurrence of ischemic events during follow-up: cardiac death and all-cause mortality, acute myocardial infarction, stroke, stent thrombosis, and need for emergency revascularization. Moreover, the hemorrhage rate (defined as BARC grade ≥ 2 bleeding events) will be compared. The definitions of all study endpoints are shown in table S2.

Statistics

Sample size calculation

Sample size was calculated for the randomized clinical trial cohort. The total number of patients (including those not randomized with PRU > 30) will depend on the total required to reach the estimated sample size for the randomized clinical trial.

We estimate a smaller difference in event rates across the groups than that observed in the TOPIC trial,[4] specifically, 14% in the de-escalation group vs 22% in the standard therapy group. Assuming a significance level of 0.05, a power of 80%, a 2-tailed *P*-value and a 10% loss to follow-up, a total of 634 randomized patients (317 per group) will be required.

Statistical analysis plan

Quantitative variables will be expressed as mean and standard deviation if normally distributed, or as median and interquartile range otherwise. Categorical variables will be expressed as absolute values and percentages. Study data will be analyzed using one-way analysis of variance (ANOVA) for continuous variables, and Fisher's exact or chi-square tests for categorical variables, as appropriate. Nonparametric tests will be used for variables that are not normally distributed or cannot be normalized. For the main outcome measure, Kaplan-Meier survival curves with log-rank statistics will be presented for prespecified criteria, and multivariable Cox regression will be performed to adjust for known risk factors and potential confounders. Hazard ratios and 95% confidence intervals will be reported for all statistically significant variables.

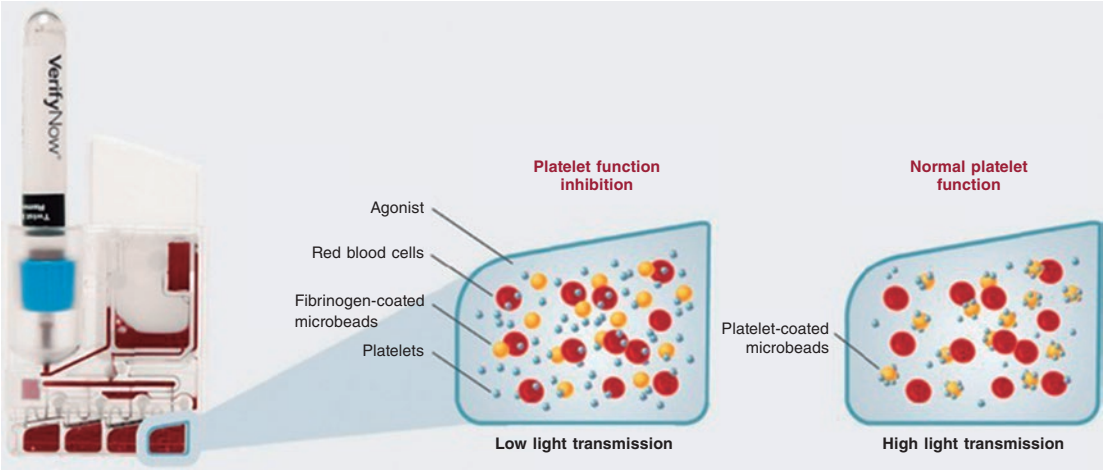

Figure 3. Performance of the VerifyNow system based on light transmission aggregometry. Light transmission increases as activated platelets bind and aggregate to the fibrinogen-coated microbeads in the kit. Therefore, high light transmission (corresponding to elevated platelet reactivity unit [PRU] values) indicates normal platelet function, whereas low light transmission (decreased PRU values) reflects platelet inhibition induced by the tested drugs.

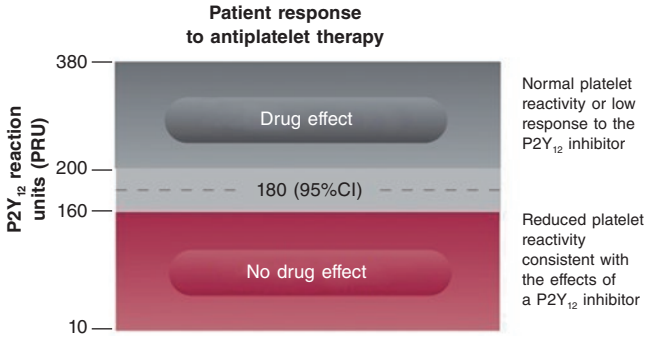

Figure 4. Reference levels for platelet reactivity units (PRU). 95%CI, 95% confidence interval.

Table 3. Endpoints of the study

Primary endpoint
To compare the percentage of net adverse cardiovascular events between the 2 subgroups of patients with low platelet reactivity (PRU ≤ 30) who were randomized to de-escalation to clopidogrel vs standard therapy
Secondary endpoints
To compare the rate of cardiac death between the 2 randomized patient subgroups
To compare the rate of all-cause mortality between the 2 randomized patient subgroups
To compare the rate of acute myocardial infarction between the 2 randomized patient subgroups
To compare the rate of stroke between the 2 randomized patient subgroups
To compare the rate of stent thrombosis between the 2 randomized patient subgroups
To compare the rate of emergency revascularization between the 2 randomized patient subgroups
To compare the rate of bleeding events (defined as BARC ≥ 2) between the 2 randomized patient subgroups

BARC, Bleeding Academic Research Consortium; PRU, platelet reactivity units.

Intention-to-treat (according to randomization assignment) and per-protocol analyses (in case of crossover) will be conducted. The former will serve as the study primary analysis.

DISCUSSION

The EPIC17-VERONICA trial aims to demonstrate the efficacy of a VerifyNow platelet aggregation test-guided de-escalation strategy in reducing hemorrhagic events without increasing ischemic events in patients with ACS who have undergone percutaneous revascularization and exhibit very low platelet reactivity after the first month of treatment with prasugrel or ticagrelor.

The initial lack of expected results from platelet function testing to identify patients at risk for thrombotic events while on clopidogrel in the GRAVITAS,[9] TRIGGER-PCI,[10] and ARCTIC[11] trials relegated its use to a class IIb recommendation in the European Society of Cardiology antiplatelet guidelines for determining the optimal timing of cardiac surgery after ACS.[8] However, the 1-year results of the large-scale multicenter ADAPT-DES trial[12] with 8500 PCI patients demonstrated that platelet reactivity assessed with the VerifyNow platelet aggregation test is an independent predictor of bleeding events.

In the TOPIC[4] and TALOS-AMI[7] trials, the unguided de-escalation strategy significantly reduced bleeding events without increasing ischemic events. In the TROPICAL-ACS[5] trial, this platelet aggregation test–guided de-escalation strategy showed a trend toward fewer hemorrhages, with a similar rate of thrombotic complications.

The EPIC17-VERONICA study further seeks to improve the application of this de-escalation strategy by using the VerifyNow platelet aggregation test to identify patients with very low platelet reactivity (PRU ≤ 30) as those most likely to benefit from de-escalation.

CONCLUSIONS

The EPIC17-VERONICA trial has been designed to investigate the efficacy of de-escalating from the most potent antiplatelet agents (ticagrelor and prasugrel) to clopidogrel after the first month of

therapy in patients with ACS and very low platelet reactivity, aiming to reduce bleeding events without increasing ischemic complications. Furthermore, it will provide evidence on the clinical utility of the VerifyNow platelet aggregation test for patient selection.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

The study is being conducted in full compliance with the principles outlined in the Declaration of Helsinki on clinical research and has been approved by the central ethics committee (*Comité del Bierzo*, León, Spain) and endorsed by the ethics committees of all participant centers. Written informed consent is required prior to performing ant platelet aggregation measurements. Sex and gender bias considerations have been addressed.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this manuscript.

AUTHORS' CONTRIBUTIONS

C. Garilleti Cámara and I. Lozano Martínez-Luengas drafted the manuscript; the remaining authors critically revised the document and approved the final version.

CONFLICTS OF INTEREST

J.M. de la Torre-Hernández is Editor-in-Chief of *REC: Interventional Cardiology*; A. Pérez de Prado is Associate Editor of *REC: Interventional Cardiology*. In both cases, the journal's editorial procedure to ensure impartial handling of the manuscript has been followed. The remaining authors declared no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- De-escalation from the most potent antiplatelet agents to clopidogrel is one of the strategies used to reduce hemorrhage after percutaneous revascularization in acute coronary syndrome. This de-escalation can be performed guided or unguided by genetic or platelet function testing.

WHAT DOES THIS STUDY ADD?

- The EPIC17-VERONICA trial is the first to use the VerifyNow platelet aggregation test to select patients eligible for de-escalation.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000544.

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Original article

DEB or DES for the treatment of calcified nodules after intravascular lithotripsy: the DEBSCAN-IVL trial design

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ABSTRACT

Introduction and objectives: Calcified coronary nodules (CN) are among the most challenging lesions for percutaneous coronary intervention, as drug-eluting stents (DES) frequently result in suboptimal expansion, malapposition, and recurrent adverse events. Although intravascular lithotripsy (IVL) provides effective plaque modification, the optimal definitive strategy remains unclear. Drug-eluting balloons (DEB) have demonstrated potential in the treatment of complex lesions in which stent implantation may be less desirable. This trial aims to compare the safety and efficacy profile of DEB vs DES after IVL in patients with CN.
***Methods*:** We conducted a retrospective, investigator-initiated, multicenter, non-inferiority, randomized clinical trial.
Results: A total of 128 patients with de novo CN confirmed by intracoronary imaging in vessels measuring 2.5 mm to 4.0 mm in diameter will be enrolled across 10 high-volume percutaneous coronary intervention centers. After lesion preparation with IVL, patients will be randomized on a 1:1 ratio to receive a DEB or a DES. The co-primary endpoints are late lumen loss and net luminal gain at 9 ± 1 months of angiographic follow-up, both assessed by an independent core laboratory. Secondary endpoints include procedural, angiographic, and clinical outcomes, adjudicated by a blinded clinical events committee. Clinical follow-up will be conducted at 1 month, 1 year, and 2 years.
Conclusions: The DEBSCAN-IVL trial will provide the first randomized evidence comparing DEB and DES after IVL for CN. Registered at ClinicalTrials.gov: NCT06657833.

Keywords: Calcified nodule. Intravascular lithotripsy. Drug-eluting balloons. Drug-eluting stents. Complex percutaneous coronary intervention.

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BFA o SFA para el tratamiento de nódulos calcificados tras litotricia intravascular: diseño del ensayo DEBSCAN-IVL

RESUMEN

Introducción y objetivos: Los nódulos coronarios calcificados (NC) se encuentran entre las lesiones más desafiantes para la intervención coronaria percutánea, ya que los *stents* farmacoactivos (SFA) con frecuencia presentan expansión subóptima, mala aposición y eventos adversos recurrentes. La litotricia intravascular (LIV) permite una modificación eficaz de la placa, pero la estrategia definitiva óptima sigue sin estar clara. Los balones farmacoactivos (BFA) han mostrado resultados prometedores en lesiones complejas en las que la implantación de *stents* podría ser menos favorable. Este ensayo tiene como objetivo comparar la seguridad y la eficacia del BFA frente al SFA después de la LIV en pacientes con NC.
Métodos: Ensayo clínico prospectivo, por iniciativa del investigador, multicéntrico, de no inferioridad y aleatorizado.
Resultados: Un total de 128 pacientes con NC *de novo* confirmados mediante imagen intracoronaria en vasos de 2,5-4,0 mm de diámetro serán incluidos en 10 centros de intervencionismo coronario percutáneo de alto volumen. Tras la preparación de la lesión con LIV, los pacientes serán aleatorizados 1:1 para ser tratados con BFA o SFA. Los criterios de valoración coprimarios son la pérdida luminal tardía y la ganancia luminal neta en el seguimiento angiográfico a 9 ± 1 meses, evaluadas por un laboratorio central independiente. Los criterios secundarios incluyen resultados procedimentales, angiográficos y clínicos, adjudicados por un comité de eventos clínicos enmascarado. El seguimiento clínico se realizará a 1 mes, 1 año y 2 años.
Conclusiones: El ensayo DEBSCAN-IVL proporcionará la primera evidencia de comparación de BFA y SFA aleatorizados después de IVL en NC.
Registrado en ClinicalTrials.gov: NCT06657833.

Palabras clave: Nódulo calcificado. Litotricia intravascular. Balón farmacoactivo. *Stent* farmacoactivo. Intervención coronaria percutánea compleja.

Abbreviations

CN: calcified coronary nodule. **DEB:** drug-eluting balloon. **DES**: drug-eluting stent. **IVL:** intravascular lithotripsy. **OCT:** optical coherence tomography. **PCI:** percutaneous coronary intervention.

INTRODUCTION

Calcified coronary nodules (CN) represent the most complex type of calcified lesion for percutaneous coronary intervention (PCI), as they are associated with worse angiographic and clinical outcomes after drug-eluting stent (DES) implantation.[1-8]

Intravascular lithotripsy (IVL) has shown favorable results in this context.[9] However, stent implantation after IVL may not always be the best treatment option due to suboptimal stent expansion and severe malapposition in a non-negligible percentage of patients which, along with possible nodule protrusion through the stent struts, may be associated with an increased need for new target lesion revascularization (TLR), and a higher rate of major adverse cardiovascular events (MACE).[10-12]

Drug-eluting balloons (DEB) have demonstrated to be a safe and effective alternative to DES in various settings, especially in those in which stenting is associated with worse outcomes, such as small vessel disease and in-stent restenosis.[13] Therefore, their use has increased exponentially in recent years and has expanded to other lesion types.[14]

In the specific setting of calcified lesions, there are some data on the safety and efficacy profile of DEB after an adequate plaque modification.[15-19] Moreover, in this setting, DEB have shown similar clinical outcomes with favorable late lumen loss rate compared with DES.[20-23]

Despite the increasing use of DEB in calcified lesions, evidence on the safety and efficacy profile of CN treatment is lacking. In this setting, where the risj of suboptimal stent expansion and apposition—and the consequent likelihood of MACE— is higher,[24] a leave-nothing-behind strategy using DEB following optimal plaque modification technique may be a more appealing approach.Therefore, our aim is to compare the safety and efficacy profile of the use of DEB or DES after IVL in CN within the context of a randomized controlled trial.

METHODS

Patients and study design

The DEBSCAN-IVL trial is an investigator-initiated, multicenter, open-label, prospective, randomized, controlled clinical trial including 10 high-volume centers.

Patients will be randomized to receive a DEB or a DES after optimal treatment with IVL if they meet all the inclusion criteria and have no exclusion criteria. Inclusion criteria are age ≥ 18 years with a clinical indication for PCI (presenting with chronic or acute coronary syndromes) in a CN-induced de novo severe coronary lesion (confirmed via intracoronary imaging) in vessels with a reference diameter between 2.5 mm and 4.0 mm. Patients who meet at least 1 of the following conditions will be excluded: inability to provide oral and written informed consent or unwillingness to return for systematic angiographic follow-up; pregnant or breastfeeding patients; cardiogenic shock or cardiac arrest at the time of the index procedure; inability to maintain dual antiplatelet therapy for at least 1 month; life expectancy < 1 year; index lesion located at the left

Table 1. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients must meet all inclusion criteria: • Patients > 18 years admitted for stable coronary artery disease or acute coronary syndromes and indication for PCI and • Severe coronary lesion with a calcified nodule, highly recommended confirmation with intracoronary imaging (OCT or IVUS) and • Target lesion located in a vessel measuring between 2.5 mm and 4.0 mm in diameter	Patients must not meet any criteria: • Inability to provide oral and written informed consent or unwillingness to come back for systematic angiographic follow-up • Pregnant or breastfeeding patients • Cardiogenic shock or cardiac arrest at the index procedure • Impossibility to maintain dual antiplatelet treatment for at least 1 month • Life expectancy < 1 year • Index lesion at left main coronary artery • Aorto-ostial lesion • Target lesion previously treated with stents or DEB • High thrombus burden in the target lesion (TIMI thrombus grade ≥ 3)

DEB, drug-eluting balloon; IVUS, intravascular ultrasound; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

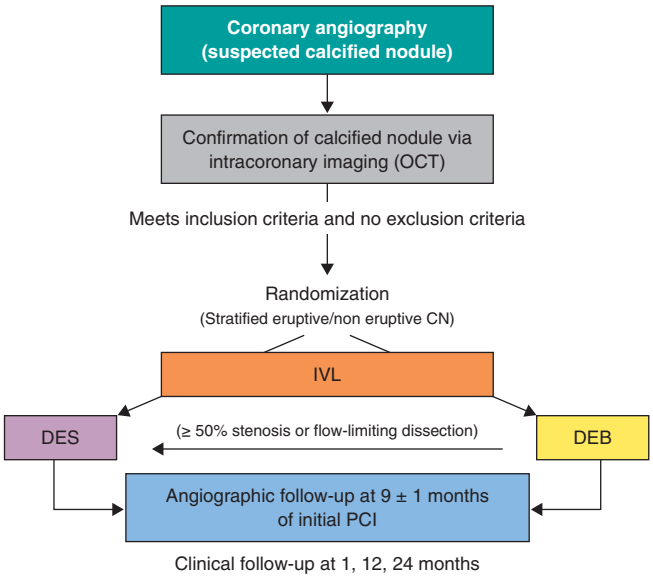

Figure 1. Central illustration. Study design flowchart. CN, calcified coronary nodule; DEB, drug-eluting balloons; DES, drug-eluting stents; IVL, intravascular lithotripsy; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

main coronary artery or in an aorto-ostial location; target lesion previously treated with stents or DEB or with high thrombus burden at the time of PCI (Thrombolysis In Myocardial Infarction [TIMI] thrombus grade ≥ 3).

Patients who meet all the inclusion criteria and none of the exclusion criteria will be treated with IVL and randomized to receive final therapy with DEB or DES. Randomization will occur via a web-based system. The complete inclusion and exclusion criteria are shown in table 1, and the study flowchart in figure 1.

Primary and secondary endpoints

The endpoint of this study is to evaluate and compare the safety and efficacy profile of DEB or DES as final treatment strategies for CN previously modified by IVL.

Co-primary endpoints will be the late lumen loss (LLL) and net luminal gain at 9 ± 1 months of angiographic follow-up, as assessed by an independent core laboratory, with a non-inferiority hypothesis between the 2 groups. LLL is defined as the difference between postoperative and follow-up minimal lumen diameter, whereas net gain is defined as the difference between follow-up and preoperative minimal lumen diameter, according to the latest Drug Coated Balloon Academic Research Consortium Consensus Document.[25]

Secondary endpoints of the study will include procedural, angiographic and clinical outcomes. Procedural endpoints will include the rate of crossover between treatment groups, angiographic success (defined as final TIMI grade-3 flow and a residual final percent diameter stenosis < 30% in the DEB group or < 20% in the DES group), device success (defined as angiographic success without crossover between treatment group), procedural success (defined as angiographic success without the occurrence of severe procedural complications, including cardiac death, target vessel perioperative myocardial infarction [MI], need for new clinically driven TLR, stent thrombosis [ST], stroke, flow-limiting dissection or vessel perforation). Angiographic endpoints will include the minimal lumen diameter measured immediately after the intervention and at the time of angiographic follow-up, the residual percent diameter stenosis at both timeframes, and the rate of binary restenosis, defined as a luminal diameter reduction o≥ 50% during follow-up.[25] Secondary endpoints will include procedural adverse events (such as dissection, perforation, acute vessel occlusion, slow flow or no-reflow, and intraoperative thrombosis), major hemorrhagic events (classified as Bleeding Academic Research Consortium [BARC] type ≥ 3),[26] and hemodynamic instability (requiring unplanned administration of vasopressors, inotropes, or ventricular support devices), cardiac death, target lesion-related MI (TL-MI), need for TLR, and ST, and MACE (defined as a composite of cardiac death, TL-MI, and TLR). TLR and ST are defined according to the Academic Research Consortium criteria.[27] MACE and its components will be assessed during the index hospitalization and at 6-month, 1-year, and 2-year follow-up visits. Detailed endpoints definitions are shown in appendix S1.

Primary outcome assessment will be conducted by a central independent core laboratory. All medical data will be anonymized and stored, and confidentiality will be protected at any time in full compliance with the current legislation. The clinical events committee (CEC) and the independent core laboratory will be blinded to the treatment group. Secondary outcomes will be assessed via centralized angiographic analysis and structured clinical follow-up, either in person or via telephone, at scheduled time points.

Devices

- IVL: Shockwave Balloon (Shockwave Medical, United States).
- Optical coherence tomography (OCT) or intracoronary ultrasound (IVUS) system, based on availability at each participating center.
- DEB: paclitaxel-eluting balloon (Pantera Lux, Biotronik, Switzerland).
- DES: new-generation zotarolimus eluting stent (Onyx Frontier, Medtronic, United States).

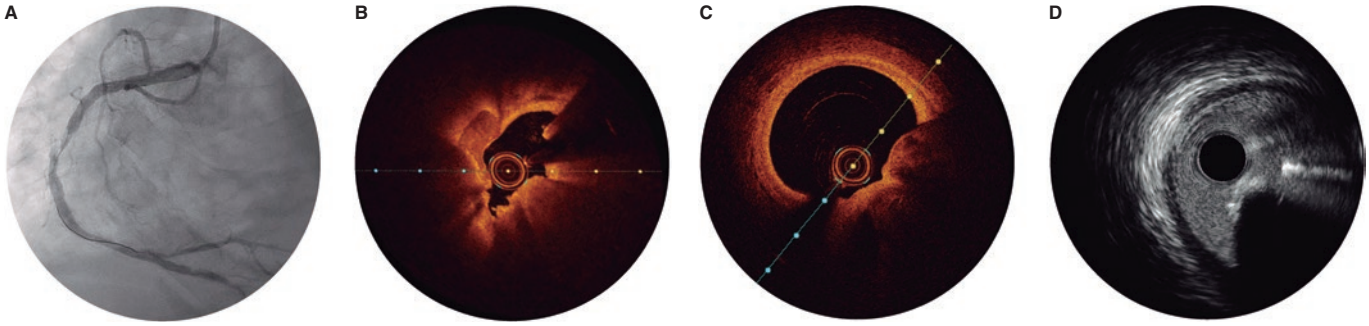

Figure 2. Calcified nodule appearance on angiography (**A**), optical coherence tomography (eruptive [**B**] and non-eruptive [**C**]) and intravascular ultrasound (**D**).

Procedure

When a CN is suspected on coronary angiography, intracoronary imaging—preferably OCT, with IVUS as an alternative—will be performed to confirm the diagnosis. After confirmation of a CN in the target lesion, patients will be randomized on a 1:1 ratio to receive a DEB or a DES. Randomization will be stratified to ensure a balanced distribution of eruptive and non-eruptive nodules across both treatment groups. A CN (figure 2) will be defined as a calcified segment with an accumulation of protruding nodular calcification (small calcium deposits) with disruption of the fibrous cap (eruptive CN) or an intact thick fibrous cap (non-eruptive CN).[28-30]

All patients will be treated with IVL, using a balloon sized 1:1 to the vessel reference diameter. A minimum of 80 pulses per lesion is recommended. If the IVL balloon cannot cross the lesion, predilation with smaller balloons is permitted. Additionally, the use of adjuvant techniques such as rotational atherectomy or excimer laser coronary atherectomy will be allowed only when deemed necessary to facilitate IVL balloon crossing. Postdilation with a non-compliant balloon after IVL is recommended before proceeding with the final assigned treatment modality.

Once optimal lesion preparation has been achieved, defined as > 80% balloon expansion in 2 orthogonal projections with a balloon sized 1:1 to the vessel, patients will receive a DEB or a DES, according to their initial randomization. If a patient randomized to the DEB group experiences a flow-limiting dissection or exhibits a percent diameter stenosis > 50%, conversion to DES implantation will be permitted at the operator's discretion. Similarly, any crossover from DES to DEB will be documented, along with the reasons for these procedural decisions.

It is recommended that the DEB reach the target lesion within 2 minutes, as drug loss may occur during transit.[13] Thus, operators need to anticipate difficulties in reaching the target lesion (proximal coronary disease or tortuosity) and ensure optimal support prior to using the DEB. If difficulties in reaching the target lesion are anticipated, the use of guide extension catheters is recommended. The recommended DEB inflation time is 60 seconds.

The PCI will be performed according to current European Society of Cardiology (ESC) guidelines, including perio- and postoperative antithrombotic management.[31,32] Patients should ideally receive dual antiplatelet therapy at least 2 to 4 hours prior to the PCI to ensure optimal platelet inhibition. In cases where this is not feasible, administration of IV antiplatelet agents, such as acetylsalicylic acid with or without cangrelor, immediately before the procedure is recommended.

Intracoronary imaging with either OCT or IVUS (the same imaging modality that was initially used) is recommended at the end of the procedure.

Angiographic analysis

Quantitative coronary imaging and intracoronary analysis of baseline and follow-up angiographies will be conducted by an independent central laboratory (Barcicore, Spain). At least 2 well-selected orthogonal views—free of foreshortening and side-branch overlap—focused on the target lesion are required after intracoronary nitroglycerine administration. These views should be obtained before treatment, after the intervention, and during follow-up angiography to ensure consistent angulation and enable accurate, reproducible measurements.

Follow-up

Post-PCI antithrombotic therapy will abide by the latest ESC clinical practice guidelines, considering the individual ischemic and bleeding risk profile of each patient.[31,32] Regardless of the assigned treatment group (DEB or DES), a 6-month regimen of dual antiplatelet therapy (aspirin and clopidogrel) is recommended in patients with stable coronary artery disease, and a 12-month regimen of dual antiplatelet therapy (preferably using prasugrel or ticagrelor as a $P2Y_{12}$ inhibitor) in patients with acute coronary syndrome. For patients requiring chronic oral anticoagulation, the choice and duration of antithrombotic therapy will follow current guideline recommendations, with triple therapy (oral anticoagulant + aspirin + clopidogrel) limited to 1 month, whenever feasible. Electrocardiogram and troponin assessment will be performed 24 hours after the PCI. All patients will be discharged with a scheduled angiographic follow-up at 9 ± 1 months. OCT is recommended during this follow-up, especially if angiography suggests progression of coronary artery disease in the target lesion. In cases where angiography or intracoronary imaging indicates disease progression, but the percent diameter stenosis is < 90%, revascularization should be guided by ischemia and confirmed with a pressure guidewire. Clinical follow-up visits are scheduled at 12 and 24 months. Schedule of visits and data assessment throughout the study are shown in table S1.

Statistical analysis

The primary endpoint analysis will be performed by lesion and by intention-to-treat with a 1-sided Student *t* test with an alfa of 0.05 between the DES and the DEB group. A per-protocol analysis, including crossover cases, will also be conducted for sensitivity purposes. If the hypothesis of non-inferiority is confirmed, a superiority 2-sided analysis will be performed. Clinical endpoints will be analyzed on a per-patient basis.

Quantitative variables will be expressed as mean ± standard deviation if normally distributed, and as median with minimum and

maximum values if they do not follow a normal distribution. Normality will be assessed using the Kolmogorov-Smirnov test. Qualitative variables will be described by their absolute values and frequencies, and will be expressed as absolute counts and percentages. A $P < .05$ will be considered statistically significant, and 95% confidence intervals (95%CI) will be reported for all main analyses. For comparisons of continuous variables between the 2 groups, the Student *t* test will be used if normality is confirmed, or the Mann-Whitney *U* test if non-parametric. For comparisons across > 2 groups, the ANOVA test or the Kruskal-Wallis test will be applied, as appropriate. Associations across categorical variables will be analyzed using the chi-square test or Fisher's exact test when expected frequencies are small. Correlations between continuous variables will be explored using Pearson's or Spearman's correlation coefficient, depending on their distribution.

A multivariate analysis will be conducted using Cox proportional hazards regression with forward stepwise selection, including variables that are significantly associated with outcomes (or show a trend) in the univariate analysis. Kaplan-Meier curves will be generated for event-free survival, and differences will be assessed using the log-rank test.

Prespecified subgroup analysis

Subgroup analysis will be performed according to the following prespecified categories: type of calcified nodule (eruptive vs non-eruptive), age (< 75 vs ≥ 75 years), sex (male vs female), presence of diabetes mellitus (yes vs no), location of the calcified nodule within a true bifurcation lesion involving a side branch ≥ 2.5 mm (yes vs no), and clinical presentation (acute coronary syndrome vs chronic coronary syndrome). In addition, a prespecified OCT subgroup analysis will be performed in patients with available OCT imaging at both the end of the procedure and follow, including assessments of minimal lumen area (or minimal stent area in stented segments) and minimal lumen diameter.

Sample size calculation

The hypothesis is that DEB-PCI for CN is not inferior to state-of-the-art DES-PCI in terms of LLL and net luminal gain at the lesion. The sample size calculation was based on an expected LLL of 0.20 mm in the DES group, with a non-inferiority margin (delta) of 0.30 mm, a significance level (alpha) of 5%, and a statistical power of 80%. The estimate of LLL in the control group was derived from previous studies evaluating the same DES platform.[33-35] Assuming a 20% attrition rate for angiographic follow-up, 64 patients per group (128 patients in total) will be required to provide adequate statistical power. The study is not powered for clinical endpoints, which will be considered exploratory and hypothesis-generating.

Organization and ethical concerns

The study protocol has been approved by the local ethics committees of all participant centers. Written informed consent will be obtained from all patients prior to enrollment. The DEBSCAN-IVL trial is an investigator-initiated study conducted in full compliance with Good Clinical Practice guidelines applicable to interventional and epidemiological research. The rights, safety, and well-being of all participants will be protected full compliance with the principles set forth in the Declaration of Helsinki, applicable EU legislation, and local legal requirements. Participant data will be handled confidentially and anonymously. The trial is registered at ClinicalTrials.gov (NCT06657833). The sponsor of the study is Fundación EPIC. The study is supported by unrestricted research grants from Fundación EPIC, Shockwave Medical, Biotronik, and Medtronic.

The steering committee serves as the primary decision-making body of the trial and bears full responsibility for its scientific and clinical conduct. A clinical events committee (CEC), composed of independent interventional cardiologists not participating in the study and blinded to treatment allocation, will adjudicate all clinical events and endpoints. The CEC will operate according to pre-specified definitions outlined in the study protocol and will remain blinded to the overall trial outcomes.

DISCUSSION

CN represent the most complex type of calcified lesion for PCI, as they are associated with the worst angiographic and clinical outcomes after DES implantation.[1-8] Three main factors may contribute to these unfavorable results: the nature of the nodule *per se*, the plaque modification technique used, and the final revascularization strategy (DES or DEB). Although our understanding of the origin and behavior of calcified nodules has grown, it remains unclear which lesions are likely to respond favorably to PCI, and which are not. Eruptive CN, for instance, may be more amenable to initial modification, yet paradoxically, they have also been associated with higher rates of adverse clinical events during follow-up.[29,36]

Regarding plaque modification techniques, current evidence is limited. Rotational atherectomy (RA), while commonly used, is constrained by wire bias and frequently requires large burr sizes.[2] Although orbital atherectomy might overcome some of these limitations, randomized data comparing it with other advanced plaque modification techniques are lacking.[37] Balloon-based techniques, in contrast, may fail to cross severely stenotic nodular lesions but have the advantage of avoiding the wire bias inherent to atherectomy.

However, conventional or scoring/cutting balloons often prove insufficient to fully modify the depth of nodular calcium, and very high-pressure special balloons carry the risk of overstretching the usually normal opposite vessel wall causing perforation. In this context, IVL has emerged as a promising alternative, offering the most robust evidence to date for nodular plaque modification.[29,38]

Traditionally, stent implantation has been the standard definitive treatment for CN.[23] However, stenting in nodular lesions frequently leads to suboptimal expansion and incomplete apposition, particularly at the shoulders of the nodule. Moreover, In these patients, TLR is often driven not by classic in-stent restenosis, but by late protrusion of the calcified nodule through the stent struts.[10,11,39] These limitations have generated interest in a "leave nothing behind" strategy after effective plaque modification.

DEB have demonstrated to be safe and effective in various settings, particularly small vessel disease and in-stent restenosis, where DES implantation may be less favorable.[13] Therefore, their use has grown significantly in recent years.[14] In the context of calcified lesions, there are concerns that adequate drug-uptake may be compromised, but preliminary evidence suggests DEB may offer good outcomes after adequate plaque preparation.[15-17] For instance, Ito et al.[18] evaluated a total of 81 patients with de novo lesions treated with DEB, including 46 with calcified lesions. While LLL and restenosis appeared slightly higher in the calcified group, these differences were not statistically significant and did not translate into worse clinical outcomes at 2 years. Notably, 82% of these lesions were pre-treated with RA. Similarly, Nagai et al. reported a TLR rate of 16.3% in 190 severely calcified lesions treated with RA followed by DEB.[19] Rissanen et al. found MACE rates of 14% and 20% at 12 and 24 months, respectively, in 82 complex de novo calcified lesions treated with DEB after RA and balloon predilation, with very low rates of clinically driven TLR.[20] Furthermore,

favorable findings have been reported by Shiraishi et al., including a subset of calcified nodules.[16]

Comparative studies have further explored DEB vs DES in calcified lesions. Ueno et al.[21] conducted a single-center cohort study comparing the clinical outcomes of 166 severe calcified lesions treated with either DEB or DES after RA at a median follow-up of 3 years. The TLR rates were similar across the groups (15.6% vs 16.3%; $P = .99$), while LLL was significantly lower in the DEB group (0.09 mm vs 0.52 mm; $P = .009$). Iwasaki et al.[22] compared 194 patients with de novo calcified lesions in non-small vessels the RA + DEB vs RA + DES strategies. There were no significant differences at 1 year in terms of MACE, cardiac death, myocardial infarction, TLR or hemorrhage.

Despite this data on the performance of DEB in calcified lesions, evidence on the safety and efficacy profile in the CN setting is lacking. However, given the high likelihood of suboptimal stent expansion and malapposition in this setting, which may lead to increased MACE risk,[24] a metal-free strategy using DEB following optimal plaque modification seems to be an attractive and feasible approach.

Intracoronary imaging-guided PCI has been consistently associated with improved procedural outcomes and a reduction in major adverse cardiovascular events, including mortality, particularly in complex lesions.[40] Intracoronary imaging plays a pivotal role in this context. Compared with conventional angiography, it provides a far more accurate assessment of coronary disease severity and plaque morphology.[1] This is particularly relevant in calcified and complex lesions, where procedural planning and outcomes are significantly impacted by the detailed anatomical insights obtained. OCT, in particular, offers superior spatial resolution compared to IVUS, allowing for precise quantification of the calcium burden.[28,41]

In the case of CN, OCT enables accurate assessment of the plaque substrate and procedural results, including stent expansion and apposition, or in DEB-treated lesions, the extent of plaque modification.

The DEBSCAN-IVL trial will be comparing the safety and efficacy profile of DEB vs DES after lesion preparation with IVL in patients with CN, assessing both angiographic and clinical outcomes. Moreover, the trial will provide valuable information on the underlying plaque morphology and the response to different PCI strategies following the systematic use of intracoronary imaging. The central hypothesis of the study is that a DEB strategy, after IVL-based plaque modification in calcified nodules, is not inferior to DES implantation in terms of LLL and net gain, while potentially reducing the risk of long-term adverse events through improved biocompatibility and vessel healing. In addition, the analysis will be stratified according to nodule morphology, specifically differentiating eruptive vs non-eruptive CN, 2 entities that are thought to have distinct biological behavior and potentially different response to plaque modification and PCI.[6,7,29,36] This stratified analysis may provide novel insights into the prognostic and therapeutic implications of nodule subtype and guide future individualized interventional strategies.

CONCLUSIONS

The DEBSCAN-IVL trial is an investigator-initiated, multicenter, open-label, prospective, randomized, controlled clinical trial designed to compare the safety and efficacy profile of the use of DEB or DES after IVL in CN. The co-primary endpoints are LLL and net gain at 9 ± 1 months of angiographic follow-up. The findings are expected to inform clinical decision-making and support a more individualized approach on the management of this specific type of calcified coronary disease.

DATA AVAILABILITY

This manuscript refers to the protocol of a study, therefore there is not available data related to this manuscript.

FUNDING

The DEBSCAN-IVL study was supported by non-restricted grants from Shockwave, Biotronik and Medtronic.

ETHICAL CONSIDERATIONS

The study was conducted in full compliance with the principles set forth in the Declaration of Helsinki. Institutional Ethics Committee approval was obtained, and all participants gave their written informed consent prior to enrollment. The confidentiality and anonymity of participants were strictly preserved throughout the study. Sex and gender considerations were addressed following the recommendations of the SAGER guidelines to ensure accurate and equitable reporting.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence assisted technologies were used exclusively to support language editing and improvement of style. No artificial intelligence tools were employed to generate, analyze, or interpret the data. The authors take full responsibility for the integrity, accuracy, and originality of the manuscript content.

AUTHORS' CONTRIBUTIONS

A. Jurado-Román, M. Basile and R. Moreno drafted the manuscript. The remaining authors performed a critical review, and all authors approved the final version for publication.

CONFLICTS OF INTEREST

A. Jurado-Román is a proctor for Abbott, Boston Scientific, World Medica, and Philips; has received consulting fees from Boston Scientific and Philips; and has received speaker fees from Abbott, Boston Scientific, Shockwave Medical, Philips, and World Medica. J.M. Montero-Cabezas received a research grant from Shockwave Medical and speaker fees from Abiomed, Boston Scientific, and Penumbra Inc. A. Pérez de Prado reports receiving institutional research grants from Abbott and Shockwave Medical and speaker honoraria and consulting fees from iVascular, Boston Scientific, Terumo, B. Braun, and Abbott Vascular. I.J. Amat-Santos is proctor for Boston Scientific. A. Pérez de Prado, F. Alfonso 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. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

WHAT IS KNOWN ABOUT THE TOPIC?

- CN are among the most complex calcified lesions for PCI, as DES often result in suboptimal expansion, malapposition, and long-term adverse events. IVL is an effective and safe technique for modifying nodular calcium. DEB have proven effective in complex lesions such as small vessel disease and in-stent restenosis, suggesting potential utility where stent implantation might be suboptimal. However, robust evidence on the safety and efficacy of DEB specifically for CN after IVL is currently lacking.

WHAT DOES THIS STUDY ADD?

- The DEBSCAN-IVL trial will be the first randomized study to compare DEB and DES after IVL in patients with CN. It will evaluate angiographic endpoints such as late lumen loss and net luminal gain, as well as procedural and clinical outcomes. The study is expected to provide crucial insights into whether a "leave-nothing-behind" approach with DEB can achieve comparable efficacy to DES while potentially improving vessel healing and reducing long-term complications in this challenging patient population.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000551.

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Review article

Transcatheter treatment of aortic coarctation

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ABSTRACT

Aortic coarctation is a congenital disease that consists of the narrowing of the thoracic aorta, leading to distal blood flow obstruction. Significant aortic coarctation is associated with hypertension and distal hypoperfusion, with a poor prognosis without intervention. Initially, treatment was surgical; however, less invasive techniques such as percutaneous balloon angioplasty later emerged and proved effective in selected patients.
The introduction of stent implantation significantly improved the outcomes, making percutaneous repair the preferred option, especially in adolescents and adults.
However, immediate and long-term complications persist, which has driven research efforts aimed at improving the safety and efficacy profile. Modern strategies now focus on advanced stent designs, offering better delivery profiles and high redilatation potential. Gaps in knowledge remain, and data from studies with longer follow-up will be essential to further elucidate disease progression in these patients. This review aims to offer a comprehensive overview of these percutaneous procedures, discussing recent advancements, clinical outcomes, and future perspectives.

Keywords: Aortic coarctation. Percutaneous repair. Complications. Advanced stent designs.

Tratamiento percutáneo de la coartación de aorta

RESUMEN

La coartación de aorta es una enfermedad congénita caracterizada por el estrechamiento de la aorta torácica, que provoca una obstrucción del flujo sanguíneo distal. Una coartación de aorta significativa se asocia con hipertensión arterial e hipoperfusión distal, así como con un mal pronóstico sin intervención. Inicialmente el tratamiento era quirúrgico, pero fueron surgiendo técnicas menos invasivas, como la angioplastia percutánea con balón, que mostró eficacia en ciertos pacientes. La incorporación del implante de *stents* mejoró de manera significativa los resultados, convirtiendo la reparación percutánea en la opción preferida, en especial en adolescentes y adultos. Sin embargo, siguen produciéndose complicaciones inmediatas y a largo plazo. Esto ha impulsado esfuerzos destinados a mejorar su seguridad y eficacia. Las estrategias modernas se enfocan en *stents* de diseño avanzado, con mejor perfil de entrega y un alto potencial de redilatación. Persisten vacíos por llenar, y nuevos datos provenientes de estudios con seguimientos más prolongados permitirán comprender mejor la evolución de estos pacientes. Esta revisión tiene como objetivo ofrecer una visión integral de estas intervenciones percutáneas, abordando los avances, los resultados y las perspectivas futuras.

Palabras clave: Coartación de aorta. Reparación percutánea. Complicaciones. *Stents* de diseño avanzado.

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INTRODUCTION

Aortic coarctation (AC) is a congenital heart disease (CHD) that is defined as a narrowing of the thoracic aorta. This defect is usually located distal to the left subclavian artery and near, or at, the insertion of the ductus arteriosus remnant. Severity may vary, and AC can present as a discrete stenosis or as a long and/or tortuous stenotic segment.[1,2] AC is one of the most common CHD, accounting for 5% to 8% of this group of defects,[3] with a rate of 3 to 4 cases per 10 000 live births. Male sex is more prevalent, with a 2:1 predominance.[4] Other congenital cardiovascular defects are usually found accompanying this disease, with a rate of 70% to 87%.[1,5,6] The most common is the bicuspid aortic valve (BAV), which has been reported in up to 60% of cases.[1,2]

The clinical presentation depends on the severity of the obstruction and the presence of other accompanying CHD. Severe cases present in the neonatal age, often with cardiogenic shock. In contrast, less severe obstructions can be detected in childhood or even adulthood with upper body hypertension, ventricular hypertrophy, thoracic aorta dilatation, and progressive collateralization.[7,8] Signs and symptoms are listed in table 1.[9]

The natural history of unrepaired aortic coarctation is associated with a markedly poor prognosis. Campbell et al. reported the leading causes of death in unrepaired AC: congestive heart failure (25%), aortic rupture (21%), bacterial endocarditis (18%), and intracranial hemorrhage (11%).[10] Therefore, AC repair in patients with significant stenosis is mandatory to improve prognosis and quality of life. Currently, clinical practice guidelines suggest intervention when AC is accompanied by hypertension and a peak-to-peak invasive gradient > 20 mmHg.[11] Surgery was the first repair technique, with percutaneous treatment subsequently established as a viable therapeutic option for eligible patients. This review aims to summarize available evidence on percutaneous interventions, discussing advancements, outcomes, and future perspectives.

HISTORICAL PERSPECTIVE

The first AC surgery was performed by Crafoord in 1944, and consisted of resection and end-to-end anastomosis.[12] Since then, other surgical techniques have evolved to prevent recoarctation and aneurysm formation, including patch aortoplasty, subclavian flap aortoplasty, and coarctectomy with graft interposition.[2]

Although surgery was the gold standard for many years, the introduction of percutaneous therapies opened a new spectrum of possibilities. The first percutaneous treatment for AC was published in 1982 by Singer et al. They successfully performed a balloon angioplasty (BA) to treat an AC in a newborn.[13] Despite the effectiveness of this technique, it was associated with a high rate of recoarctation and aneurysm formation.[14,15]

The first documented case of stent implantation in a patient with AC was published in 1991[16], and later, in 1995, Suárez de Lezo et al. reported the first series of patients treated with the same approach, showing safety and efficacy.[17] The main advantage of stent implantation is the provision of structural support, which reduces complications.[18] In 1999, Gunn et al. and subsequently other authors reported the use of covered stents with good results.[19-21]

Currently, stent implantation is recommended by the European clinical practice guidelines as the first option in adult patients with appropriate anatomy.[11] However, surgical repair remains essential in some instances, requiring careful determination of the optimal approach.

Table 1. Signs and symptoms of aortic coarctation in adults with unrepaired AC[9]

Signs	Symptoms
Upper extremity hypertension	Exertional intolerance/dyspnea
Weak or absent femoral pulses	Headache
Brachio-femoral delay	Epistaxis
Blood pressure gradient between the upper and lower extremities	Dizziness
Systolic or continuous murmur between the scapulae	Lower extremity claudication
Aortic regurgitation murmur (in cases of dilated aortic root with or without bicuspid valve)	Abdominal angina
Apical impulse displaced (in cases of dilated left ventricle)	Tinnitus
	Cold feet

BALLOON ANGIOPLASTY

BA was initially used in neonates and infants with AC and heart failure as a bailout strategy or as definitive therapy in cases of high surgical risk.[13] However, this technique was subsequently tested in older children and adults. The main advantage of BA is its simplicity, with good results in discrete coarctation. However, balloon dilatation inside the aorta can rupture the intima and damage the media layers, with subsequent potential complications.[22]

Disadvantages include lower efficacy in complex anatomies, such as isthmic hypoplasia and diffuse stenosis.[23,24] The most common complications are aortic dissection and elastic recoil in the short term, and recoarctation and aneurysm formation in the long term.[23,25,26] A retrospective registry of children treated with BA reported aortic rupture/dissection in 2% of cases, recoarctation in 26% and aneurysm formation in 34%.[27] Similarly, a randomized clinical trial comparing balloon angioplasty vs surgical treatment in children revealed that aneurysm formation occurred in 20% and restenosis in 25% of the patients treated with angioplasty.[28] On the other hand, in older patients with discrete coarctation, Walhout et al. and Fawzy et al. have found a low rate of recoarctation (≈3%).[29,30] Similarly, aneurysm formation in adults appears to be lower vs children (1.8-6%).[31,32]

BA shows a good efficacy profile in 67%-90% of cases of recurrent coarctation (postoperative or patients with a previous BA), especially in children. Therefore, currently, recurrent AC is one of the main indications for BA.[25,33-35] Furthermore, it is used in native coarctation in children to delay stent implantation until adulthood, when adult-sized stents can be implanted as definitive therapy. Despite these primary indications, in selected cases with discrete, non-critical obstruction, BA may be effective and stent implantation can be avoided, as we previously mentioned.[36]

TRANSCATHETER STENT PLACEMENT

The introduction of stent implantation in AC aimed to improve short- and long-term outcomes after balloon angioplasty, reducing complications due to aortic elasticity, recoil, and wall rupture.[35] The radial strength of the stent opposes the aortic recoil and helps to improve vessel integrity after the trauma inherent to balloon dilatation.[35]

Zabal et al. found that the residual gradient was significantly lower in patients treated with stent implantation vs those undergoing BA. This difference was more evident in patients with non-discrete coarctation (tubular coarctation or isthmic hypoplasia), in whom a residual gradient > 20 mmHg was observed in 57% of cases after BA vs 0% in the stenting group.[36] Furthermore, stenting reduces the rate of recoarctation and aneurysm formation.[37-39]

Moreover, stent implantation has demonstrated to be safe in the treatment of recoarctation, especially in patients who have undergone surgical repair. Despite several complications having been described, long-term follow-up has shown promising efficacy.[40,41]

Currently, stent implantation is preferred over BA in adults and adolescents. Furthermore, the European clinical practice guidelines recommend stenting over surgical repair when the anatomy is favorable.[42]

Despite the advantages, stenting in children younger than 8-10 years is still limited by the risk of vascular complications at the access site (greater sheaths needed), and the additional limitation of being unable to implant an adult-sized stent in a still-growing aorta, as well as the challenge of placing stents that can be adequately postdilated to accommodate future aortic growth.[25,43]

Covered vs uncovered stents

First, it is essential to note that balloon-expandable stents are preferred over the self-expandable ones due to the greater radial strength of the former, which enhances AC dilatation and prevents aortic recoil. Among balloon-expandable stents, covered stents are preferred over the bare-metal (uncovered) ones in most clinical scenarios. Covered stents can create a sealing effect at the implantation site, providing an additional safety feature.[44]

Currently, covered stents are considered first-line stents for percutaneous management of native AC, stent fracture, recoarctation, and aneurysm formation.[11] In the native AC scenario, covered stents are preferred, especially in complex anatomies, older patients, patients with connective tissue disease, or Turner syndrome (TS) to prevent aortic wall rupture or aneurysm formation.[25,38] The "sealing effect" is advantageous in previously treated patients who develop aneurysm formation or rupture of the vessel wall.[45]

Uncovered stents are preferred in children due to the possibility of redilating the stent to accommodate aortic growth. Covered stents can only be dilated up to a specific diameter without damaging their covering material. This is why covered stents are indicated for adult patients.[46]

HYBRID APPROACHES

A hybrid approach combining surgical procedures with percutaneous treatment is currently an option in patients with CHD. In the context of AC, a hybrid approach is typically necessary when the patient presents with another additional congenital heart defect that requires surgical repair. A common scenario is the coexistence of a dilated ascending aorta and a BAV with significant regurgitation or stenosis.[47] The management of such cases is always challenging due to the lack of standard guidelines and recommendations. The timing of the corrections and the type of procedures to be applied are still under discussion.

Several authors have reported cases of patients with BAV disease accompanied by ascending aorta dilatation and aortic regurgitation, which were initially treated with a percutaneous technique for the AC and later underwent a Bentall procedure.[47,48] Probably, AC repair before valvular replacement can decrease the risk of hypoperfusion of organs distal to the coarctation. However, the evidence remains inconclusive; first-stage surgical repair of valvular disease has nonetheless been reported as successful.[49]

As a new approach, Russell et al. reported their experience with a patient with BAV, ascending aorta dilatation, and AC. They performed a single-stage hybrid approach that included endovascular repair of the aortic root (AC), followed in the same session by surgical replacement of the aortic valve and ascending aorta.[50]

IMAGING, PATIENT SELECTION, AND PROCEDURAL CONSIDERATIONS

Imaging

Multimodal imaging evaluation is mandatory in patients with suspected AC to adequately characterize the anatomy, rule out accompanying malformations, and help to decide the best therapeutic option.

Transthoracic echocardiography

Transthoracic echocardiography is usually the first imaging modality performed in patients with suspected AC. Transthoracic echocardiography can reveal ascending aorta dilatation and, in some cases, allows localization of coarctation in the suprasternal view with 2D imaging and color Doppler. Additionally, spectral Doppler in the suprasternal view can display the typical "saw tooth" pattern with continuous wave Doppler, enabling the measurement of the gradient in favorable cases.[51]

Computed tomography angiography

Computed tomography angiography (CTA) is considered the imaging modality of choice for evaluating the thoracic aorta in patients with contraindications to cardiac magnetic resonance (CMR), such as pacemakers and defibrillators. Furthermore, it is the gold standard for aortic dissection, a known complication of AC, and the preferred imaging modality for evaluating luminal patency and ruling out restenosis or stent fracture in patients who have undergone a previous AC repair.[52]

Compared with CMR, the CTA provides a higher spatial resolution of the aorta, requires shorter acquisition times, and is better tolerated by claustrophobic patients; however, its disadvantages include the use of ionizing radiation and the need for IV dye, which can lead to kidney damage.[53]

Cardiac magnetic resonance

CMR is currently considered the gold standard imaging modality for evaluating adult patients with suspected AC and other CHD. This modality can accurately identify the location and significance of the coarctation using phase-contrast flow analysis. Furthermore, CMR facilitates measurement of the coarctation segment length and aortic dimensions to select an appropriate stent size, identifies collateral flow in the intercostal arteries, assesses cardiac function, and the presence of other concomitant CHD. All of these advantages are achieved without the use of ionizing radiation.[54,55] Moreover, CMR is used for postoperative surveillance after stent implantation and surgery to detect potential complications.[2]

Patient selection and indications

Native AC or recoarctation repair (either surgical or transcatheter) is mandatory in patients with hypertension and a confirmed peak-to-peak gradient across the coarctation > 20 mmHg (class I indication), with a preference for stenting when technically feasible in both most recent European and American clinical practice guidelines.[11,56] Furthermore, according to European clinical practice guidelines, AC percutaneous repair should be considered in patients

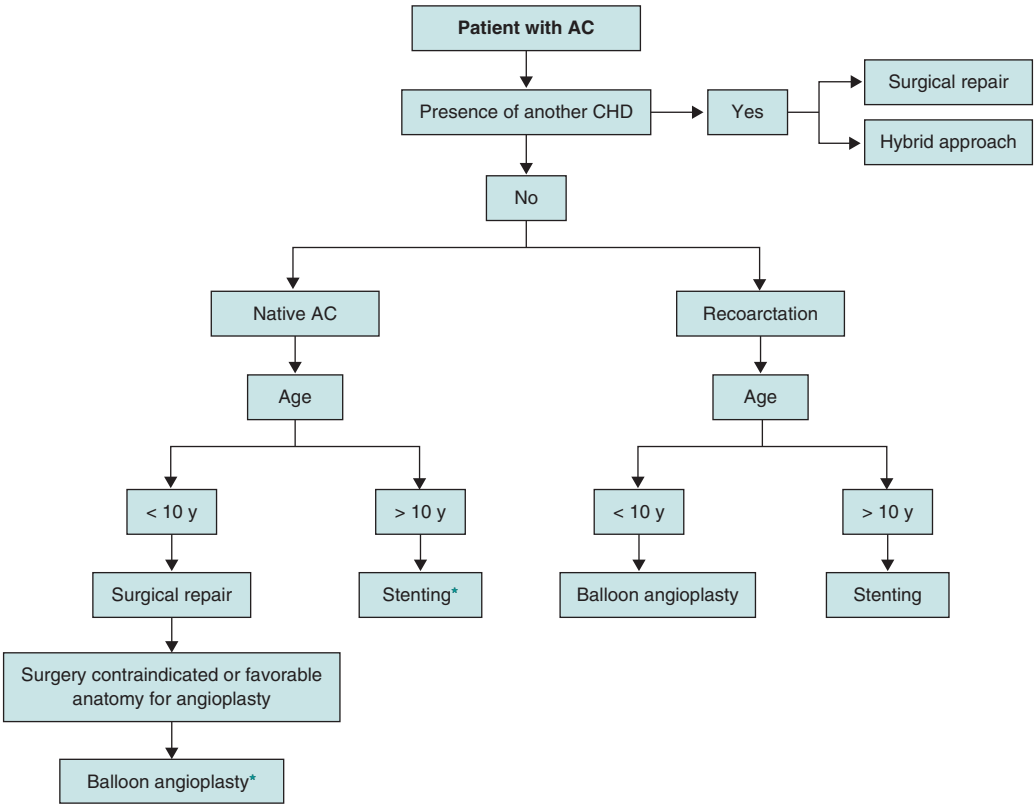

Figure 1. Proposed algorithm of first-line therapies according to the age of patients with aortic coarctation. The suggested approach in each case and age group is general, and the decision on the selected strategy will depend on the anatomic characteristics and the centers' experience. AC, aortic coarctation; CHD, congenital heart disease.
* Some authors suggest a "threshold" of 25 kg, below which the use of a stent would be inadvisable.

with hypertension and 50% narrowing without peak-to-peak gradient < 20 mmHg, and normotensive patients without significant gradients (class IIa indication).[11]

Repair strategy selection in patients with AC should be based on meticulous analysis, considering key factors such as patient age and weight, anatomic characteristics of the coarctation, and a history of prior surgical procedures. Typically, percutaneous repair is considered a lower-risk alternative to surgery in correctly selected patients. A schematic representation of the decision-making process is shown in figure 1.

In infants and children aged 8-10 years with native AC, surgical repair is preferable to percutaneous techniques. If an endovascular intervention is selected, BA will be the preferred approach.[25] Furthermore, some authors suggest a "threshold" of 25 kg, below which stenting is not recommended due to greater sheaths needed, and represents a high risk for vascular complications.[57]

In adolescents and adults, if the anatomy is adequate and there is no accompanying CHD requiring surgical repair, percutaneous stenting is currently considered the first-line therapy.[25] These considerations will depend on the patient's individual anatomic characteristics. Additionally, each center's experience with these cases will influence clinical decision-making.

Procedural considerations

Adequate planning will be crucial in ensuring better outcomes and minimizing the risk of complications associated with coarctation stenting. Several steps may coincide with the BA. The main steps and technical considerations will be addressed below. Figure 2 illustrates a case of an AC successfully treated with stent implantation.

First, before the procedure, managing hypertension is crucial as a hypertensive crisis is commonly observed after stent implantation. Beta-blockers can help to prevent such crises. Furthermore, strict postoperative monitoring is recommended to detect and manage hypertension effectively, ensuring better patient outcomes. Some authors recommend performing any percutaneous treatment under general anesthesia. AC dilatation is often painful, and the use of this approach could ensure a more comfortable procedure.[35] However, in general, light or moderate sedation is usually sufficient for adult patients.

- Access: typically, the common femoral artery (right or left) is used. Preclosure with a Perclose ProGlide (Abbott Vascular, United States) should be considered. The sheath size should be selected based on the balloon or stent diameter; delivery sheaths 2-3-Fr sizes larger than the minimum required for the balloon are recommended. Unfractionated heparin is administered to achieve an activated clotting time > 250 seconds. Furthermore, a prophylactic dose of cefazolin should be administered.

- Coarctation crossing: AC can usually be crossed with a conventional 0.035 in polytetrafluoroethylene guidewire, and sometimes a hydrophilic guidewire. In extremely difficult anatomies, retrograde access from the radial artery with externalization via femoral artery may be necessary. New

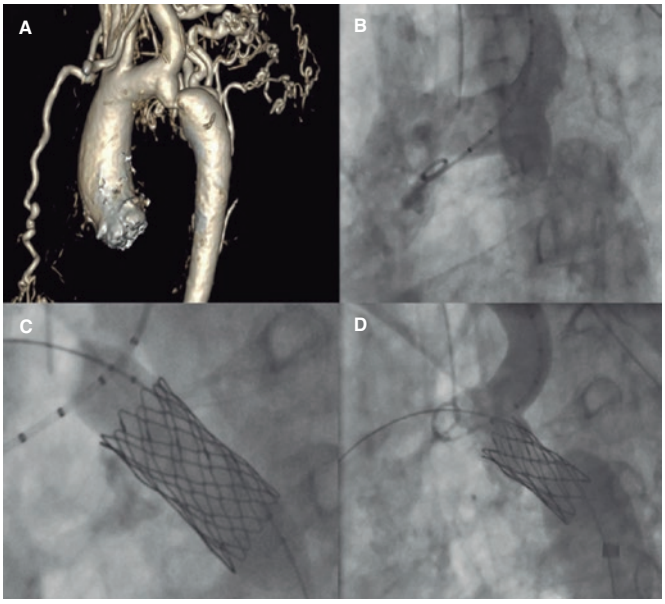

Figure 2. A successful treatment of aortic coarctation in an adult. **A:** computerized tomography showing aortic coarctation. **B:** angiography confirming aortic coarctation. **C:** balloon angioplasty and stent implantation. **D:** final fluoroscopic result after stent implantation.

gradient measurements and angiographies should be obtained to evaluate the defect. The initial guidewire will be exchanged for an extra-stiff guidewire that will be positioned in the ascending aorta or the left subclavian artery (only if the distance from the subclavian ostium to the defect is > 10 mm).

- Balloon and stent size selection: stent (and balloon) should be sized according to the diameter of the proximal arch without exceeding the diameter of the diaphragmatic aorta.[57] Stent length should be adequate to cover the stenotic segment, bearing in mind that over-dilation may result in shortening of up to 30%. Several of the stents currently available for AC treatment are listed in table 2.

- Dilatation and stent implantation: Predilatation is not routinely recommended as anchorage and stent implantation are generally more effective with direct stent placement. However, in cases of critical stenosis, predilatation turns out to be unavoidable.

  After dilatation, the ratio of the final stent diameter vs the most stenotic region of the AC should be < 3.5.[57]

- Effectiveness: The procedure will be considered successful when the invasively measured residual gradient is < 10 mmHg.[58]

OUTCOMES AND COMPLICATIONS

Immediate and short-term outcomes

Percutaneous treatment of AC has proven safe and effective, with success rates varying by intervention type and patient population. Immediate complications related to transcatheter repair include aortic wall rupture, stent malapposition, and vascular access site complications; their rate varies across groups and reports. Steiner and Prsa found that BA achieved a success rate of 71% in native AC and 69% in recoarctation. On the other hand, stent implantation showed a 100% success rate in both situations.[59] A meta-analysis conducted by Nana et al. found that the technical success rate of stenting in adults was 97%, with intraoperative and 30-day mortality rates of 1%.[60] Another meta-analysis by Yang et al. reported an overall success rate of 98% for stent implantation in native AC.[61]

Long-term outcomes

Transcatheter treatment using stents, both bare-metal and covered, has demonstrated excellent long-term outcomes. Schleiger et al. reported a procedural success rate of 88.2% and survival rates of 98.1% at 5 years, 95.6% at 10 years, and 95.6% at 15 years. Reintervention rates were 27.8% at a median follow-up of 7.3 years, with no significant difference between bare and covered stents.[62] The COAST and COAST II trials showed a good efficacy profile at the follow-up and less antihypertensive drug use.[63]

Long-term complications include aneurysm formation, restenosis, stent fracture, and stent migration.[64] Of note, the COAST and COAST II trials reported a cumulative rate of stent fractures of 24.4% at late follow-up. Reintervention rates were 21.3%, with predictors including younger age and smaller stent diameters.[63]

Table 2. Stents used for AC repair

Covering	Assembly	Stent model	Manufacturer	Metal	Expansion range (mm)	Shortening	Cell type*
Uncovered	Pre-assembled	Formula	Cook Medical	Stainless steel	8-20	~ 10-15%	Closed-cell
	Not pre-assembled	Andrastent XL and XXL	Andramed	Cobalt-chromium alloy	12-32	< 5%	Open-cell
		CP stent	NuMED	Platinum-iridium alloy	12-30	≈ 15-20%	Closed-cell
		Optimus	AndraTec GmbH	Cobalt-chromium alloy	10-28	~ 5%	Open-cell
Covered	Pre-assembled	Begraft aortic	Bentley Innomed GmbH	Cobalt-chromium alloy	12-24	< 5%	Closed-cell
		Atrium Advanta V12	Maquet	Stainless steel	12-16	0-15%	Closed-cell
		NuDEL	NuMED	Platinum-iridium alloy	12-24	~ 10%	Closed-cell
	Not pre-assembled	CP covered	NuMED	Platinum-iridium alloy	12-24	~ 15-20%	Closed-cell
		Optimus covered	AndraTec GmbH	Cobalt-chromium alloy	12-28	< 5%	Open-cell

* Open-cell stents have larger gaps and fewer connecting struts, offering greater flexibility and conformability to curved vessels. Closed-cell stents feature more interconnections, providing higher radial strength and uniform coverage but reduced flexibility and adaptability in tortuous anatomies.

Pan et al. provided one of the longest published follow-up (from 4 to 30 years). The cumulative rate of stent fracture at the long-term follow-up was 34%, while aneurysm formation occurred in 13% of cases.[65]

Overall, stenting is associated with high procedural success rates, significant long-term survival benefits, and a lower rate of hypertension. However, long-term follow-up is essential due to the risks of stent fractures, reinterventions, and potential late complications such as aneurysm formation.[42,56]

ADDRESSING LIMITATIONS IN SPECIFIC PATIENT POPULATIONS

Turner syndrome and connective tissue diseases

CHD can be found in approximately one-third of patients with TS, of which 75% correspond to AC or BAV.[66,67] Although the usual first-line therapy for AC in children is surgical repair, patients with TS exhibit high rates of aortic dissection (11%) and aneurysm formation (30%) after surgery.[68] These results are attributed to inherent aortic wall weakness due to cystic medial necrosis observed in TS.[68] Therefore, percutaneous treatment with covered stent implantation is currently the preferred treatment option in patients with adequate anatomy. Covered stents can cover the injured area in the stented wall and help to reduce the risk of aneurysm formation in this particular vascular situation.[69]

Regarding connective tissue diseases, such as Marfan or Ehlers-Danlos syndrome, there is insufficient evidence to select the optimal treatment for AC in these cases. However, similar considerations to those outlined previously outlined for TS may be applied, selecting covered stents when percutaneous treatment is anatomically feasible.

Adults and elderly patients

Elderly patients usually present with severe calcification at the coarctation site, which complicates the stent implantation and expansion, which can lead to suboptimal outcomes and increased risk of complications. In this regard, some authors recommend performing a series of dilations of the implanted stent to restore the physiological aortic diameter gradually. The use of covered stents to treat AC should be advised in elderly patients with a calcified aortic wall.[70]

In selected complex cases, such as adults with longstanding severe coarctation leading to near or complete aortic occlusion, percutaneous treatment may still be feasible. These cases require careful procedural planning, often using staged balloon dilations or covered stents to restore aortic patency safely. Advanced techniques such as guidewire escalation strategies, retrograde or antegrade access, and careful predilatation may be employed to minimize the risk of aortic injury and optimize stenting. Case reports and small series have demonstrated that, with experienced operators and appropriate planning, percutaneous repair can achieve satisfactory outcomes even in these challenging anatomies.[65]

INNOVATIONS AND EMERGING TECHNIQUES

Advances in stent technology

Biodegradable stents

An alternative to bare-metal stents for children and newborns could be bioabsorbable polymers, such as PLLA (poly-L-lactic acid) and PLA (poly-lactic acid).[71] These stents must provide structural support through their geometry; however, their lower strength compared with bare-metal metals makes them unsuitable for larger, stiffer vessels, such as the aorta.[72,73] Currently, no polymeric bioabsorbable stents exist for treating AC in children.[74] Despite this, bioresorbable stents could reduce the costs and risks associated with permanent implants. Advances in stent technology may soon provide biodegradable solutions, enabling nonsurgical management and allowing infants with AC to grow normally.

Expandable stents

One limitation of stenting in infants is the size of the delivery sheath required for stent implantation, which can later be redilated to accommodate somatic growth.[75] Balloon-expandable stents are the gold standard for treating AC.[76] However, self-expandable stents are still in the early stages of research, which may reduce the risk of stent fracture, vessel dissection, and aneurysm formation.[77]

Efforts to address growth challenges include the development of self-disrupting stents, such as the Growth stent (QualiMed, Germany), designed for AC. The device is composed of 2 halves of laser-cut, electropolished stainless steel, joined with bioabsorbable sutures to form a circular structure. The sutures are fully absorbed within 6 months, after which the 2 separate halves will remain safely in position without limiting natural growth, facilitating the implantation of a larger traditional stent that can potentially expand to adult dimensions. Despite initial promise, these stents ultimately failed due to high reintervention rates and inadequate growth adaptability.[78]

Modern strategies now focus on newer stent designs with low delivery profiles and high redilation potential, such as the Palmaz Genesis XD, Intrastent Mega, and Cheatham Platinum stent, the latter being the first approved for AC. These stents significantly reduce the risk of restenosis and the need for additional implantation. The Cheatham Platinum stent (NuMED, United States) is made from platinum and iridium wires arranged in a zigzag configuration capable of expanding to a diameter of up to 30 mm. Its significant dilation capability greatly reduces the need for additional stent implantation, leading to a lower rate of restenosis vs other devices.[58,79]

Emerging technologies include the Minima stent (Renata Medical, United States), designed for congenital vascular stenosis allows for an initial size < 4 mm for implantation at birth, with the possibility to expand to over 22 mm, maintaining structural integrity and radial strength,[80] and the BeGrow stent (Bentley InnoMed, Germany), developed for pulmonary artery stenosis to allow for dilation up to 11.5 mm, which features controlled breaking points to accommodate growth and future interventions.[81]

Imaging and navigation enhancements

Three-dimensional (3D) printed models are proving invaluable for planning complex procedures in CHD.[82,83] 3D-printed models have demonstrated utility in surgical and percutaneous planning, including for aortic arch hypoplasia and transcatheter valve implantation. These models are created using imaging modalities such as CMR, CTA, or echocardiography, followed by segmentation and printing. While rigid models are ideal for stent positioning, flexible models assess vessel wall dynamics.[83] Clinically, 3D printing enhances procedural precision, reduces complications, and shortens procedural time being beneficial for high-risk patients or challenging anatomies.

Future directions

Advanced imaging modalities, innovative stenting technologies,[74] and hybrid approaches could enhance AC treatment results. Additionally, rigorous long-term follow-up protocols are crucial for monitoring treatment durability and assessing late complications in patients.

Unmet needs for percutaneous treatment exist, including non-standardized techniques and ideal approaches for different patient profiles.[84,85] We need to refine patient selection criteria, enhance the management of complications, and collect more extensive long-term clinical data to ensure optimal outcomes and patient safety.

Finally, key research priorities in this field include conducting randomized clinical trials comparing new stent designs, optimizing stent implantation techniques, evaluating the role and timing of post-dilation, improving imaging modalities to guide and assess outcomes, determining the indications and optimal timing for percutaneous reintervention, and addressing the management of patients during the transition from pediatric to adult care.[86]

Without a doubt, artificial intelligence will play an important role in the percutaneous treatment of CHD. In the case of AC, it will enable a more precise analysis of imaging modalities to characterize its severity. Moreover, AI will enable better treatment planning, allowing selection of the most suitable approach and device, as well as individualized stents tailored to each patient's profile, thereby optimizing long-term results.

CONCLUSIONS

Percutaneous stenting has become the standard of care for eligible patients with AC, supported by consistent procedural success and favorable long-term outcomes. Future research should focus on optimizing device design, pediatric adaptability, and standardized follow-up protocols.

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STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this review.

AUTHORS' CONTRIBUTIONS

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CONFLICTS OF INTEREST

None declared.

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Scientific letter

Prognostic determinants in patients with severe aortic stenosis and moderate fragility following TAVI

Factores pronósticos en pacientes con estenosis aórtica grave y fragilidad moderada tras TAVI

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To the Editor,

Transcatheter aortic valve implantation (TAVI) is a well-established technique for the treatment of severe symptomatic aortic stenosis.

Frailty is a multidimensional clinical syndrome that reflects a patient's vulnerability to adverse events. Its evaluation is complex, with multiple scales available: the Fried scale, which includes parameters such as weight loss or grip strength; the Short Physical Performance Battery (SPPB), which evaluates balance, gait speed, and the ability to rise from a chair; and others such as the Essential Frailty Toolset, the Clinical Frailty Scale, etc.[1] In addition to classical features such as age and comorbidity, it is essential to assess frailty before deciding on valve intervention, as it correlates with prognosis after TAVI.[2]

In patients with mild or severe frailty, the decision-making process regarding the procedure is clearer. However, patients with moderate frailty—defined as the presence of 1 or 2 frailty criteria—represent an intermediate group between robustness and advanced frailty. These patients have a moderate risk of falls, disability, hospitalization, and death, and are more likely to progress to severe frailty in the coming years.[3]

We evaluated the characteristics and prognosis of patients with moderate frailty treated with TAVI. For this purpose, we conducted a single-center retrospective study of patients with severe symptomatic aortic stenosis and moderate frailty who underwent TAVI between 2016 and 2023. The outcomes analyzed were overall mortality, all-cause readmissions, and heart failure (HF) decompensation. The study was approved by our center ethics committee (No. 2019/8735/I).

The geriatrics department performs a comprehensive evaluation, classifying frailty as mild, moderate, or severe. To assess frailty in patients with severe aortic stenosis who are eligible for TAVI, we used the SPPB scale[4] due to its high ability to discriminate between robust and frail patients in a rapid and objective manner, allowing identification of irreversible frailty. The SPPB provides greater precision than other scales in predicting adverse events and readmissions, and it is simple to apply in clinical practice. Moderate frailty was defined as a score < 10 on the SPPB, along with dependence for instrumental activities and mild dependence for basic activities of daily living, mild-to-moderate cognitive impairment, and risk of malnutrition.

Of the 306 patients evaluated, those with severe frailty, major comorbidity, or who declined the procedure were excluded and received conservative treatment. A total of 236 patients underwent TAVI, 54 of whom exhibited moderate frailty and constituted the study cohort.

Clinical, functional, and laboratory data were collected at the time of the procedure. Variables were analyzed using the chi-square or Fisher's exact tests for categorical variables, and the Student's t test or nonparametric tests for continuous variables. The Kaplan-Meier method was used to analyze the association between previous HF and events of mortality, HF decompensation, and hospital readmission. Survival curves were compared using the log-rank test. Previous HF was analyzed as a potential independent prognostic factor using a Cox regression model, adjusted for clinically relevant variables: diabetes mellitus, left ventricular ejection fraction prior to TAVI, chronic kidney disease, and ischemic heart disease.

The patients' mean age was 83.4 ± 4 years, with a predominance of women (81.5%) and a mean Barthel index of 89. The most common comorbidities were hypertension (94.5%), chronic kidney disease stage ≥ 3 (50%), diabetes mellitus (22.2%), atrial fibrillation (44.4%), and ischemic heart disease (31.5%). The mean left ventricular ejection fraction was 60 ± 10%. A total of 59.3% had a prior diagnosis of congestive HF requiring IV diuretic therapy.

Regarding the clinical presentation that led to the indication for TAVI, 48.2% exhibited congestive HF; 40.7%, dyspnea without signs of congestion; 7.4%, angina pectoris; and 3.7%, syncope.

During a mean follow-up of 25.5 months, 26 deaths (48.1%) were reported, with cardiovascular causes being the most frequent (51.9%). The median time to death was 24 months [10.5–41.5]. A total of 57.4% of patients were readmitted, most commonly for infection (24.1%); 42.6% presented with HF decompensation and required IV diuretics.

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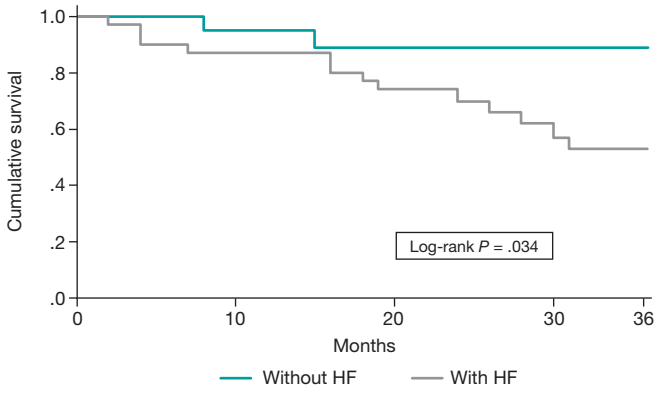
Table 1. Clinical characteristics associated with events after TAVI in patients with moderate frailty (n = 54)

Variable	Composite endpoint* (n = 39)	No composite endpoint (n = 15)	*P*
Female sex, n (%)	32 (82.1)	12 (80)	1
Cardiovascular comorbidity, n (%)			
Hypertension	37 (94.9)	14 (93.3)	1
Diabetes mellitus	11 (28.2)	1 (6.7)	.145
Dyslipidemia	19 (48.7)	11 (73.3)	.133
Ischemic heart disease	12 (70.6)	6 (29.4)	1
Atrial fibrillation	19 (48.7)	5 (33.3)	.28
Previous heart failure	28 (71.8)	4 (26.7)	.003
Previous valvuloplasty	9 (23.1)	6 (40)	.309
Other comorbidity, n (%)			
COPD	8 (20.5)	3 (20)	1
OSAHS	4 (10.3)	1 (6.7)	1
CKD (eGFR < 60)	19 (48.7)	8 (53.3)	.761
Stroke	6 (15.4)	2 (13.3)	1
Peripheral vascular disease	4 (10.3)	1 (6.7)	1
Neoplasm	3 (7.7)	3 (20)	.331
Functional and cognitive aspects, n (%)			
Lives alone	14 (35.9)	2 (13.3)	.182
Cognitive impairment	5 (12.8)	6 (40)	.054
TAVI, n (%)			
Intraoperative complications	21 (53.8)	6 (40)	.362
Post-TAVI pacemaker implantation	7 (17.9)	2 (13.3)	1

CKD, chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2); COPD, chronic obstructive pulmonary disease; OSAHS, obstructive sleep apnea-hypopnea syndrome; TAVI: transcatheter aortic valve implantation.
* Composite endpoint: hospital admission, heart failure decompensation, or death.

In the analysis of variables, only prior HF was significantly associated with higher overall mortality, all-cause readmissions, and higher risk of HF decompensation during follow-up (table 1). The Kaplan-Meier curve showed a higher proportion of decompensations in patients with previous HF during follow-up (figure 1). Statistical significance was not reached for mortality or readmission. In multivariate analysis, prior HF was the only variable significantly associated with HF decompensation (adjusted hazard ratio, 5.4; 95%CI, 1.2-24.1; $P < .026$).

HF is associated with higher mortality and readmission rates after TAVI.[5] The risk scores proposed by the European Society of Cardiology clinical practice guidelines for pre-TAVI assessment (FRANCE-2 Risk Score and PARTNER Risk Score) do not include previous HF as a risk factor, although FRANCE-2 considers New York Heart Association functional class IV as a futility factor after TAVI. Even the CAPRI risk score,[6] which predicts the risk of HF after TAVI based on comorbidities and echocardiographic parameters, does not take it into account.



Without prior HF	22	21	20	20
Prior HF	32	28	24	20

Figure 1. Kaplan-Meier curve for the event of heart failure (HF) decompensation during follow-up based on the presence of prior HF.

In the group of patients with moderate frailty, in whom clinical decision-making is more complex, identifying the factors that predict unfavorable outcomes after TAVI is of paramount importance. However, the available evidence on this issue is limited. Our results are consistent with former studies, showing that a history of congestive HF is significantly associated with a higher risk of HF readmission during follow-up after TAVI.

Identification of this high-risk subgroup for new decompensations would allow individualized follow-up and optimization of postoperative management to prevent adverse events and improve prognosis. Larger prospective studies are needed to confirm these findings and strengthen the available evidence. Despite these limitations, our study underscores the importance of prior congestive HF as a key predictor of HF development after TAVI in frail patients.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This study is in full compliance with relevant ethical considerations and was reviewed and approved by *Hospital del Mar* Ethics Committee (Barcelona, Spain) in December 2019 (Research Project 2019/8735/I). We confirm that informed consent for publication of patient cases was obtained and is archived. Similarly, we confirm that the SAGER guidelines were appropriately followed. Sex/gender of participants was considered as a potentially relevant variable, and this information was reported transparently. Differences according to sex/gender were also analyzed and reported when pertinent.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

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

AUTHORS' CONTRIBUTIONS

C. Belmonte Herrera: data collection and management, manuscript drafting. D.M. Rojas Aguirre: data collection and management. L.C. Belarte Tornero: statistical analysis. S. Ruiz Bustillo: validation and review. B. Vaquerizo Montilla: validation and review. S. Valdivielso Moré: study design, validation and review.

CONFLICTS OF INTEREST

None declared.

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Scientific letter

Off-label use of rotational atherectomy in STEMI: a single-center experience

Uso off-label de aterectomía rotacional en IAMCEST: experiencia en nuestro centro

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To the Editor,

Coronary artery calcification occurs in up to 1 in 5 patients with ST-segment elevation myocardial infarction (STEMI),[1] and its prevalence is expected to rise with population aging and the increasing burden of associated comorbidities. Calcification complicates percutaneous coronary intervention (PCI) and is associated with worse technical and clinical outcomes, including higher rates of in-stent thrombosis, target-lesion revascularization, reinfarction, and mortality.[1,2] Therefore, appropriate lesion preparation using plaque modification techniques is essential. Although rotational atherectomy (RA) (ROTABLATOR/ROTAPRO, Boston Scientific, United States) is a widely used procedure for treating severely calcified lesions, evidence on its safety and efficacy profile in patients with STEMI remains limited.

We present a retrospective case series of patients with STEMI treated with RA between 2011 and 2023 at our center. Clinical and angiographic data were collected. Success rate was defined as successful stent implantation with residual percent diameter stenosis < 20% and distal Thrombolysis in Myocardial Infarction (TIMI) grade-III flow, without major in-hospital complications. Clinical follow-up was performed according to the standard practice of the unit.

Between 2011 and 2023, only 4 of 2490 patients with STEMI (0.16%) required RA due to severely calcified lesions that prevented conventional balloon dilation or in which such dilation was insufficient to achieve successful PCI (table 1). The main clinical aspects of each case are described below (figure 1).

Case No. 1 involved a 74-year-old woman referred for emergency PCI due to an inferior subepicardial lesion. The right coronary artery showed severe calcification with acute proximal occlusion. A work guidewire was successfully advanced distally using a XBRCA catheter (Cordis Corporation, United States). However, further attempts to pass a thrombus aspiration catheter or a 1-mm balloon were unsuccessful. The guidewire was exchanged for a ROTAWIRE Floppy (Boston Scientific, United States) using a microcatheter, and RA was performed with a 1.25-mm burr after placement of a temporary pacemaker via femoral vein. After RA, antegrade flow was restored, allowing dilation with 2.5-mm and 3.0-mm balloons. A drug-eluting stent (DES) was then implanted in the right coronary artery, yielding an optimal final result.

Case No. 2 was a 67-year-old man who presented with anterior STEMI. Coronary angiography revealed a proximal medial occlusion of the left anterior descending coronary artery (LAD). Using a 6-Fr EBU 3.75 catheter (Medtronic, United States), the lesion was crossed, restoring distal flow, and a critically calcified plaque was identified. Predilation with semi- and noncompliant balloons achieved inadequate expansion. Although intracoronary lithotripsy was attempted, the balloon could not be advanced despite the use of a catheter extension system. RA was performed with a 1.25-mm burr, and due to persistent poor balloon expansion, it was repeated with a 1.75-mm burr. Subsequent dilation with a 3-mm cutting balloon was satisfactory. Intravascular ultrasound (IVUS) showed multiple calcium fractures. A 3.5 mm × 30-mm DES was ultimately implanted, and IVUS confirmed an optimal result.

Case No. 3 involved an 84-year-old man with anterior STEMI. Angiography revealed acute proximal occlusion of the LAD. Thrombus aspiration was performed with a 6-Fr EBU 4 catheter, which retrieved abundant thrombotic material. The lesion was unsuccessfully predilated with a 2.5-mm cutting balloon and a 2.5-mm noncompliant balloon at high pressure. RA with a 1.5-mm burr allowed adequate balloon expansion. A 3 mm × 38 mm drug-eluting stent was subsequently implanted, achieving an optimal final result without complications.

Case No. 4 was an 83-year-old man who presented with ventricular tachycardia treated with procainamide. The electrocardiogram showed anterior ST-segment elevation, and emergency PCI was indicated. Acute occlusion of the mid-LAD was identified. Using a 6-Fr EBU 3.75 catheter, the lesion was crossed with a Pilot 50 guidewire. Although IVUS was attempted, the device could not fully cross the lesion; however, concentric calcification was confirmed at the site of maximal stenosis. RA was performed with a 1.25-mm burr. During the procedure, the patient developed hypotension requiring low-dose norepinephrine infusion. After RA, dilation was achieved with cutting and noncompliant 2.5-mm balloons, followed by the successful implantation of a 2.75 mm × 15 mm DES. Norepinephrine was progressively withdrawn in the cath lab.

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Table 1. Main characteristics of the procedures

Case	Sex and age	Comorbidity	Clinical presentation	Vascular access	Target vessel	Devices used	Burr size	Type and size of stent	Procedural time (min)	Contrast (mL)
1	Female, 74 years	Hypertension, diabetes mellitus, dyslipidemia, prior STEMI treated with thrombolysis	Inferior STEMI	Radial artery	RCA	1.25 mm × 10 mm semicompliant balloon, 2 mm × 6 mm cutting balloon, 3 mm × 6 mm cutting balloon, 3.5 mm × 8 mm noncompliant balloon, 3.5 mm × 10 mm high-pressure balloon	1.25 mm	3.5 mm × 38 mm DES	174	200
2	Male, 67 years	Current smoker, dyslipidemia, prior PCI in left circumflex artery	Anterior STEMI	Radial artery	LAD	2.5 mm × 15 mm noncompliant balloon, 2.75 mm × 15 mm, noncompliant balloon, 3 mm × 12 mm intracoronary lithotripsy balloon, 3 mm × 8 mm noncompliant balloon	1.25 mm and 1.75 mm	3.5 mm × 30 mm DES	115	159
3	Male, 84 years	Hypertension, diabetes mellitus, dyslipidemia, peripheral vascular disease	Anterior STEMI	Femoral artery	LAD	2.5 mm × 15 mm noncompliant balloon, 2.5 mm × 6 mm cutting balloon, 3 mm × 14 mm noncompliant balloon, 3.35 mm × 15 mm noncompliant balloon	1.5 mm	3 mm × 38 mm DES	113	250
4	Male, 83 years	Hypertension, dyslipidemia, peripheral vascular disease	Anterior STEMI	Femoral artery	LAD	2 mm × 15 mm noncompliant balloon, 2.5 mm × 15 mm noncompliant balloon, 2.5 mm × 6 mm cutting balloon, 3 mm × 8 mm noncompliant balloon	1.25 mm	2.75 mm × 13 mm DES	112	111

DES: drug-eluting stent; LAD: left anterior descending coronary artery; PCI: percutaneous coronary intervention; RCA: right coronary artery; STEMI: ST-segment elevation myocardial infarction.

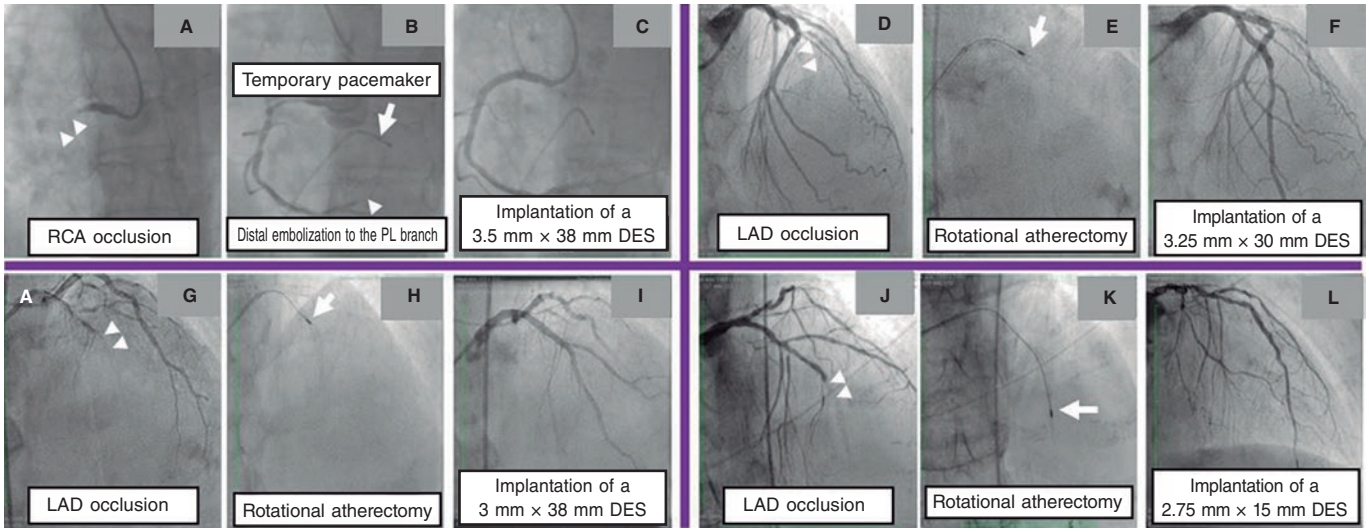

Figure 1. Images of percutaneous coronary interventions in the patient series. **A:** proximal occlusion of the right coronary artery (RCA) (arrowheads mark the occlusion site). **B:** temporary pacemaker implantation (arrow); after rotational atherectomy, distal embolization of the posterolateral artery (PL) is observed (arrowhead). **C:** deployment of a 3.5 mm × 38 mm DES. **D:** mid-LAD occlusion with severely calcified lesion (arrowheads). **E:** rotational atherectomy with a 1.25-mm burr (arrow). **F:** deployment of a 3.25 mm × 30 mm DES. **G:** mid-LAD occlusion (arrowheads). **H:** rotational atherectomy with a 1.5-mm burr (arrow). **I:** deployment of a 3 mm × 38 mm DES. **J:** mid-LAD occlusion (arrowheads). **K:** rotational atherectomy with a 1.25-mm burr (arrow). **L:** deployment of a 2.75 mm × 15 mm DES.

In all cases, flow was restored, adequate predilation achieved, and a DES successfully deployed with satisfactory angiographic results (table 1). IVUS was used in 2 of the 4 patients; notably, these were the most recent cases, reflecting increased awareness of the benefits of imaging modalities to optimize procedural outcomes in patients with coronary calcification over the past decade. The mean procedural time was 133 ± 31 minutes. At the 2-year follow-up, all 4 patients were alive, and did not require any additional interventional procedures or hospital readmissions for cardiovascular causes.

Coronary artery calcification is associated with advanced age, smoking, and chronic kidney disease, and is present in up to one-third of patients undergoing PCI.[2,3] Severe calcification, defined visually or by intracoronary imaging, hinders stent implantation and expansion

and increases the risk of complications.[4] Newer plaque modification techniques promise improved outcomes.[5] RA enables calcium fracture using a diamond-coated rotating burr, increasing arterial compliance and facilitating device passage and stent expansion.

Large RA studies have systematically excluded acute coronary syndrome, particularly STEMI, due to the higher risk of complications. The ROTATE Registry,[5] which included primarily patients with non–ST-elevation acute coronary syndrome or chronic coronary disease, found comparable success rates but higher complication rates in the acute setting. The ROTA-STEMI Registry[6] analyzed 104 patients with STEMI treated with RA during PCI across 12 European centers from 2002 through 2021. RA was mainly used as a bailout strategy (76.9%). Although the procedural success rate (stent implanted, TIMI grade-3 flow, and residual percent diameter stenosis < 30%) was 86.5%, the in-hospital mortality rate reached 18.3% overall, with marked differences depending on hemodynamic status (50% in shock vs 1.5% without shock). These findings support the feasibility of RA in selected cases of STEMI.

Relative contraindications for RA in STEMI include the risk of distal embolization, vasospasm, and the RA-induced prothrombotic state, which enhances platelet activation and worsens slow-flow/no-reflow.[4] In our case series, the rate of technical success was 100%, with no major complications or cardiovascular events during 2-year follow-up. Although our study did not include a systematic analysis of unsuccessful primary PCI, RA seems to be a safe and effective technique for treating severely calcified lesions even in the acute STEMI setting, when performed by experienced operators.

In conclusion, multicenter clinical trials with robust design and adequate sample size are needed to specifically assess the safety and efficacy profile of plaque modification strategies in patients with STEMI and severe coronary calcification, including RA, traditionally reserved for bailout cases.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

The study was approved by *Hospital del Mar* Research Ethics Committee. Because of its retrospective design and anonymization of data, the requirement for informed consent was waived. According to SAGER guidelines, sex and gender variables were considered.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this article.

AUTHORS' CONTRIBUTIONS

A. Prieto-Lobato drafted the manuscript and was responsible for data acquisition and analysis. H. Tizón-Marcos conceived the study and reviewed the manuscript. J.C. Betancourt and X. Armario participated in data collection. B. Vaquerizo and H. Cubero reviewed the manuscript. All authors approved the final version.

CONFLICTS OF INTEREST

None declared.

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Ventricular tachycardia after mitral valve-in-valve implantation

Taquicardia ventricular secundaria a valve-in-valve *mitral*

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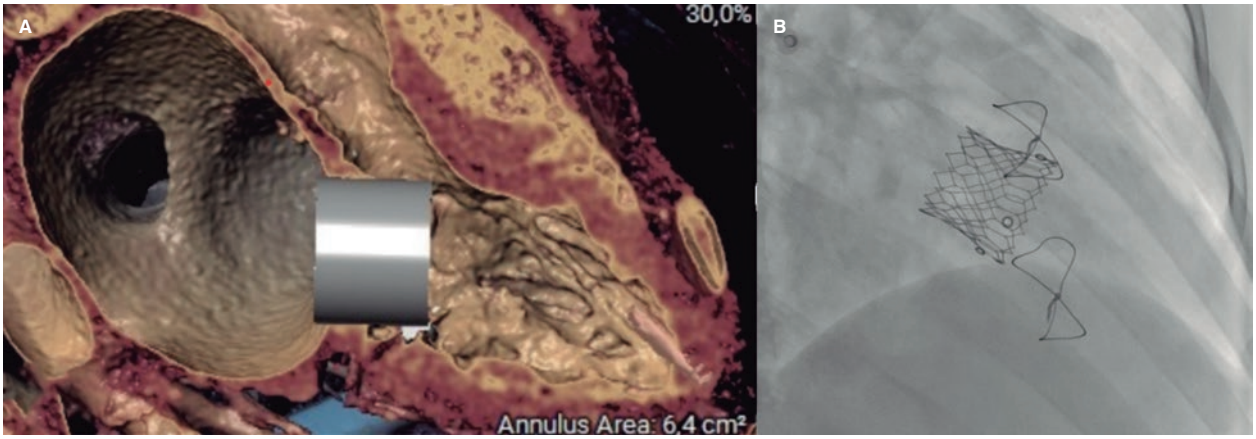

Figure 1.

We present the case of a 14-year-old girl with a double mitral lesion due to a dysfunctional 31 mm Mosaic biological prosthetic valve (Medtronic, United States) implanted for symptomatic congenital mitral valve disease. Prosthetic valve replacement was indicated due to severe stenosis and functional deterioration (video S1 and video S2).

Using coronary computed tomography angiography and the 3Mensio software (PIE Medical, the Netherlands) for virtual simulation of a 29 mm SAPIEN heart valve (Edwards Lifesciences, United States), we deemed the valve suitable, which had an estimated left ventricular outflow tract area of 1.8 cm^2 (figure 1A).

We performed transseptal access with an echo-guided BRK needle and interatrial septum dilatation with a 16 mm × 40 mm Atlas balloon (Bard Medical, United States). Afterwards, we advanced the 29 mm SAPIEN 3 transcatheter valve delivery system and implanted it with simultaneous left ventricular overdrive pacing with excellent results (figure 1B, video S3, and video S4).

The patient developed several episodes of monomorphic ventricular tachycardia not previously documented (figure 2). Telemetry suggested a probable origin in the papillary muscles, confirmed by transthoracic echocardiography, which showed systolic contact of the valve with the posterior papillary muscle (video S5). Holter monitoring showed frequent ventricular tachycardias despite treatment with beta-blockers. Due to the low likelihood of success with ablation, we decided to explant the transcatheter valve (figure 3) and implant a 31 mm ATS mechanical mitral prosthesis (Medical Open Pivot, United States).

The postoperative course was favorable, without any new episodes of ventricular tachycardia.

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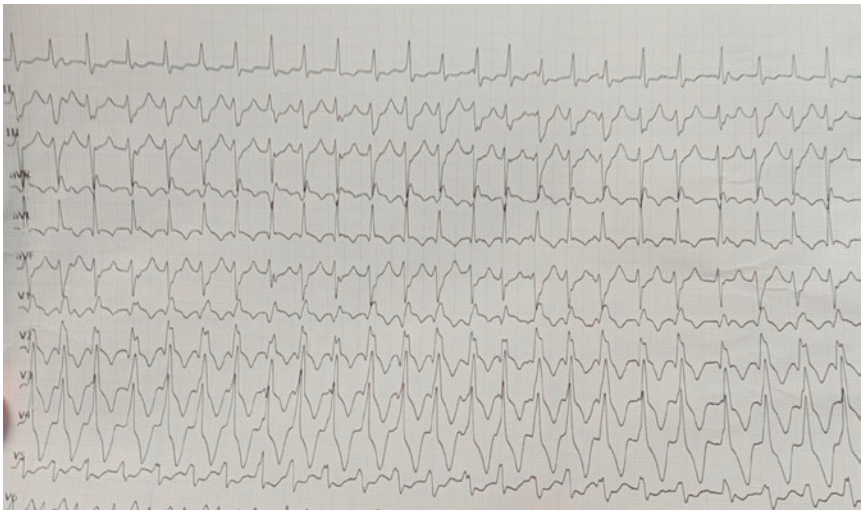

Figure 2.

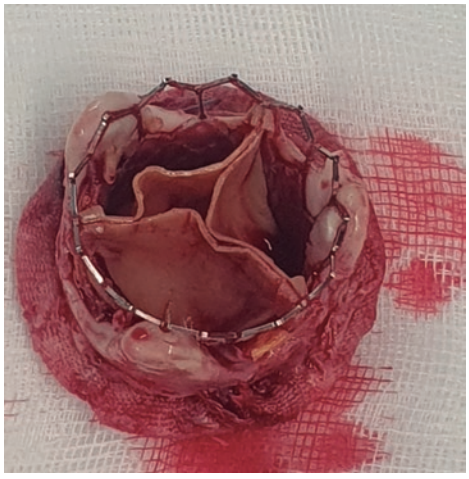

Figure 3.

ETHICAL CONSIDERATIONS

Informed consent was obtained from the patient's legal tutors.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this article

AUTHORS' CONTRIBUTIONS

A. Villanueva García, C. Abelleira Pardeiro, E.J. Balbacid Domingo, M. Larman Tellechea, N. Guillén, and F. Gutiérrez-Larraya Aguado participated in the drafting, critical review, and final approval of the manuscript.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000525.

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Mitral valve-in-valve with severe atrial septum calcification

Valve-in-valve *mitral con septo interauricular gravemente calcificado*

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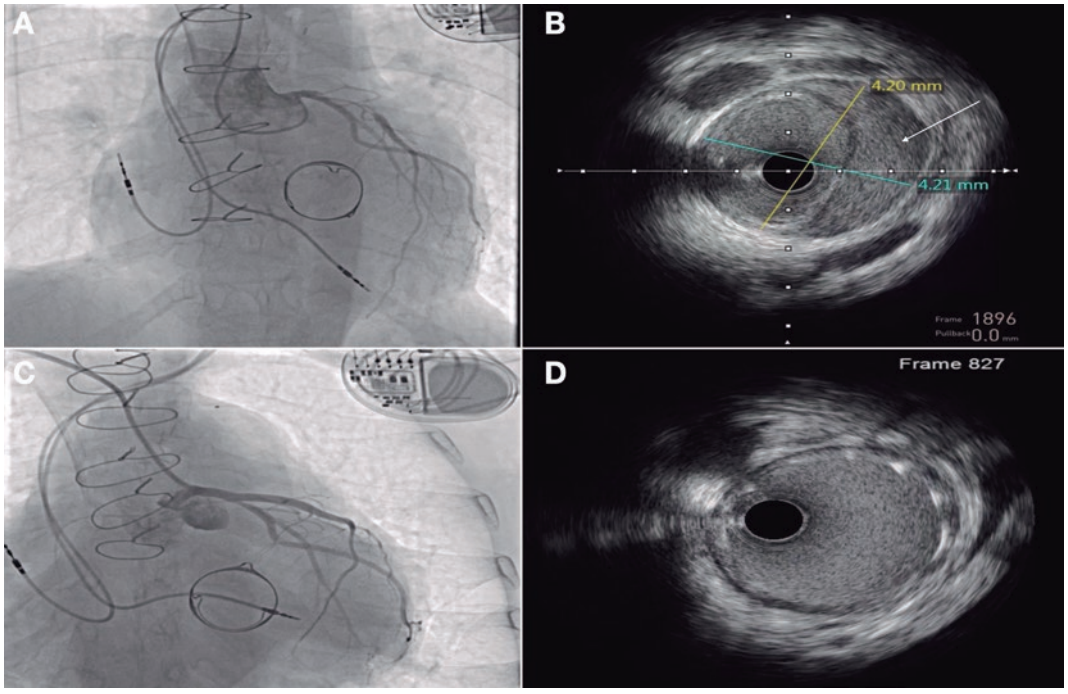

Figure 1.

A 55-year-old woman with an incomplete atrioventricular canal, who underwent repair of the mitral cleft and patch closure of the ostium primum type defect, followed by mitral bioprosthesis implantation (Carpentier PERIMOUNT 27, Edwards, United States) in adulthood. She developed episodes of left atrial flutter. Due to the inability to perform a transseptal puncture, we proceeded with retroaortic atrioventricular node ablation, resulting in iatrogenic left main coronary artery dissection, which resolved after drug-eluting stent implantation (figure 1A-D, videos S1 and S2). During follow-up, she showed signs of progressive prosthetic degeneration (figure 2A-B, videos S3 and S4), which led to transcatheter mitral valve-in-valve implantation. We performed a transseptal puncture of the severely calcified patch (figure 2C-D) using a Versacross system (Boston Scientific, United States). Then, we used a deflectable catheter to advance a high-support guidewire, which was, eventually, captured in the left ventricle, establishing a venoarterial loop. Afterwards, we performed a septostomy with an Atlas Gold 16 mm × 45 mm balloon catheter (BD, United States) and with great difficulty given the anatomical complexity, we advanced a 26-Fr DRYSEAL sheath (Gore, United States) into the left atrium through which we implanted a SAPIEN 3 Ultra 26 bioprosthesis (Edwards, United States) with a nominal +2 cm³ inflation. Good expansion was observed, with slight protrusion into the left ventricle without conflict with the outflow tract (figure 3A-D, video S5). The patient was discharged with normal prosthetic valve function, which was maintained at the 1-year follow-up (video S6). The patient signed the informed consent form.

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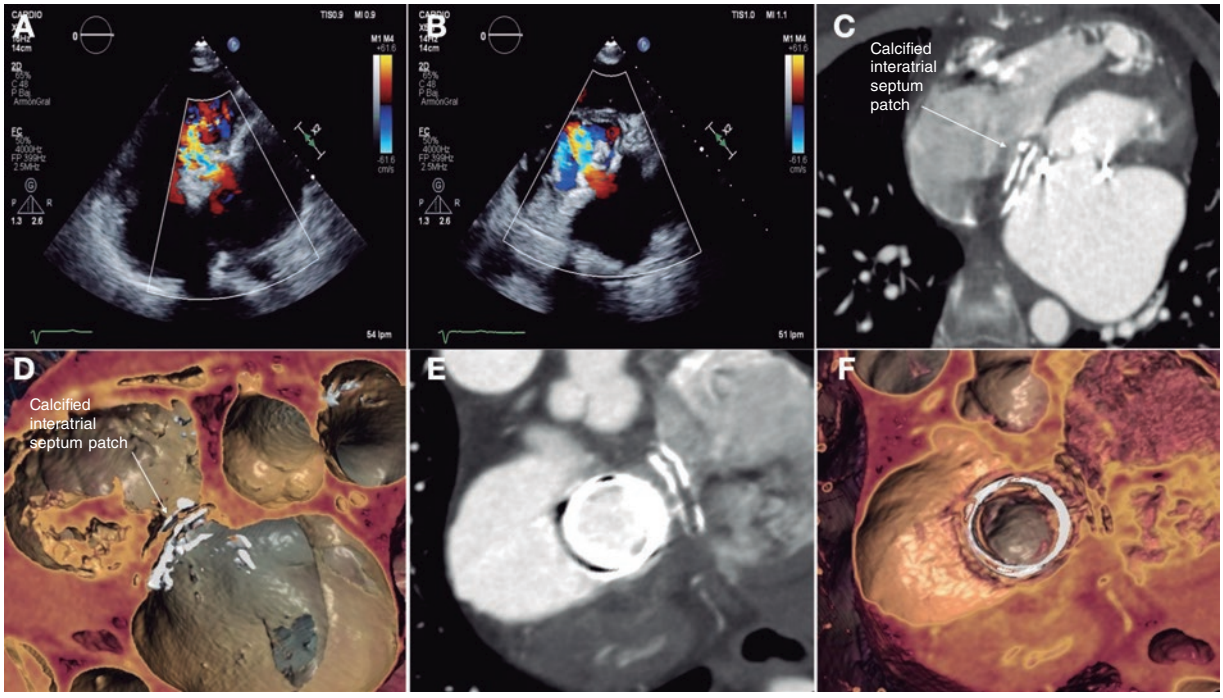

Figure 2.

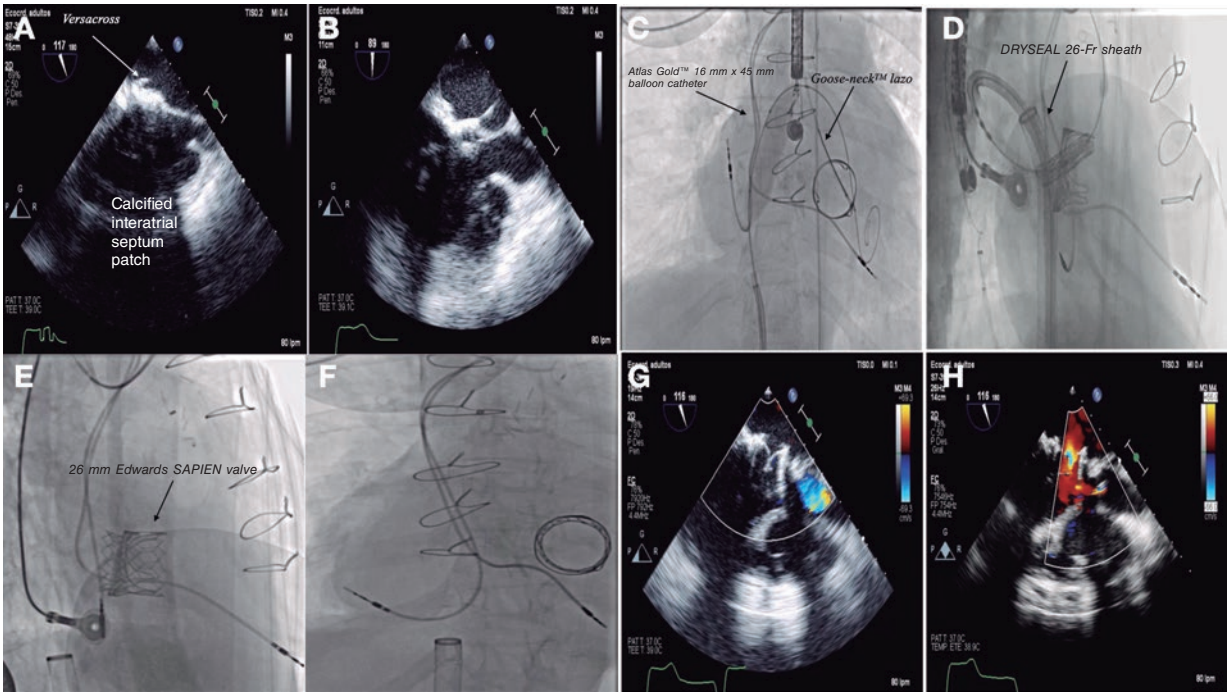

Figure 3.

FUNDING

None declared.

ETHICAL CONSIDERATIONS

This work was accepted by our center ethics committee. Informed consent for publication of this case was obtained and has been archived. SAGER guidelines regarding potential sex/gender biases have been followed.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

No artificial intelligence was used in the preparation of this work.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to the preparation of the text.

CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M25000530.

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Interview

An interview with Bruno Scheller

Una entrevista con Bruno Scheller

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Bruno Scheller, MD, PhD, is Professor of Clinical and Experimental Interventional Cardiology at Saarland University and Deputy Director of the Clinic for Internal Medicine III, University Hospital of Saarland, Homburg, Germany. As Head of Interventional Cardiology, he oversees catheter-based treatment of coronary artery and structural heart disease including transcatheter aortic valve implantation and transcatheter edge-to-edge repair. His research group is at the forefront of preclinical and clinical research on local drug delivery and the development of novel catheter based interventional therapies.

Let's start from the beginning — what first inspired you to study medicine?

I was born into a working-class family. My father, a coal miner, taught me skills in manual work, from which I still benefit every day in the cath lab. During secondary school, my strongest subjects were mathematics and physics. Toward the end of my schooling, I worked part-time in an industrial plant to co-finance my education. I tried to decide which subject to study by doing internships. In late summer 1988, the region in which I lived was affected by the Ramstein air show disaster. Our university hospital was among the centers responsible for treating civilian casualties. At that time, I was completing a nursing internship in the intensive care unit, which carried much of the clinical burden of the response. The professional attitude of the nursing staff made a deep impression on me and ultimately shaped my decision to study medicine. Nevertheless, during the early years of medical stidues, I continued to question whether this had been the right choice.

Why did you specialize in cardiology? Why did you decide to be an interventional cardiologist?

During an internal medicine lecture in the winter of 1990, our cardiologists proudly demonstrated how they could reopen an occluded right coronary artery in a patient with ST-segment elevation myocardial infarction (STEMI) during the night. At that time, percutaneous coronary intervention (PCI) for STEMI was still regarded as an experimental approach. I realized that interventional cardiology was my destiny.

Describe your initial interest and work with drug-coated balloons. What were the preclinical trials?

I completed my doctoral thesis on the effects of of X-ray contrast media on microcirculation. This work was supported by the head of the R&D department for contrast media of Schering AG in Berlin, Professor Ulrich Speck. In December 1999, he invited me to Berlin (Germany), shortly after I attended the Transcatheter Cardiovascular Therapeutics (TCT) meeting in Washington DC (United States) for the first time in my life. In DC, I was impressed by preclinical data on drug-eluting stents. In Berlin we discussed ideas to use contrast media as carriers for antiproliferative agents.

A few months later, Speck moved to the Radiology Department at Charité hospital, Berlin, for a professorship under the direction of Bernd Hamm. We established a porcine stent restenosis model and conducted the first study of contrast agent-taxane formulations. We showed that a short-term contact of antiproliferative drugs with the vessel wall, such as paclitaxel, led to a dose-dependent, long-lasting biological effect. However, a more lesion-specific technique was required. Remarkably, coating of a conventional angioplasty balloon catheter with the contrast agent and paclitaxel resulted in a significant inhibition of neointimal formation after experimental stent implantation in the porcine model. This observation marked the birth of the drug-coated balloon (DCB) technology.

When we presented the preclinical results of DCB in the early 2000s, the prevailing reaction was that it would not work at all, even if it worked on pigs, it would not work on humans, and even if it worked on humans, nobody would need such technology, let alone use it.

Briefly summarize your clinical research in DCB for in-stent restenosis (ISR) and de novo lesions.

In 2003, we discussed several options for a first-in man study. At that time, it was not possible to predict from animal data whether efficacy could be clinically proven at all, or whether patients would be harmed by an excessive effect. My proposal was to start with a safe indication that also represented an unmet clinical need, namely coronary ISR, where a stent is already in place and surrounded by

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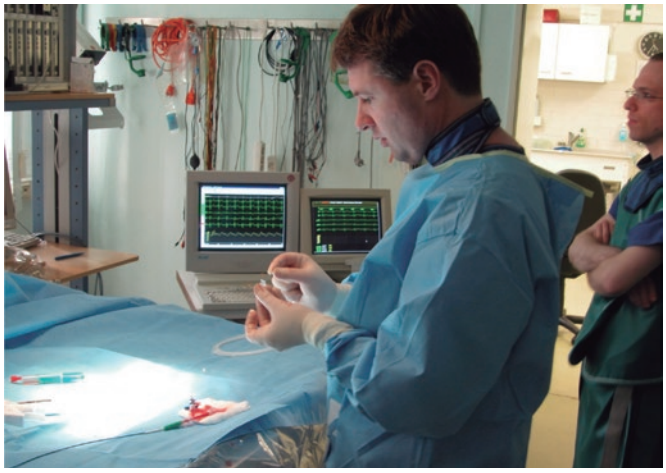

Experimental work in the animal cath lab (2006).

substantial tissue coverage. Our first clinical trial[1] in the ISR indication was successful and paved the way for the indication of DCB for coronary ISR. Meanwhile, our Paccocath ISR trial is seen as one of the milestones in interventional cardiology.[2]

The concept of treating de novo lesions was initially proposed by colleagues performing peripheral vascular interventions. Gunnar Tepe and Thomas Zeller encouraged us to support a trial on the treatment of femoropopliteal lesions, an approach toward which I was initially very skeptical. Fortunately, the THUNDER trial[3] demonstrated the utility of DCB in peripheral arteries and fundamentally transformed strategies in peripheral vascular intervention.

One of the early trials on coronary de novo lesions was the PEPCAD I study.[4] It was a prospective, non-randomized series of patients with small coronary arteries. At that time, we had no understanding of lesion preparation and only a DCB, with a diameter of 2.5 mm, which we attempted to use for lesions ranging from 2.0 mm to 2.75 mm. The positive result was that approximately 70% of lesions could be successfully treated with DCB alone, with event rate in the mid-single-digit percentage range. Conversely, we learned that combining DCB therapy with stent implantation was detrimental, especially in cases of geographical mismatch.

Based on this, shortly after Eastern 2010, we organized the first meeting of the initially German, later international DCB Consensus Group in the timely context of the annual conference of the German Cardiac Society in Mannheim (Germany). My idea was to predilate the lesions to identify those requiring stent implantation. Along with Franz Kleber, I proposed the now widely accepted concept of 'DCB only', focusing on lesion preparation to decide between drug-eluting stents (DES) and DCB as the final treatment.[5]

Criteria were chosen pragmatically. Achievement of TIMI grade-3 flow was considered essential, and the classification of dissections smaller than type C was based on old data from the pioneering days of Grüntzig. The threshold of 30% residual diameter stenosis arose from the recognition that achieving 10% to 20% with conventional angioplasty was challenging (the advantages of specialty balloons were little known at the time) and, at the same time, 50% percent diameter stenosis would, by definition, mean restenosis. We, therefore, proposed a 30% cutoff, which has remained the standard to this day. These criteria are certainly not the last word on wisdom, and we must work to find better standards. Until then, we will continue to work with it, and for small coronary arteries, this concept has performed well in the Basket Small 2 trial,[6,7] and larger studies such as Selution de novo have also successfully implemented these criteria.

Which were, and still are, the technical hurdles in the development and advancement of this technology?

The fundamental goal of DCB technology is to deliver as much drug as possible to the vessel wall for as long as possible, despite the short contact time between the balloon and the vessel wall. Accordingly, improvements include reducing drug loss, improved transfer to the vessel wall, a depot effect in the vessel wall, and reduced loss of the coating to the periphery.

Not all drug-coated balloons are the same. How do paclitaxel-based DCB compare with limus-based DCB in terms of efficacy and clinical outcomes?

The central issue is not so much which drug is better or worse, but rather how good or poor the coating technology actually is. Currently, there are significant and clinically relevant differences in this regard for both paclitaxel and sirolimus.

What is the current role of DCB in routine clinical practice?

At present, this very much depends on each center, the investigator and, most importantly, geographic region. In Asia, DCB have already been adopted by 40% in many countries, while in Europe we are slowly approaching the 20% mark. The United States, on the other hand, is just getting started.

For many years, our center has followed the principle of focusing on esion preparation, which we do for every lesion. This ultimately results in a mix of DCB and DES, whereby the number of lesions and, above all, the length of the lesions have led to a predominance of DCB. We now encounter ISR almost exclusively in patients who previously received long stents at other centers.

Why are DCB currently in the spotlight?

That's a question I ask myself every day these days, and I do not really have an answer. We have been following the basic principles of lesion preparation and the decision between DCB and DES for almost 15 years. For me, not much has changed in daily practice. The current hype is certainly mainly psychological. The important aspect is that we use this new dynamic to create reliable clinical evidence.

Where do you see this treatment modality in the next 5 to 10 years?

I am, of course, biased here. Patrick Serruys has just published a forecast in the *European Heart Journal* predicting an almost equal mix of DES and DCB by 2032.[8] Whether this will actually be the case depends on many factors. For me, the most important thing is that we conduct high-quality scientific research.

Before we finish, how do you like to spend your time outside of your professional life?

The most important part of my life is my family. I deliberately reserve my free time exclusively for my wife, my son and our puppy.

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STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

None used.

CONFLICTS OF INTEREST

None declared.

ABOUT THE AUTHOR

Fernando Alfonso is associate editor of *REC: Interventional Cardiology*, with research interest is drug-coated balloons.

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