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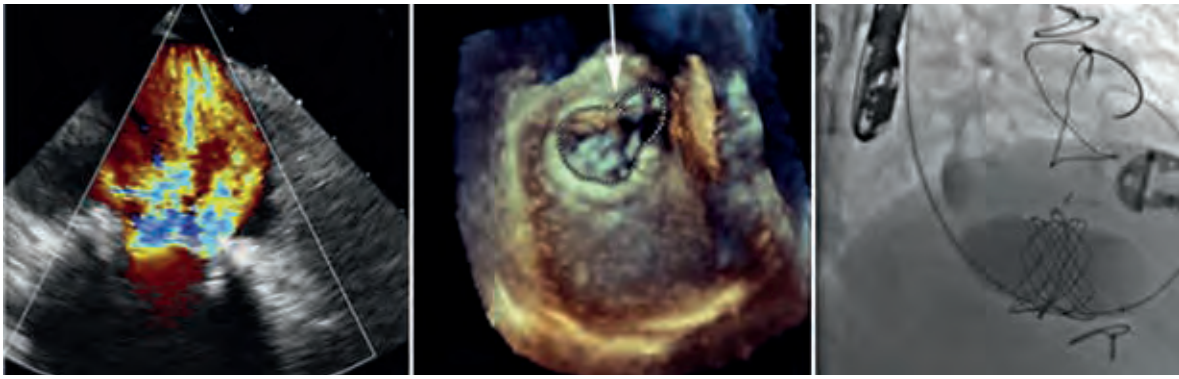

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REC: INTERVENTIONAL CARDIOLOGY

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Editorial

Cardiac allograft vasculopathy. A disease on the search for therapy

Vasculopatía del injerto cardiaco: una enfermedad en busca de un tratamiento

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To this day, heart transplant is the treatment of choice in patients with heart disease and functional repercussions that is refractory to treatment (both drugs and electrical or mechanical devices) and has no contraindications. The milestone that made heart transplant take the spotlight in the management of these patients was the introduction of calcineurin inhibitors as basic immunosuppressants, which allowed the effective control of acute graft rejection. Immunosuppression patterns based on cyclosporine at the beginning and then on tacrolimus have led to really long survivals with means of up to 12 years.[1] After acute rejection was no longer the main cause of graft failure and occasionally the patient, the long-term survival of the graft is basically limited by the development of coronary vascular disease.

Graft vascular disease represents an accelerated phase of the underlying fibroproliferative process that affects the entire coronary vascular bed diffusely. On the pathological analysis, its appearance is different from classic atherosclerosis of complex and multifactor etiology in that it includes non-immunity factors and, in particular, immunity factors.[2] As a matter of fact, it is the most conspicuous manifestation of antibody-mediated late rejection, which is why it has sometimes been referred to as "chronic graft rejection". Its incidence based on the angiographic data we have is over 30%-50% from the third to the fifth year after the transplant which has a significant impact on prognosis: it is the leading cause of graft failure and one of the leading causes of death in recipients with long survival rates.[3] Also, the management of this process is relatively limited because of its diffuse nature that makes coronary revascularization procedures more difficult.

In the study conducted by Solano-López Morel et al.[4] and recently published on *REC: Interventional Cardiology*, authors from 2 experienced groups revealed their results with percutaneous revascularization with drug-eluting stents in one of the most severe forms of graft vascular disease: chronic total coronary occlusion. The authors confirmed that the technique was feasible since it used state-of-the-art diagnostic and therapeutic technological means, although they restricted it to highly selected patients. The findings show that chronic total coronary occlusion has a low but still significant prevalence (12.2% of the patients), late onset (mean, 10 years after the transplant), and even in experienced hands it is barely eligible for percutaneous revascularization (13.5% of the patients with chronic total coronary occlusions). Although the angiographic results are promising (93% of initial success and 2% restenosis only), the prognosis of these patients is still poor (a 21.4% cardiovascular mortality rate with a mean at follow-up of 2.8 years) even compared to graft vascular disease without complete occlusion treated percutaneously (21.4% vs 8.3%). Although the study sample is limited, it would have been interesting to draw a comparison between patients with chronic total coronary occlusions treated percutaneous or medically.

The most important thing of the study conducted by Solano-López Morel et al.[4] is that it is the first time that the feasibility of the recanalization of chronic total coronary occlusions in graft vascular disease is ever reported. The results are indicative that in these patients, percutaneous procedures are nothing more than palliative care *sensu stricto* whose effectiveness in clinical terms has not been confirmed yet (and probably never will). This comes as no surprise since graft vascular disease is a diffuse and progressive disease that affects both the epicardial coronary arteries and the intramyocardial trajectories and especially the capillary bed. Therefore, same as it happens with other conditions, the most effective management is preventive treatment targeted at well-known etiopathogenic factors including taking good care of the donor, preventing graft primary failure, preventing and treating cytomegalovirus-related infections, the universal use of statins (such as hypolipemiant and immunomodulating statins), and preventing antibody-mediated acute and chronic cell rejection through the use of individual immunosuppression therapies for each patient.[5]

CONFLICTS OF INTEREST

None declared.

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REC Interv Cardiol. 2019;1(3):147-149

Editorial

Novel oral anticoagulants, diagnostic catheterization, and coronary intervention: another step forward towards the optimal strategy

Nuevos anticoagulantes orales, cateterismo diagnóstico e intervencionismo coronario: otro paso hacia la estrategia óptima

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The optimal management of chronic anticoagulation is still controversial to this day both in clinical cardiology and particularly in interventional cardiology. The progressive aging of the population has increased exponentially the percentage of patients with an indication for chronic oral anticoagulation who undergo percutaneous invasive procedures to up to 5%-10% of the total. Also, most of them suffer from atrial fibrillation.[1]

Until the arrival of new direct-acting oral anticoagulants (DOAC), most of these patients were anticoagulated with vitamin K antagonists (VKA). Invasive procedures used to be performed after withdrawing oral anticoagulation and using bridging anticoagulation with low molecular weight heparin.[2] We believe that this widely used strategy in our setting should be put into question though. In the first place, the prothrombotic rebound effect has been reported as associated with the withdraw and reset of VKA.[3] Secondly, the interaction of anticoagulants with a different mechanism of action used in patients on bridging therapy can have pro-hemorrhagic and procoagulant consequences. As a matter of fact, the actual clinical guidelines recommend avoiding the concomitant use of unfractionated heparin in patients undergoing percutaneous coronary interventions (PCI).[4] Also, more hemorrhagic complications associated with bridging therapy have been confirmed in patients treated with invasive or surgical procedures (1.3% vs 3.2%),[5] in patients undergoing PCI (8.3% vs 1.7% and 6.8% vs 1.6%[7]), and in one meta-analysis (odds ratio, 5.40; 95% confidence interval, 3.00-9.74).[8] Overall, none of these studies revealed more thromboembolic events associated with the absence of bridging therapy.[5-8] With the actual evidence available today, we should ask ourselves why many clinical practice protocols in our setting recommend the use of bridging therapy with VKA and low molecular weight heparin in patients on chronic anticoagulation

There is little evidence from the studies published so far that specifically compare uninterrupted strategies with anticoagulation and interrupted strategies without bridging therapy. We could argue that vascular access is safer if used in uncoagulated patients. However, the PCI is a low-risk of bleeding procedure[9] when performed through the access of choice which is the radial access[1,4] (used in Spain in up to 90% of the cases).[10] Also, yet despite the doubts of many interventional cardiologists, therapeutic warfarin treatment seems to provide sufficient anticoagulation for PCI, and additional heparins are not needed and may increase access site complications.[11] Actually this is what the clinical guidelines establish when the international normalized ratio (INR) is above 2.5[4]. In any case, we always have this possibility of adding heparin during the PCI, always bearing in mind that when choosing radial access, the incidence of bleeding is low, and the chances of radial occlusion or thrombosis of the materials drop.

Yet despite the growing use of DOACs in the clinical practice, the evidence available today for its use during the procedure is scarce in patients undergoing PCI. This contrasts with the benefit shown with the use of VKA in revascularized patients who need antiplatelet therapy[12] or even as adjuvant therapy for the management of acute coronary syndrome.[4] In an article published on *REC: Interventional Cardiology*, Ramírez Guijarro et al.[13] talk about their own initial experience with same-day diagnostic catheterizations without DOAC withdrawal in patients on chronic anticoagulation. It is interesting that no differences were seen in the incidence of hemorrhages or radial occlusions compared to patients without prior antiplatelet therapy or with uninterrupted therapy with VKA. The way we see it, this is a pioneering strategy in our setting which, although it does not validate its use in PCIs with stent implantation, it provides evidence in the right direction. In our opinion, the uninterrupted strategy of anticoagulation when using the radial access has 2 main advantages. The first advantage is the simplification of the procedure for doctors and patients alike especially in outpatient same-day procedures. The benefit of this simplification is potentially higher in patients treated with DOACs since the monitoring of the INR is not necessary at admission and the complexity of withdrawal protocols is avoided based on the half-life of DOACs and renal function. The second advantage is the safety shown with its use since it reduces bleeding complications without improving thromboembolic complications.

In sum, with the evidence available today we know that: *a)* we should avoid prescribing systematic bridging therapy with low molecular weight heparin in patients undergoing catheterizations/PCI. When dealing with a procedure where there is a high risk

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Table 1. Summary of actual anticoagulation recommendations in patients who are going to undergo invasive procedures

Group	Recommendations for patients treated with VKA	Recommendations for patients treated with DOAC
ACC 2012 Consensus Document on standards at the cath lab[2]	- Withdraw - INR < 2.2 for radial access	- Always withdraw dabigatran
ESC 2015 Guidelines on the management of NSTEACS[4]	- Uninterrupted strategy - Without parenteral anticoagulation when INR > 2.5 - Additional dose of parenteral anticoagulation when INR < 2.5	- Uninterrupted strategy - Always administer additional dose of parenteral anticoagulation (60 IU/kg of UFH)
ESC 2017 Guidelines on the management of STEMI[14]	- Uninterrupted strategy - Always administer additional parenteral anticoagulation	- Uninterrupted strategy - Always administer additional parenteral anticoagulation
ACC 2017 Consensus Document on the management of anticoagulation during the procedure in patients with non-valvular atrial fibrillation[9]	- Uninterrupted strategy without bridging therapy	- Withdraw for 24-96 h - No bridging therapy
AHA Position Statement on DOAC therapies[15]		- Withdraw for 12-48 h - Consider bridging therapy with heparin in the presence of high embolic risk - Add heparin during the procedure
European EHRA, EAPCI, ACCA Consensus Document 2018 on anticoagulation in patients undergoing interventional procedures[1]	- Uninterrupted strategy - Administer 30-50 IU/kg of UFH	- Withdraw for 12-48 h without bridging therapy with elective percutaneous coronary interventions - Administer 70-100 IU/kg of UFH

ACC, American College of Cardiology; ACCA, European Association of Acute Cardiac Care; AHA: American Heart Association; DOAC, direct-acting oral anticoagulants; EAPCI, European Association of Percutaneous Cardiovascular Interventions; EHRA: European Heart Rhythm Association; ESC, European Society of Cardiology; INR, international normalized ratio; NSTEACS, non-ST-segment elevation acute coronary syndrome; STEMI, ST-elevation acute myocardial infarction; UFH, unfractionated heparin; VKA, vitamin K antagonists.

of bleeding, the best thing to do is to withdraw anticoagulation without using bridging therapy in patients with non-valvular atrial fibrillation; *b)* we should keep VKAs during catheterizations/PCIs performed through radial access; *c)* stent implantation seems safe with VKA, but heparin can also be prescribed based on the INR and experience; *d)* diagnostic catheterizations on DOAC therapy seem safe.

In sum, we still need more evidence on this ongoing debate. Studies like the one conducted by Ramírez Guijarro et al.[13] are extremely useful but future randomized trials should elucidate what the best antithrombotic strategy is for stent implantation in patients treated with DOAC or VKA. Similarly, clinical guidelines should come to terms on the actual recommendations based on the evidence available today since they do not agree on many issues as table 1 shows. The ultimate goal should be finding the optimal strategy which should be easy to implement, effective, and safe for our patients.

CONFLICTS OF INTEREST

None reported.

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Editorial

From Prometheus to Element Care

De Prometeo a Element Care

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When Prometheus' liver was daily devoured by the eagle that Zeus would send each day to the Caucasus mountains where the titan was kept in chains, pain was the price to pay for disobedience and immortality. Prometheus' insurrection was sealed after he stole the fire from the gods and gave it to men so they could heat themselves, cook food, make utensils, and have a divine spark inside of them to become spiritual and intelligent beings, thus bringing them a little closer to the gods and away from the animal kingdom. The immortal nature of Prometheus would regenerate the liver only to see it devoured again the next day. Only Hercules put an end to Prometheus' torment when he broke the chains of his sentence.

This Greek myth of the demi-god is a good analogy of the evolution of medicine from ancient to modern times. Suffering; disease; wisdom; hope; cure, and eventually immortality. It has been the greed shown by Homo sapiens that has tried to conquer the fire stolen by the Greek hero.

It is precisely this human exchange that has allowed us to evolve as a species. We have been able to conquer our planet, cure diseases, control epidemics, and fight our kind to the benefit but also to the detriment of our own world and at the expense of the extinction of millions of species, the very subjugation of death, and the suffering of millions of our own people.

Throughout history, doctors have been perceived by others has holders of some sort of a special talent. The first physicians were healers, shamans who understood the laws of the ancient universe and had a special connection with the divine. In addition to having a secret knowledge of plants, herbs, and minerals with healing potential, their wisdom had been transmitted through oral tradition from one family to the other or through genetic inheritance as some sort of natural selection of only those individuals with the necessary conditions to become healers. These were exceptional individuals among the ancient human groups who were measured by the highest standards and revered by the different societies. They were possibly Prometheus' chosen ones as holders of that "extra fire".

Medical science evolved with extraordinary advances for all mankind by drastically reducing child mortality at the end of the 20th century, improving life expectancy in most countries up to 75 years of age (by 2050 the estimates are that human beings will live up to 100 years old), and ultimately by managing successfully most of the diseases that plague the Homo sapiens.[1]

After the Second World War, medicine was revolutionized, a sort of golden age if you will, with the appearance of antibiotics, vaccines, new anesthetic agents, breaking surgical procedures, and new drugs. Doctors were respected and admired; the doctor-patient interchange was based on conversations and deep scrutiny of the intimate life of individuals and rigorous physical examinations following all rules of semiology.

These advances were followed by universal medical plans and health reforms, making medicine lose its human dimension of that doctor-patient relationship. Thus, the infamous "cost-benefit" ratio became a priority and technology was incentivized creating a gap between humanity and science and, on many occasions, verbal communication, so essential to understand each other, was simply gone and doctors became technicians or service providers overnight whose effectiveness was put under the microscope.

This was the birth of the so-called "junk consultation" that leads to countless complains from users (our patients) who are rushed inside a world of unnecessary tests, studies, and procedures that have an excessive, and in most countries, unsustainable cost for the health-care system.

The irony is that by improving life expectancy we end up having more old patients who, on many occasions, suffer from loneliness and grief. With today's medical approach, doctors simply cannot bring any remedies to them. Instead, nearness is needed here to examine the natural condition of man and be able to develop our profession fully by offering that lenitive as part of the medical prescription.

Ms. Ellen Trane Nørby, secretary of health in Denmark, one of the highest ranking countries in effective healthcare systems worldwide has said: "Something must be wrong in Denmark when we're spending 50% of the healthcare budget in the last 90 days of a human life to delay the inevitable in just a few weeks."[2]

Abandonment, sadness, and isolation in old patients who live in developed countries generates astronomical costs at the ER when they are actually looking for social support.

An article published on *The New York Times*[3] has brought the program *Element Care* –non lucrative and for old adults– to everyone's attention. This program provides those elderly who are eligible with one tablet with a software and a virtual pet that

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interacts with them, talks to them about sports and pastimes, shows them memories of their lives and, above all, tells them that they are loved.

The patients know that this device is connected to an emerging startup called Care Coach. They also know that the employees who operate this platform see, listen and give remote answers to them, but at the end of the day they come to love their little pet, feeling that they still mean something and that someone else still cares.[3]

Today's society is on a non-stop rampage towards progress. We are modernizing consumption without having developed thought first and we are embarked on a technological frenzy that perpetuates itself and turns us into isolated entities that only interact with one another through cybernetic applications. Let us commit ourselves to becoming social individuals back again and humanizing artificial intelligence. Let us be a replica of our ancestors who lived their lives around the fire given to them by the good titan Prometheus.

As physicians I think we should look in the mirror for just a second and ask ourselves whether we are treating patients the same way we would like to be treated. If the answer is no, let's make hugs last longer than our well-known narcissism.

CONFLICTS OF INTEREST

None reported.

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Original article

Outcomes of percutaneous coronary intervention of chronic total occlusions in heart transplant recipients

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ABSTRACT

Introduction and objectives: Chronic total coronary occlusion (CTO) of coronary arteries is frequent in heart transplant recipients (HTR). It is usually managed with medical therapy due to the suboptimal results shown by the percutaneous coronary intervention (PCI). Although the PCI of native CTOs is performed in experienced centres, in HTR we do not know PCI results or clinical efficacy. This is the first study ever to actually analyse the PCI-Target Lesion Procedure Success of CTO PCI and its angiographic and clinical follow-up in HTR. In addition, we compared the clinical follow-up of CTO vs non-CTO PCI in HTR.
Methods: We retrospectively analysed the baseline characteristics, procedural outcomes and clinical events during the follow-up of HTR with CTO undergoing PCI between January 1, 2006 and December 31, 2016 in 2 centres with an ongoing CTO program. Over the same period, we also compared clinical events during the follow-up of these patients vs PCI on non-CTO stenosis in HTR at one of the centres.
Results: PCI was successful in 13 out of 14 patients. A systematic follow-up angiography was conducted at centre 1 (n = 10). Two patients showed in-stent restenosis (20%), and a new PCI was performed successfully in both cases. Mortality rate was 28.5%, after a median follow-up of 33.5 months [interquartile range, 20-50]. We found no statistical differences in the clinical events after the PCI of CTO lesions vs non-CTO lesions in HTR.
Conclusions: The PCI of CTO in HTR is feasible in experienced centres and selected patients, with a high success rate and low rate of intraprocedural complications.

Keywords: Chronic total coronary occlusion. Heart transplantation. Coronary angioplasty. Cardiac allograft vasculopathy. Results.

Resultados de la intervención coronaria percutánea de oclusiones crónicas totales en pacientes con trasplante cardiaco

RESUMEN

Introducción y objetivos: Las oclusiones coronarias crónicas totales (OTC) son frecuentes en los pacientes receptores de trasplante cardiaco (PTC) y suelen tratarse con tratamiento médico debido a los resultados subóptimos de la intervención coronaria percutánea (ICP). A pesar de que la ICP de OTC en corazones nativos se lleva a cabo en centros experimentados, no se conocen sus resultados ni la eficacia clínica en PTC. Este es el primer estudio que analiza la tasa de éxito de la ICP sobre OTC en PTC, así como el seguimiento clínico y angiográfico. Así mismo, se comparan los eventos clínicos durante el seguimiento de los PTC tratados con ICP sobre OTC frente a PTC con ICP sobre estenosis no oclusivas.
Métodos: Se analizaron retrospectivamente las características clínicas basales, los resultados del procedimiento y los eventos clínicos durante el seguimiento de los PTC con OTC en quienes se realizó una ICP entre el 1 de enero de 2006 y el 31 de diciembre de 2016 en 2 centros con un programa específico de OTC. Además, se compararon los eventos clínicos durante el seguimiento de estos pacientes con los de PTC tratados con ICP sobre una estenosis coronaria no oclusiva en uno de los centros durante el mismo periodo de tiempo.
Resultados: La ICP resultó exitosa en 13 de los 14 pacientes. Se realizó un seguimiento angiográfico sistemático en el centro 1 (n = 10). Dos pacientes presentaron reestenosis en el interior del *stent* (20%), por lo que se realizó una nueva ICP sobre ellas que tuvo éxito en ambos casos. La mortalidad fue del 28,5% con una mediana de seguimiento de 33,5 meses [rango intercuartílico,

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20-50]. No se encontraron diferencias estadísticamente significativas entre los eventos clínicos tras la ICP sobre una OTC y tras la ICP sobre una estenosis no oclusiva en PTC.
Conclusiones: La ICP sobre OTC en PTC es factible en centros con experiencia y en pacientes seleccionados, con una alta tasa de éxito y una baja frecuencia de complicaciones periprocedimiento.

Palabras clave: Angioplastia coronaria. Enfermedad vascular del injerto. Oclusión total crónica. Resultados. Trasplante cardiaco.

Abbreviations

CAV: cardiac allograft vasculopathy. **CTO:** chronic total coronary occlusion. **HTR:** heart transplant recipient. **PCI:** percutaneous coronary intervention.

INTRODUCTION

Nowadays the orthotopic cardiac transplantation is the endgame for many patients with end-stage heart failure in developed countries.[1] After the third year of heart transplantation, chronic rejection is one of the leading causes of morbidity and mortality.[2] One of the main manifestations of chronic rejection is cardiac allograft vasculopathy (CAV) that affects nearly 50% of transplanted hearts at 5 years.[3] CAV is characterized by diffuse intimal thickening that leads to progressive coronary luminal narrowing, with similar consequences to native heart atherosclerotic disease.[4] It typically shows diffuse lesions in the distal territories with more focal stenosis in the proximal segments.[5] Although the main treatment of CAV is based on titrating immunosuppressive therapy, a PCI is usually conducted here.

The use of PCIs for the management of CAVs has been reported to have success rates above 90% but with long-term restenosis rates of up to 36%.[6] On the other hand, as a result of denervation following transplantation and subsequent incomplete reinnervation, most patients are asymptomatic or show atypical symptoms, despite silent progression to advanced stages of the disease. Therefore, angiographic findings of a CTO in this population are not rare.

Due to the high rate of restenosis associated with these procedures[7] and the lack of solid evidence of a clinical benefit, medical treatment is advised in these patients especially when it comes to CTOs. Nevertheless, CTO recanalization has experienced a significant boost due to new techniques and technological advances made over the last few years. Therefore, in highly experienced centres performing PCIs of CTOs, this kind of procedures can be an alternative.

We know from registries published in recent years that the success rates of PCIs on CTOs, in non-transplanted patients are between 60% and 80% in the United States, Canada, and Europe.[8,9] However, there are no studies of the success rates and results of PCIs on CTOs in patients in whom CAV can play an important role. We don't have data on short and long-term clinical benefits either.

Consequently, the main goal of our study is to evaluate the characteristics of this population, the feasibility of PCI in these patients and its clinical results. In addition, we will make a comparison with heart transplant recipients (HTR) who underwent a PCI on lesions without CTO criteria.

METHODS

Definitions

For the purpose of this paper, the main conditions are defined as follows. According to the EuroCTO definition, chronic total coronary occlusion (CTO) is defined as the presence of Thrombolysis in Myocardial Infarction 0 flow within the occluded coronary segment with an estimated occlusion duration of > 3 months.[10] Percutaneous coronary intervention (PCI)-target lesion procedure success is defined as the achievement of < 30% residual diameter stenosis of the target lesion as assessed by visual inspection or quantitative coronary angiography, without an in-hospital major adverse cardiac event (death, acute myocardial infarction, or repeated coronary revascularization of the target lesion).[11] In-stent restenosis is the re-narrowing of a stent implanted at a lesion site to treat a prior stenosis, to an in-stent diameter stenosis of > 50%, including the original treated site plus the adjacent vascular segments 5 mm proximal and 5 mm distal to the stent.[11] Regarding PCI-related myocardial infarction related (and according to the 4th universal definition of myocardial infarction), stand-alone post-procedural increases of cardiac troponin values are enough to establish a diagnosis of procedural myocardial injury but not for the diagnosis of a type 4a myocardial infarction. Type 4a myocardial infarction requires the elevation of cardiac troponin values greater than 5 times the 99th percentile URL in patients with normal baseline values or patients with elevated pre-procedural cardiac troponin in whom the cardiac troponin levels are stable (≤ 20% variation) or dropping. The post-procedural cardiac troponin needs to rise > 20% to an absolute value more than five times the 99th percentile upper reference limit. In addition, there should be evidence of new myocardial ischaemia, either from electrocardiogram changes, imaging evidence, or procedural-related complications associated with reduced coronary blood flow such as coronary dissections, occlusions of a major epicardial artery or side branch occlusion/thrombi, collateral flow disruptions, slow flows or no-reflow, or distal embolizations.[12]

Patients and data analysis

First, we performed an analysis of the incidence of CTO in the context of coronary angiography screening of CAV in one of our centres. We also show the proportion of patient who underwent PCIs. Secondly, we conducted a retrospective analysis of all HTRs who underwent PCIs on a coronary CTO between January 1, 2006 and December 31, 2016 in 2 centres with an ongoing CTO program. Data from both centres were used for the analysis of the

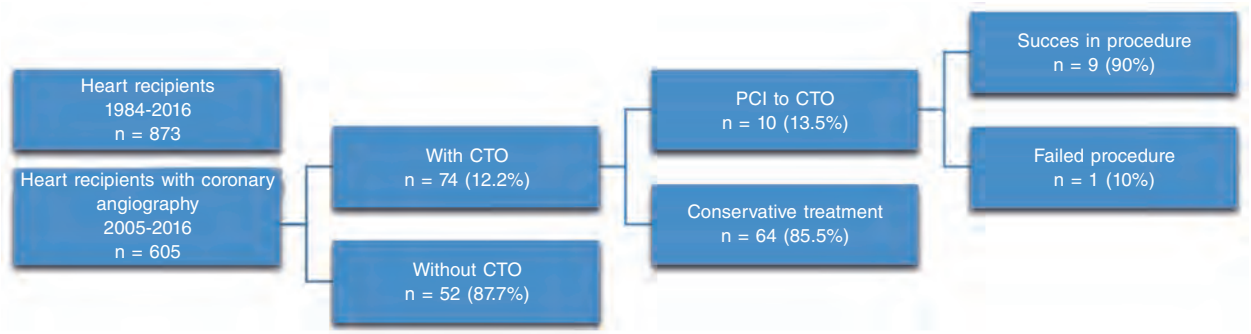

Figure 1. Study flowchart. CTO, chronic total coronary occlusion; PCI, percutaneous coronary intervention.

CTO PCI procedure characteristics, immediate results, clinical events and coronary angiography during follow-up. Also, we analysed clinical events during follow-up of the same previous HTR with PCI on a CTO and compared it to HTRs with PCI on a non-CTO lesion. The clinical endpoints analysed were these: re-admission for heart failure or acute myocardial infarction, sustained ventricular arrhythmias, cardiovascular death, and all-cause mortality. Patient demographics and PCI-related data have been extracted from hospital databases. Digital images have been mined from dedicated storage servers. Transthoracic echocardiography images were obtained before and after CTO recanalizations to assess variations in the left ventricular ejection fraction using the Simpson method. Diagnostic coronary angiographies were analysed to assess the CTO characteristics prior to the PCI. Short- and long-term complications were obtained from medical records. In addition, follow-up coronary angiographies were performed in most patients, according to the protocols of the different centres.

This study was approved by the clinical trials committee of the *Hospital Universitario Puerta de Hierro de Majadahonda*, Madrid, Spain, in full compliance with the principles of the Declaration of Helsinki.

Statistical methods

For the assessment of the differences in the baseline demographic characteristics between the CTO group and the non-CTO group, the qualitative variables were expressed in percentages and analysed using the chi-square test. The quantitative variables were expressed as mean ± standard deviation and analysed using the Student *t* test. The quantitative variables without normal distribution were expressed as median ± interquartile range and analysed using the Wilcoxon test.

When it comes to the size of the sample, a comparative analysis of the clinical outcomes between CTO and non-CTO group was conducted using Fisher's exact statistical test. To compare mortality between the CTO with the non-CTO group we used the Kaplan-Meier survival analysis. For all the tests, a P values < .05 were considered statistically significant. The statistical analysis was performed using the software SPSS package (V 21.0.0.0).

RESULTS

Incidence of chronic total coronary occlusion in heart transplant recipients

On the incidence of CTOs, only patients from *Hospital Universitario Puerta de Hierro* were studied. During the analysed period, 605 coronary angiographies were performed in HTRs. Among these, 74 patients (12%) had a CTO according to the EuroCTO criteria. Of these patients, PCIs were performed in only 10 (13%), leaving the remaining 64 patients under medical treatment (figure 1).

Clinical characteristics. Procedural outcomes and follow-up

Clinical characteristics

Ten patients patients from *Hospital Universitario Puerta de Hierro* and 4 patients from Hospital Clinic de Barcelona, Barcelona, Spain were included in the study.

The baseline clinical characteristics and follow-up of each patient are shown on table 1. Eighty-five percent were males with an average age of 57 years [46.2-66] at the time of the PCI.

On the clinical manifestations when the CTO was diagnosed, 4 patients had angina or angina-like symptoms (28%), 2 patients required hospitalization for decompensated heart failure (14%) and the remaining 8 (57%) were asymptomatic. In asymptomatic patients, the diagnosis of ischemia was achieved by studying regional wall motion abnormalities in the follow-up echocardiograms (62%) and electrocardiographic changes suggestive of ischemia (12%). In the remaining patients (26%), the diagnosis was achieved based on the CAV screening coronary angiography.

The time elapsed from cardiac transplantation to coronary CTO PCI procedure varies from a minimum of 5 years to a maximum of 18 years (median 10 years).

Baseline coronary angiography and procedure

The angiographic characteristics of CTOs and details of each patient's procedure can be found on table 2 and table 3.

The occluded artery was the left anterior descending artery in 8 patients (57%), the right coronary artery in 4 patients (29%) and the left circumflex artery in 2 patients (14%). Only in one case (patient 8) a distal occlusion was treated, while the remaining patients showed proximal or mid segment occlusions. No patient had more than 1 CTO.

Fifty percent of the patients (7 patients) had 1 vessel disease, 28% (4 patients) 2 vessels disease and 21% (3 patients) 3 vessels disease. Other non-CTO severe lesions were treated before the CTO procedure in those patients with multivessel disease. The mean J-CTO[13] score was 1 (± 0.78).

Table 1. Clinical variables and follow-up

Patient	Age, y	HT	DM	DL	Clinical presentation prior to CTO diagnosis	Time from heart transplantation to PCI, years	Time from CTOs PCI to FUCA, days	ISR in follow-up	LVEF prior PCI	LVEF post-PCI	Follow-up post-PCI
1	73	Yes	No	No	Asymptomatic	14	238	No	59%	52%	Alive at 4 and 1 months
2	64	No	No	No	HF	8	192	No	30%	45%	Alive at 4 and 4 months
3	25	No	No	No	HF	5	1122	Yes	35%	40%	Alive at 10 and 4 months
4	31	Yes	No	Yes	Asymptomatic	8	175	-	50%	55%	Alive at 9 and 6 months
5	60	Yes	No	Yes	Angina	16	210	No	Unknown	Unknown	Death at 1 and 8 months due to ruptured iliac artery aneurysm.
6	57	Yes	No	Yes	Asymptomatic	10	No FUCA	Unknown	40%	60%	Alive at 4 and 2 months
7	53	Yes	No	Yes	Asymptomatic	12	No FUCA	Unknown	60%	Unknown	Sudden death at 2 and 4 months
8	32	No	Yes	No	Asymptomatic	-	No FUCA	Unknown	35%	40%	Alive at 3 and 1 months
9	73	Yes	Yes	No	Asymptomatic	10	161	No	50%	65%	Death due to metastatic pancreatic cancer at 2 and 3 months
10	63	Yes	No	No	Angina	6	No FUCA	Unknown	60%	55%	Sudden death at 267 d
11	57	No	No	No	Dyspnea	14	134	No	60%	Unknown	Alive at 1 and 6 months
12	51	No	No	No	Asymptomatic	10	246	No	55%	Unknown	Alive at 2 and 6 months
13	53	Yes	No	Yes	Dyspnea	18	90	Yes	55%	Unknown	Alive at 1 y
14	72	No	No	Yes	Asymptomatic	18	1439	No	65%	63%	Alive at 4 y

CTO, chronic total coronary occlusion; DL, dyslipidemia; DM, diabetes mellitus; FUCA, follow-up coronary angiography; HF, heart failure; HT, hypertension; ISR, in-stent restenosis; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention.

Table 2. Chronic total coronary occlusion angiographic characteristics

Patient	CTO location	J-CTO score	Blunt entry	Calcification	Occlusion length > 2 cm	Bending > 45º	Re-try lesion
1	Proximal RCA	0	-	-	-	-	-
2	Proximal LAD	0	-	-	-	-	-
3	First OM	2	+	-	-	+	-
4	Mid LAD	1	-	-	+	-	-
5	Mid RCA	2	-	-	+	+	-
6	Proximal LAD	1	-	-	+	-	-
7	Mid LAD	1	-	-	-	+	-
8	Distal RCA	1	-	-	-	+	-
9	Mid LAD	0	-	-	-	-	-
10	Second OM	1	+	-	-	-	-
11	Mid RCA	2	-	+	-	+	-
12	Mid LAD	0	-	-	-	-	-
13	Mid LAD	2	-	+	+	-	-
14	Mid LAD	1	+	-	-	-	-

CTO, chronic total coronary occlusion; LAD, left anterior descending artery; OM, obtuse marginal artery; RCA, right coronary artery.

In 11 patients (79%), the femoral artery was used as the main access, in 5 of these patients the radial approach was used simultaneously. In the remaining 3 patients (21%), only radial approach was used. Contralateral injections were used in 6 interventions (43%).

In all cases, the anterograde strategy was used. An average of 1.9 guidewires were used per procedure and an intravascular ultrasound was performed in 3 of the procedures. In 10 patients (71%), at least one dedicated microcatheter was used. In every case, a guidewire escalation approach was performed, starting with guidewires with lower tip load and penetration capacity to guides with higher tip load and penetration capacity.

In every case, drug-eluting stents were deployed with an average of 1.57 stents per patient and an average stent length of 41.5 mm.

The amount of contrast used in the procedures went from 117 to 468 mL with a median of 209 mL. However, no events of contrast-induced nephropathy were reported.

The PCI was successful in 13 patients (92.8%). The only failed attempt (patient 4) was a mid-segment left anterior descending artery CTO with a J-CTO score of 1. Three drug-eluting stents were deployed but final Thrombolysis in Myocardial Infarction flow was 1. Follow-up coronary angiography showed no improvement in coronary flow. No further attempts were made to recanalize the vessel.

In-hospital results

Regarding cardiovascular events during hospitalisation after the PCI, only 1 patient had a procedural myocardial injury, with a significant increase of myocardial necrosis markers (troponin I peak of 9 µg/dL for a 99th percentile upper reference limit of 0.06 µg/dL) but without haemodynamic impairment or new regional wall motion abnormality. No radiodermatitis was reported.

Clinical and angiographic follow-up

During a median follow-up of 33.5 months [20-50] mortality rate was around 28.5% (4 out of 14 CTO patients). Among these, 2 deaths were due to sudden cardiac death, 1 to advanced stage pancreatic carcinoma and 1 death was due to suspected ruptured right iliac artery aneurysm (unrelated to the procedure).

The improvement of left ventricular ejection fraction measured using the Simpson method was confirmed in 6 of the 9 patients who underwent an echocardiogram both before and after the CTO procedure, with 5.8% (± 0.87) of global mean improvement (P = NS).

All patients from centre #1 had a coronary angiography during follow-up. The median time from the CTO PCI to the follow-up angiography was 201 days (161-246). Two patients had in-stent restenosis (20%) after 3 and 37.4 months, respectively (one first-generation drug-eluting stent and one second-generation stent). In both cases reintervention was successful, and new drug-eluting stents were deployed with no further events at follow-up.

CTO versus non-CTO PCI in heart transplant recipients

We compared the results of 14 HTRs in whom one CTO lesion PCI was performed and 36 HTRs with non-CTO lesion PCI over the same period of time.

The long-term follow-up of patients was 100% (CTO and non-CTO patients), with median follow-up of 27 months [14.7-50.2], a minimum of 3, and a maximum of 124 months.

No statistically significant differences were found when the clinical and demographic baseline variables were compared in both groups (table 4).

During follow-up, there were no statistically significant differences in the all-cause mortality rate and cardiovascular mortality

Table 3. Variables related to the percutaneous coronary intervention

Patient	Access	Guide catheter	Guidewires	Successful guidewire	Microcatheter	Stent	Total length treated with stent	Successful intervention	Contrast
1	Femoral	AR 2-6 Fr	2	Miracle 3g	Yes	CYPHER	33 mm	Yes	241 mL
2	Femoral-radial	EBU 3.5-6 Fr	2	PT Graphics	No	CYPHER SELECT	23 mm	Yes	218 mL
3	Radial	AL 2-6 Fr	2	Miracle Bros 3	No	CYPHER	33 mm	Yes	117 mL
4	Femoral-radial	EBU 4-8 Fr	3	Miracle 6	Yes	TAXUS Liberté x3	96 mm	No	132 mL
5	Femoral-radial	JR 4-6 Fr	2	Miracle 3	No	TAXUS Liberté XIENCE V x2	83 mm	Yes	300 mL
6	Femoral	EBU 3.5-7 Fr	Unknown	Pilot 50	Yes	CYPHER x3 Vision x1	66 mm	Yes	468 mL
7	Femoral	JL 4-7 Fr	Unknown	Miracle 3	Yes	CYPHER	33 mm	Yes	158 mL
8	Femoral-radial	JR 4-6 Fr	Unknown	Fielder FC	Yes	CYPHER	18 mm	Yes	182 mL
9	Femoral	EBU 3.5-6 Fr	2	Fielder XT	Yes	XIENCE V Prime x2	43 mm	Yes	225 mL
10	Femoral-radial	Hockey S	Unknown	Fielder XT	Yes	XIENCE Xpedition	22 mm	Yes	240 mL
11	Femoral	JR 4-6 Fr	1	Gaia third	Yes	Resolute Onyx	38 mm	Yes	224 mL
12	Radial	EBU 4-6 Fr	1	Fielder XT	No	Resolute Integrity	22 mm	Yes	154 mL
13	Radial	EBU 4-7 Fr	2	Fielder XT	Yes	BioMatrix x2	53 mm	Yes	129 mL
14	Femoral-femoral	EBU 4-8 Fr	2	Fielder XT	Yes	PROMUS Element	18 mm	Yes	200 mL

rate between both groups (table 5). The mortality rate was 28% (4 out of 14) in the CTO group and 14% (5 out of 36) in the non-CTO group (P = .245). The cardiovascular mortality rate was 21% (3 out of 14) in the CTO group and 8% (3 out of 36) in the non-CTO group (P = .331).

Regarding the 3 patients with cardiovascular death in the non-CTO group, all had severe CAV and advanced chronic kidney disease: 2 of them died due to refractory heart failure and 1 due to humoral rejection. The causes of death in the CTO group are described in the dedicated section.

The rate of readmission for heart failure or acute myocardial infarction during follow-up was 28.6% (4 of 14) in the CTO group and 31.4% (11 of 35) in the non-CTO group (P = .844).

No ventricular tachycardias were reported at follow-up in any of the groups.

DISCUSSION

There is little experience in the percutaneous management of CAVs. Until recently, CAV was considered a progressive and irreversible process with few therapeutic options. Since treatment with m-TOR inhibitors to delay the progression of the disease is effective in many cases, the PCI has emerged as an adjunctive treatment in these patients with good results.[14] However, the results of the CTO PCI in this context are largely unknown. Considering CAV as a diffuse vessel disease, the clinical and angiographic outcomes of CTO recanalization in transplanted hearts are difficult to extrapolate based on the results observed in atherosclerotic coronary occlusions.

As far as we know, this is the very first systematic study on the prevalence of CTOs in HTRs. Also, it is the very first analysis of PCI results of CTOs in this population.

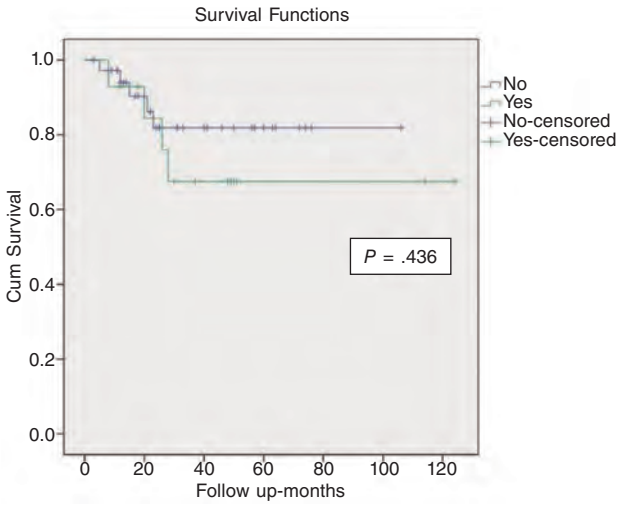

Figure 2. Kaplan-Meier survival analysis comparing chronic total coronary occlusion (green) vs non-chronic total coronary occlusion (blue) percutaneous coronary intervention.

We have found a PCI-target lesion procedure success rate very similar to that of studies published in CTO secondary to atherosclerotic coronary heart disease (92.8%). The rate of intrastent restenosis is similar to that found in large series of PCI in CTO in non-transplanted patients. Although the procedures were performed over an extended period of time, there were no differences in success rate between older and recent procedures in witch we cannot exclude an inclusion bias.

Regarding the safety of PCI, there has only been one procedural myocardial injury with elevation of cardiac necrosis markers,

Table 4. Demographic characteristics of heart recipient patients with percutaneous coronary intervention. Period 2005-2016

Variable	CTO	Non-CTO stenosis	*P*
Patient	14	36	-
Mean age, y [IQR]	57 [46.2-66]	62 [47.5-68.7]	.552
Woman (%)	14.3	22.2	.538
HT (%)	57.1	63.9	.667
DM (%)	21.4	22.2	.953
DL (%)	50	52.8	.863
Actual smoker/former smoker (%)	50	23	.685
CKD (%)	90	74.3	.303
Statins (%)	90	82.4	.572
Median age at the time of heart transplant in years [IQR]	44 [37.5-58]	46 [35.7-54]	.709
Drug-eluting stent (%)	100	100	1
Acute rejection (%)	70	51.4	.259
Mean LVEF (%) (standard deviation)	50 (11.4)	52.7 (10.2)	.558

CKD, chronic kidney disease; CTO, chronic total coronary occlusion; DL, dyslipidemia; DM, diabetes mellitus; HT, hypertension; IQR, interquartile range; LVEF, left ventricular ejection fraction.

Table 5. Major cardiac events. Period 2005-2016

Variable	CTO	Non-CTO	*P* Fisher's exact test
HF or AMI hospital admissions- n (%)	4 (28.6%)	11 (31.4%)	.844
Death-n (%)	4 (28.6%)	5 (13.9%)	.245
Cardiovascular death-n (%)	3 (21.4%)	3 (8.3%)	.331
Sustained ventricular arrhythmias-n (%)	0 (0%)	0 (0%)	-

AMI, acute myocardial infarction; CTO, chronic total coronary occlusion; HF, heart failure.

although there has been no haemodynamic involvement or impact on the ejection fraction of the left ventricle.

Despite the fact that our patients were treated with immunosuppressants, we found no contrastinduced nephropathy events, which may reflect that an optimization in contrast volume, adequate prophylaxis and the correct selection of cases can decrease the rate of renal impairment.

Unexpectedly, given the progressive nature of CAV, only 2 of the cases developed in-stent restenosis that was successfully treated in both cases with no other restenosis during long-term follow-up.

Consistent with the poor clinical prognosis of CAV in series already published, in our registry there is a high mortality rate during the long-term follow-up (28.5%). Of the 3 patients who died of cardiovascular death, 2 of them developed sudden death (271 and 856 days after PCI to CTO) and 1 patient died due to hypovolemic shock secondary to the suspected and unrelated to the procedure ruptured iliac artery aneurysm.

Although statistically irrelevant, there is an apparent higher mortality rate in HTRs with CTOs compared to HTRs with nonocclusive stenosis, which may have to do with a more advanced stage of CAV or with more associated comorbidities.

We should mention here that in our study, the CTO recanalization produces a statistically nonsignificant improvement of the ejection fraction.

Accordingly, our study suggests that following an adequate selection of cases, centres experienced in the management of CTOs can feasibly handle PCIs on CTOs in transplanted hearts with a high PCI-target lesion procedure success and low periprocedural complications. However, probably due to the underlying disease, medium and long-term results are still poor with a high mortality rate and a significant rate of restenosis.

Limitations

Although it should be noted here that this is the first study ever on this subject, there are several limitations. First of all, its retrospective nature. Secondly, the number of heart transplant patients is limited despite combining the experience of 2 high volume HTR centres. Nevertheless, we should keep in mind that the overall experience with these patients is very scarce considering their special characteristics.

In addition, the proportion of HTRs in our centres who undergo CTO PCI is low. Considering the CAV inner nature, it is not rare to find CTO of distal vessels or diffuse distal disease making any PCI attempts futile if not impossible. In fact, most of our patients who underwent PCIs showed CTOs in proximal segments with a good distal vessel. We could conclude that our procedures were performed in highly selected patients. This would be a bias that would be favoring a high success rate by selecting less complex cases (medium J-CTO score 1).

When it comes to the statistical analysis, we should mention here that it has not been possible to perform more powerful analyses such as propensity score analyses due to the low number of patients included in the registry.

However, despite these limitations, we believe that our study is relevant because it shows the experience accumulated over the years in 2 high heart transplant volume centres and because it is the very first study on this subject with a long-term follow-up of the patients.

CONCLUSIONS

Coronary CTO is a common condition in HTRs. PCI is feasible in centres with extensive experience conducting CTO procedures and in selected patients, with a PCI-target lesion procedure success and periprocedural complications rate similar to global CTO procedures and non-CTO PCIs. The rate of in-stent restenosis in HTRs is similar to that found in large series of CTO PCIs in non-transplanted patients. There is a non-significantly higher all-cause and cardiovascular mortality in HTRs undergoing a CTO PCIs compared to those with non-CTO PCIs. This may have to do with more advanced stages of the CAV.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- CTOs are frequent in the context of allograft vasculopathy in heart recipient patients, being usually managed with medical treatment due to the technical difficulty and the poor results of PCIs in this population.

WHAT DOES THIS STUDY ADD?

- In this study we concluded that performing PCIs of CTOs in selected patients with heart transplantations is feasible in experienced centres, with a PCI-target lesion procedure success rates and hospital complications similar to that those of heart recipients with non-CTO lesions.

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Original article

Safety profile of outpatient diagnostic catheterization procedures in patients under direct-acting oral anticoagulants

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ABSTRACT

Introduction and objectives: Today it has become increasingly common to perform procedures without withdrawing oral anticoagulation. However, the need to withdraw oral anticoagulants prior to cardiac catheterization in patients chronically anticoagulated (OACs) remains controversial. We evaluated the efficacy and safety of performing transradial catheterization in outpatients without withdrawing direct-action oral anticoagulants (DOACs).
Methods: Prospective and observational study where 270 patients who underwent elective transradial cardiac catheterization were included from January 2013 through November 2017, divided into 3 groups of 90 patients based on their anticoagulant intake: group A (without OAC), with group B (with vitamin K antagonist), and group C (with DOACs), and matched according to the date of completion. In no case was the OAC discontinued before the procedure. We evaluated the complications of radial access within the first 24 h and 1 month after the procedure.
Results: The group of patients on DOACs had a higher proportion of men compared to the vitamin K antagonist group (71.1% vs 47.8%; P = .01) and patients were younger in the group without OAC (63.45 ± 11.47 vs 70.22 ± 9.35; P = .03). Group B had a lower percentage of diabetic patients (22.2% vs 36.67% in group C, P = .03). In group A, patients were more prone to having a history of ischemic heart disease compared to the groups of anticoagulated patients (27.84% vs 14.44% in group C, P = .028) in addition to a more frequent intake of antiplatelet drugs. Radial access was the access of choice in most patients (98.2%). There were no significant differences when it comes to vascular access complications among the groups being the rate of hematoma and/or bleeding at discharge equal to 1.1% in the DOACs group and the arterial occlusion rates both at discharge and at 1 month between 0% and 2.2%.
Conclusions: In our experience performing transradial diagnostic cardiac catheterizations without discontinuation of DOACs is safe, with low rates of thrombotic and hemorrhagic complications, without any differences with vitamin K antagonist and no OAC.

Keywords: DOACs. NOACs. Direct vitamin K anticoagulants. Non-vitamin K anticoagulants. Cardiac catheterization. Transradial.

Seguridad del cateterismo diagnóstico ambulatorio en pacientes en tratamiento con anticoagulantes orales de acción directa

RESUMEN

Introducción y objetivos: Actualmente es cada vez más habitual realizar procedimientos sin retirar la anticoagulación oral (ACO), pero la necesidad o no de suspender la ACO antes del cateterismo cardiaco sigue siendo una cuestión controvertida. Se evalúan la eficacia y la seguridad de la realización de un cateterismo transradial en pacientes ambulatorios sin retirar los anticoagulantes orales de acción directa (ACOD).
Métodos: Estudio observacional, prospectivo, que incluye 270 pacientes sometidos a cateterismo transradial electivo desde enero de 2013 hasta noviembre de 2017, divididos en 3 grupos de 90 pacientes: grupo A (sin ACO), grupo B (con antagonista de la vitamina K), grupo C (con ACOD), emparejados según la fecha de realización del cateterismo. No se suspendió la ACO antes del procedimiento. Se evalúan las complicaciones del acceso radial en las primeras 24 h y un mes después del cateterismo.
Resultados: Había más varones tratados con ACOD que con un antagonista de la vitamina K (71,1 frente a 47,8%; p = 0,01) y los pacientes eran más jóvenes en el grupo sin ACO (63,45 ± 11,47 frente a 70,22 ± 9,35 años; p = 0,03). En el grupo B hubo menos

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diabéticos (22,2 frente a 36,67% en el grupo C; p = 0,03). En el grupo A, los pacientes tenían más antecedentes de cardiopatía isquémica que los pacientes con anticoagulación (27,84 frente a 14,44% en el grupo C; p = 0,028), además de la toma concomitante de fármacos antiplaquetarios. El acceso fue radial en la mayoría de los pacientes (98,2%). No hubo diferencias significativas en las complicaciones del acceso vascular, con una tasa de hematoma o hemorragia al alta del 1,1% en el grupo con ACOD y tasas de oclusión arterial tanto al alta como al mes del 0-2,2%.
Conclusiones: En nuestra experiencia, la realización de un cateterismo diagnóstico transradial sin interrupción de los ACOD es seguro, con tasas bajas de complicaciones trombóticas y hemorrágicas, sin diferencias respecto a los pacientes en tratamiento con un antagonista de la vitamina K o sin ACO.

Palabras clave: ACOD. NACO. Anticoagulantes de acción directa. Anticoagulantes no antagonistas de la vitamina K. Cateterismo cardiaco. Transradial.

Abbreviations

BT: bridging theraphy. **COAC:** chronic oral anticoagulation. **DOAC:** direct-acting oral anticoagulants. **VKA:** vitamin K antagonists

INTRODUCTION

The number of patients who receive chronic oral anticoagulation (COAC) is huge, and is expected to increase in the future due to the overall aging of the population and the increased incidence of conditions that will require COAC.

The prevalence of COAC among patients with coronary disease who undergo percutaneous coronary interventions is between 6% and 8%.[1] Most cases are due to the concomitant presence of atrial fibrillation with moderate-to-high embolic risk.

On the other hand, up to between 20% and 30% of the patients with atrial fibrillation and an indication of COAC present with coronary disease.[2] Taking into account that the prevalence of atrial fibrillation in the population is between 1% and 2%, up to 1-2 million anticoagulated patients in Europe will end up needing one coronary angiography procedure.

There is, therefore, a significant number of patients receiving COAC with vitamin K antagonists (VKA) or one of the most recent direct-acting oral anticoagulants (DOACs, Apixaban, Rivaroxaban, Dabigatran or Edoxaban) that require coronary angiography. The routine practice with these patients is very variable, but traditionally patients with COAC have discontinued the drug and moved on to bridging therapy (BT) with low molecular weight heparin a few days before and a few days after the procedure.[3] However, an increase of hemorrhagic events with this strategy in interventional procedures and higher morbidity and mortality in these patients due to bleeding or prothrombotic situations due to the discontinuation and reset of anticoagulants has been reported.[2,4-7]

The safety of diagnostic catheterization through radial access under treatment with acenocoumarol (VKA) has been demonstrated previously. In our group, the safety profile of VKA has already been evaluated in this type of patients in the past.[8] Since there is less evidence in patients on DOACs, with this work we want to provide new evidence on this regard, given the increasing number of patients anticoagulated with these new drugs over the last few years.

In this study, we report our experience and we evaluate the safety profile of transradial diagnostic cardiac catheterizations in patients on DOACs who were discharged the same day they underwent the procedure. Also, we compared these patients with other treated with heparin during catheterization and patients on COAC with VKA.

METHODS

Study population

This is a prospective and observational study where 270 patients who underwent elective transradial cardiac catheterizations were included from January 2013 through November 2017, divided into 3 groups of 90 patients based on the intake of VKA, DOACs or without oral anticoagulant treatment, and then matched according to the date of completion. All patients who underwent diagnostic catheterization and were having DOACs during this period were recruited. As control groups, we decided to recruit the next patient who underwent a diagnostic catheterization without anticoagulant treatment and the next one that was receiving acenocoumarol without withdrawal.

In no case was oral anticoagulant therapy withdrawn prior the procedure.

In patients treated with DOACs, 20 were on dabigatran (22.22%), 38 patients on rivaroxaban (42.22%), 29 patients on apixaban (32.22%) and 3 patients on edoxaban (3.33%).

In patients undergoing VKA treatment with international normalized ratio (INR) values < 2 (underdosing) and in DOAC patients who missed their last dose by mistake, intraprocedural sodium heparin was prescribed at a dose of 2500-5000 international units in one intra-arterial bolus. In our series, 21.3% of the patients treated with VKA received underdosing (INR < 2) and, therefore, needed heparin. In this group of patients, the mean INR was 2.5 ± 0.06. The range was 1.3-4.3 (75% INR > 2.1).

In a former article of our group[8] we described the methodology of outpatient catheterizations at our center that we detail here.

Patients without COAC received the standard anticoagulant therapy with one intraarterial bolus of 5000 IU of unfractionated heparin (the routine clinical practice at our center). Also, 2.5 mg of verapamil were administered intraarterially to all patients to prevent any radial spasms.

They underwent elective transradial cardiac catheterization with same-day discharge, after removing the compression bandage and achieving hemostasis. All cases were conducted through one hydrophilic 5-Fr sheath. Hospitalized patients who underwent diagnostic catheterization were excluded as well those in whom an angioplasty procedure was anticipated.

All procedures were conducted in a single interventional cardiology unit with huge experience using transradial access (over 90% of all cases annually) and with an active program of same-day discharge outpatient cardiac catheterizations.[8,9]

Procedural characteristics

All patients are welcome at a room near the interventionist laboratory and are evaluated by a nurse specialized in their monitoring and follow-up. This nurse is in charge of informing the patients, collecting the patient's background, verifying the doses and time of the last COAC intake, and estimating the INR in patients on acenocoumarol. After informing the patient and collecting the informed consent, the best vascular access is selected, assessing the quality of the pulse and performing the Barbeau test.

Once the procedure is completed, the radial compression is performed using the patent hemostasis technique for, at least, 2 h. Radial patency and possible complications are assessed in this room prior to the patient's discharged. The complications and outcomes of the vascular approach we assessed were: acute bleeding (with need to extend the length of compression), hematoma 5-10 cm at discharge, radial patency at discharge, bleeding and/or hematoma at 24 h, radial patency at 1 month and the presence of other unusual complications (pseudo-aneurysms, fistulas, arterial perforations, or compartment syndrome). For hematoma classification, the EASY criteria were used.[10] The compression of the vascular access was made with swab and elastic bands for 2 h using the patent hemostasis technique[11] where distal permeability is verified through plethysmography. Additionally, a 30 min extra-compression was performed if the puncture bled when the bandage was removed. In order to assess radial patency after the removal of compression, the test described by Barbeau et al. was used.[12] was used here. Artery occlusion was defined by type D response (no recovery of the curve of pulse in 2 min). All patients were contacted via telephone over the following 24 h after the procedure to determine delayed local complications, and they were all followed during 1 month to determine the access occlusion.

Statistical analysis

Data are expressed as absolute rate and percentage for qualitative variables. Quantitative variables are expressed as mean (standard deviation) or median 25–75 interquartile range depending on variable distribution. Group comparisons were analyzed using the Student t test or its non-parametric equivalent; the Man– Whitney U-test for continuous variables, and chi-square test or Fisher's exact test were used for the categorical variables. Statistical significance was defined as P values < .05. The statistical analysis was conducted using the statistical package SPSS 19.0 (SPSS, Inc.; Chicago, Illinois, United States).

RESULTS

The patients included in the study were assigned to three groups of 90 individuals each and matched by date of procedure: one group without oral anticoagulation (group A), another group with anti-vitamin K treatment (group B) and another with direct-acting anticoagulants (group C).

The indication of oral anticoagulation in group B mostly corresponds to patients with atrial fibrillation (74.4%), 26.7% of patients had valvular disease and 5.6% of them were carriers of mechanical prostheses; the remaining patients received anticoagulation due to a past medical history of embolism (5.6%), dilated cardiomyopathy (1.1%) and other causes.

The baseline characteristics of our patients are shown on table 1. The group treated with DOACs had a higher proportion of men than the VKA group (71.1% vs 47.8%; P = .01) and patients were younger in the group without oral anticoagulation (63.4 ± 11.5 vs 70.2 ± 9.3; P = .03). Group B had a lower percentage of diabetic patients (22.2% vs 36.67% in group C, P = .03). Group A patients had a past medical history of ischemic heart disease more frequently than the groups of anticoagulated patients (27.84% vs 14.44% in group C, P = .028) and therefore, they had undergone previous catheterization using the same access in higher percentages (20% group A vs 5.5% in group C, P = .04).

When it comes to the concomitant treatment with antiplatelet agents, patients without COAC took acetylsalicylic acid more frequently (72.2% vs 12.2%; P < .0005) compared to the DOACs group, as well as clopidogrel (23.3% vs 4.4%; P < .0005). Acetylsalicylic acid was also more widely used in the DOACs group compared to the VKA group (12.2% vs 3.3%; P = .048). All this is probably related to a greater suspicion of ischemic heart disease in these patients. There were only 2 patients treated with prasugrel and one with ticagrelor in the group without COAC.

There were no other significant differences on the remaining baseline characteristics (high blood pressure, dyslipidemia, body mass index, smoking...).

Radial access was the access of choice in most patients (98.2%), and ulnar access in the remaining patients. Regarding complications (table 2) of vascular access, during the procedure and during the 24 h and 1 month follow-up, there were no significant differences, showing a rate of hematoma and/or bleeding at discharge of 1.1% in the DOACs group and arterial occlusion rates both at discharge and at 1 month between 0-2 an 2% in this group. Only one patient needed hospitalization due to prolonged radial bleeding.

DISCUSSION

The performance of diagnostic cardiac catheterizations without withdrawing COAC is recommended in the guidelines[13] and our standard routine here at our unit of hemodynamics and interventional cardiology is using mostly radial access (95%) excellent safety results.[8,9]

The information comes basically from studies conducted in patients under treatment with VKA. Two meta-analyses that addressed this issue[14,15] conclude that performing catheterizations without withdrawing COAC is safe and effective. The study published by the Finnish group led by Karjalainen[16] also assessed the safety profile comparing it to a group of patients on COAC and heparin BT. They found a rate of bleeding significantly higher in the latter group (1.7% vs 8.3%), being higher in the COAC-BT withdrawal group compared to the withdrawal group of COAC without BT (2.5% vs 8.3%). Also, if the procedure is done through radial access, the results in terms of bleeding are even better.[17]

Table 1. Demographic and procedural baseline characteristics

Variable	Total	Group A: no OAC (n = 90)	Group B: VKA (n = 90)	Group C: DOACs (n = 90)	*P* value
Age (years), median ± SD	68.59 ± 10.63	63.45 ± 11.47	72.09 ± 8.97	70.22 ± 9.35	.03[a] NS[b] NS[c]
Men (%)	62.6	68.9	47.78	71.1	NS[a] .001[b] .041[c]
Hypertension (%)	75.9	83.33	67.78	76.67	NS[a] NS[b] NS[c]
Diabetes mellitus (%)	32.2	37.78	22.22	36.67	NS[a] .03[b] .048[c]
Dyslipidemia (%)	48.5	53.33	52.22	40	NS[a] NS[b] NS[c]
Smoking (%)	10	10	10	10	NS[a] NS[b] NS[c]
BMI (kg/m^2) , median ± SD	30.10 ± 4.62	30.11 ± 4.45	29.22 ± 4.77	30.98 ± 4.51	NS[a] NS[b] NS[c]
Prior isquemic heart disease	17	27.78	8.89	14.44	.028[a] NS[b] NS[c]
ASA treatment	79	65	3	11	< .0005[a] .048[b] < .0005[c]
Clopidogrel treatment	25	21	0	4	< .0005[a] NS[b] NS[c]
Prior catheterization same access (%)	11.5	20	8.89	5.55	.04[a] NS[b] .031[c]

ASA, acetylsalicylic acid; BMI, body mass index; DOAC, direct-acting oral anticoagulants; NS, non-significant; OAC, oral anticoagulation; SD, standard deviation; VKA, vitamin K antagonists.
[a] No OAC (group A) vs DOAC (group C).
[b] VKA (group B) vs DOAC (group C).
[c] DOAC (group C) vs groups A+B.

However, when talking about patients on DOAC treatment, the evidence is scarce and there is no consensus. The current guidelines on revascularization[18] do not include the recommendation of keeping oral anticoagulation during the procedure, but in recent expert consensus statements published by different international societies, there is controversy on this issue. Thus, due to the lack of existing evidence, the European document of antithrombotic consensus[19] recommends to not stop anticoagulation in the case of VKA, but pre-withdraw DOACs between 12 and 24 h (24-48 h in the case of dabigatran) in patients who will undergo the intervention. On the other hand, in the document on preoperative and perioperative antithrombotic management[20] they recommend to not withdraw antithrombotic treatment with DOACs in low-risk hemorrhagic procedures such as transradial diagnostic catheterizations because of its lower rate of vascular complications, especially when it comes to bleeding.

Despite all this, the standard practice with these patients is variable, but as a rule of thumb most hemodynamic laboratories worldwide withdraw COAC and move on to BT with low molecular weight heparin a few days before and after the procedure.[3] However, there are more hemorrhagic events with this strategy when performing interventional procedures as well as more morbidity and mortality of these patients due to bleeding or prothrombotic situations that are created when withdrawing and reseting anticoagulant therapy.[2,4-7]

With the increasingly use of DOACs, new problems arise in our routine clinical practice when these drugs need to be withdrawn before performing procedures and it is common to see that in these patients BT is prescribed the same way as it is prescribed in patients undergoing VKA treatment from many medical and surgical specialties, although its use in recent consensus documents is not recommended.[20]

When it comes to cost-effectiveness, the BT strategy is a tremendous cost overrun due to several aspects: the higher incidence of hemorrhagic complications in patients who will need medical attention, the high cost of low molecular weight heparin, longer hospital stays, and the need to analyze the levels of anticoagulation

Table 2. Complications (bleedings and occlusions) and vascular access events

Variable	Group A: no OAC (n = 90)	Group B: VKA (n = 90)	Group C: DOACs (n = 90)	*P* value
Early bleeding or hematoma (%)	2.2	1.1	1.1	NS[a] NS[b]
Late bleeding or hematoma (%)	0	0	1.1	NS[a] NS[b]
Early occluded access (%)	3.3	3.3	2.2	NS[a] NS[b]
Late occluded access (%)	3	2.9	0	NS[a] NS[b]
Other complication (dissection, fistula, perforation)	0	0	0	

DOAC, direct-acting oral anticoagulants; NS, non-significant; OAC, oral anticoagulation; VKA, vitamin K antagonists.
[a] No OAC (group A) vs DOAC (group C).
[b] VKA (group B) vs DOAC (group C).

in patients under treatment with VKA. In other areas of interventional cardiology, progress has been made on this regard and cost-effectiveness studies have been conducted on this question, such as the study conducted by Coyle et al.[21] that showed that the non-prescription of BT saved US$ 1800 per patient following some the aforementioned aspects. Also, If we compare DOACs and VKA drugs, a recent study conducted by Shah et al.[22] in patients with permanent atrial fibrillation showed that all DOACs proved superior in a cost-effectiveness model that included quality-of-life adjusted survival, with dabigatran being the most cost-effective drug in patients with the highest thrombo-embolic risk of all.

The main conclusion that we can draw from this study is that it is safe to perform diagnostic cardiac catheterizations through transradial access in patients on chronic anticoagulation with DOACs. These patients do not have more frequent vascular or bleeding complications compared to those under standard therapy.

When it comes to bleeding complications, there was a low incidence rate in all groups without any significant differences. Another thing to take into consideration in the case of DOACs is the possibility of anticoagulation reversal with the specific antidote (currently only available for dabigatran and about to be on the market for factor Xa inhibitors) in case of serious complications which gives us a greater safety profile when performing invasive procedures with these drugs.[23]

In our population, the incidence of radial occlusion was exceptionally low in all groups. Early (< 24 h) and late occlusions (1 month) occurred in 2.2% and 0% of the patients from the DOAC group; in 3.3% and 2.9% of the patients from the acenocoumarol group compared to 3.3%; and in 3% of the patients from the heparin group without any statistically significant differences. Previous studies have reported extremely low rate of occlusions, even lower than 1%.[24]

We have not found in the medical literature any series similar to ours, although there are numerous series in which coronary angiographies are performed without withdrawing COAC with VKA, with results that are consistent with ours.[8,25,26]

There have been trials with DOACs in percutaneous coronary interventions that have not found any differences in the clinical adverse events (bleeding, embolism, ischemia) in patients in whom the percutaneous coronary intervention was conducted under different anticoagulation strategies.[27,28]

Study limitations and future directions

The low incidence of complications and the small size of the sample did not allow us to conclude any significant statistical differences among the groups. It would be necessary that the size of the sample was larger, which is difficult in a single center. Maybe a multicenter registry could shed some more light on this issue.

Nowadays, the number of patients under acenocoumarol or warfarin treatment is rapidly dropping due to the exponential use of new anticoagulant drugs as dabigatran, apixaban, rivaroxaban, and edoxaban. In sum, new and larger studies on direct-acting oral anticoagulants should be conducted on this regard.

CONCLUSIONS

The performance of outpatient diagnostic catheterizations using the radial access without withdrawing the DOAC treatment seems to be safe and does not bring a greater deal of complications compared to patients under treatment with acenocoumarol or without anticoagulant treatment. It would be advisable to conduct randomized studies to be able to confirm these data.

CONFLICTS OF INTEREST

We declare no conflicts of interest whatsoever.

WHAT IS KNOWN ABOUT THE TOPIC?

- Currently there is no consensus on the management of oral anticoagulation in patients taking direct-acting oral anticoagulants undergoing procedures such as diagnostic coronary catheterizations. In some centers anticoagulation is kept, resembling clinical practice in the management of antivitamin K, in others it is withdrawn even performing bridging therapy with heparin in some cases. Both the clinical practice guidelines and current consensus documents do not agree on what our approach should be with these patients since evidence is scarce.

WHAT DOES THIS STUDY ADD?

– We believe that our study is of great interest for routine clinical practice, due to the growing use of direct-acting oral anticoagulants in all physicians' daily practice, including cardiologists and interventional cardiology. The use of these drugs has increased exponentially so it is not rare to find patients who are going to undergo a coronary angiogram who are taking DOACs. That is why we wanted to share the experience of our hemodynamic laboratory with this type of patients and show the efficacy and safety profiles of these drugs in this field.

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Original article

Coronary artery calcium score with cardiac computed tomography to anticipate the need for rotational atherectomy

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ABSTRACT

***Introduction and objectives*:** This study aims to investigate if the non-invasive assessment of coronary calcium score using multislice cardiac computerized tomography (MSCT) may anticipate the need for elective rotational atherectomy (RA) during percutaneous coronary intervention.
***Methods*:** Patients were considered eligible for the study after receiving a diagnosis of severe coronary stenosis with moderate or severely calcified plaques during index coronary angiography. Those patients underwent the Agatston coronary artery calcium (CAC) score quantification using the MSCT and then underwent percutaneous intervention. Only those lesions considered non-crossable or non-dilatable according to a pre-specified revascularization protocol were treated with RA. All operators were blinded to the MSCT results. According to the study protocol, clinical, angiographic and Agatston-related variables were included in the statistical analysis. Short and long-term outcomes were investigated in both treatment groups during follow-up.
***Results*:** A total of 40 patients were included in the analysis: 20 underwent RA and 20 conventional percutaneous coronary interventions. Most patients were included after suffering from an acute coronary syndrome and had complex coronary anatomy (mean Syntax score, 25 points). The logistic regression analysis showed that creatinine levels and the per-lesion Agatston score were the only predictors of RA. No significant differences were observed regarding in-hospital or long-term procedural outcomes. A novel parameter, the CAC-Cre index, was found to be useful to anticipate the need for RA.
***Conclusions*:** Coronary artery calcification analysis using the Agatston score is a simple technique that improves the non-invasive assessment of complex coronary plaques prior to percutaneous coronary intervention. The per-lesion Agatston score, serum creatinine levels, and the CAC-Cre index may become useful parameters to anticipate the need for elective RAs during percutaneous coronary intervention.

Keywords: Rotational atherectomy. Cardiac computerized tomography. Agatston. Calcium score. Calcified coronary lesions.

Índice de calcificación coronaria en la tomografía computarizada para predecir la necesidad de aterectomía rotacional

RESUMEN

***Introducción y objetivos*:** El objetivo del estudio fue investigar si la evaluación no invasiva del índice de calcificación coronaria mediante tomografía computarizada cardiaca multidetector (TCMD) puede predecir la necesidad de una aterectomía rotacional (AR) electiva durante la intervención coronaria percutánea.
***Métodos*:** Se incluyeron pacientes diagnosticados de estenosis coronaria grave con placas moderadamente o gravemente calcificadas durante la angiografía coronaria. Esos pacientes se sometieron a la cuantificación del índice de calcificación coronaria con la escala de Agatston utilizando TCMD y posteriormente a intervención percutánea. Solo fueron tratadas con AR las lesiones que se consideraba que no era posible cruzar ni dilatar, según un protocolo de revascularización prediseñado. Ninguno de los operadores conocía de antemano los resultados de la TCMD. Según el protocolo del estudio, en el análisis estadístico se incluyeron variables clínicas, angiográficas y relacionadas con la puntuación Agatston. Durante el seguimiento se estudiaron los resultados a corto y largo plazo en ambos grupos.
***Resultados*:** Se analizaron 40 pacientes: 20 que recibieron AR y 20 con intervención coronaria percutánea convencional. La mayoría se incluyó después de un síndrome coronario agudo y tenían una anatomía coronaria compleja (puntuación media de la escala Syntax de 25 puntos). La creatinina y la puntuación de Agatston por lesión fueron los únicos factores predictivos de la AR. No se

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observaron diferencias significativas en el pronóstico dentro del hospital o a largo plazo. Un nuevo parámetro, el índice CAC-Cre, fue útil para predecir la necesidad de AR.
***Conclusiones*:** El análisis de la calcificación de las arterias coronarias mediante la puntuación de Agatston mejora la evaluación no invasiva de las placas coronarias complejas antes de la intervención coronaria percutánea. La puntuación de Agatston por lesión, la creatinina sérica y el índice CAC-Cre son parámetros útiles para predecir la necesidad de una AR electiva durante la intervención coronaria percutánea.

Palabras clave: Aterectomía rotacional. Tomografía computarizada cardiaca. Agatston. Índice de calcificación coronaria. Lesiones coronarias calcificadas.

Abbreviations

CAC: coronary artery calcium. **MSCT:** multislice cardiac computerized tomography. **PCI:** percutaneous coronary intervention. **RA:** rotational atherectomy.

INTRODUCTION

Coronary artery calcium (CAC) is a key marker of coronary artery disease and one of the most robust predictors of cardiovascular adverse events in different populations. Its prevalence increases with age and affects a large percentage of patients over 60 years of age.[1]

Increased life expectancy in developed countries has led interventional cardiologists to frequently face complex calcified lesions in patients undergoing percutaneous coronary interventions (PCI). This situation remains a challenging scenario due to lower success rate, higher risk of periprocedural complications and need for repeated revascularizations. Occasionally, plaque modification techniques such as rotational atherectomy (RA) are needed to obtain adequate stent expansion and apposition in severely calcified plaques, and they may improve angiographic and clinical outcomes in selected patients. However, the use of RA as a bailout technique may increase procedural time, the amount of contrast media and the incidence of procedural complications. Besides, the assessment of calcification using fluoroscopy only during the coronary angiography has significant limitations and cannot make reliable predictions on what lesions require RA during the intervention.

On the other hand, multislice cardiac computerized tomography (MSCT) improves the non-invasive assessment of coronary calcified lesions. The coronary artery calcium score analysis using MSCT has been related not only to the extension, complexity and severity of the obstructive coronary artery disease, but also to the risk of periprocedural complications after PCI.[2,3]

The primary objective of this study was to investigate whether accurate quantifications of CAC using MSCT may be useful to anticipate the need for RA during PCI due to calcified coronary lesions. Secondary objectives included the analysis of in-hospital and long-term outcomes.

METHODS

Study patients

Prospective, non-randomized, single-center study at a tertiary cardiac center that performs over 1100 PCI and 10-15 RA procedures per year. Between January 2011 and December 2013, patients undergoing coronary angiography who showed calcified obstructive coronary disease and were considered suitable to undergo PCI were screened to enter the study. All patients who had undergone coronary computerized tomography (CT) scans in the past, with all the inclusion criteria and without any exclusion criteria were enrolled in the present study (table 1 of the supplementary data). The exclusion criteria were: ST-segment elevation acute coronary syndrome within 7 days, previous PCI within 2 months, hemodynamic instability and total coronary occlusions. All the patients included gave their written informed consent, and the protocol was approved by the local ethics committee.

Coronary angiography

Coronary angiography was performed based on our institutional protocol and the indication for PCI was based on clinical criteria. Both the SYNTAX score[4] and coronary calcification were independently evaluated by 2 different experienced interventional cardiologists using at least 2 orthogonal fluoroscopic projections. Calcification was defined as an evident density within the arterial wall, visualized in fluoroscopy as a more radiopaque area. The degree of calcification was as follows: 1) moderate: radiopacities noted only during the cardiac cycle before contrast injection; 2) severe: radiopacities noted without cardiac motion before contrast injection usually involving both sides of the arterial lumen.[5]

Multislice cardiac computerized tomography

The MSCT was performed after the index coronary angiography and prior to the PCI procedure. All operators performing PCI were blinded to the MSCT results. CAC and non-contrast-enhanced coronary CT angiography data sets were acquired using a 64-slice single-source CT system (Aquilion-Toshiba, Medical systems corporation, Otawa, Japan). In order to quantify coronary calcification, the Agatston score was determined using the Vitrea 2 workstation (Vital Images Inc, Plymouth, MN, United States). Collimation was 4 x 3 mm; rotation time was 250 mseg; tube voltage 120 Kv; effective tube current 300 mA. Raw data from the CT scan were reconstructed using algorithms optimized for retrospectively ECG-gated segmental reconstruction with 2 mm slices thickness and at an increment of 2 mm.

Agatston score

The extent of calcification was measured individually for each patient (total calcium score), vessel (per-vessel calcium score), and segment lesion (per-lesion calcium score). Coronary calcium was

Table 1. Baseline clinical and angiographic characteristics

	RA Group	PCI Group	*P*
Age	72.4 ± 10.6	72.8 ± 10.2	.91
Men	16 (80%)	15 (75%)	.70
BMI	26.7 ± 4.8	26.6 ± 4.3	.96
Hypertension	14 (70%)	16 (80%)	.46
Dyslipidemia	12 (60%)	17 (85%)	.07
DM	9 (45%)	8 (40%)	.93
Current smoker	12 (60%)	11 (55%)	.74
Creatinine levels (mg/dL)	1.64 ± 1.48	0.96 ± 0.23	.05
STEMI	3 (15%)	1 (5%)	.5
NSTEMI	10 (50%)	10 (50%)	.5
Stable angina	7 (35%)	9 (45%)	.5
Previous MI	4 (20%)	1 (5%)	.25
Previous PCI	4 (20%)	2 (10%)	.25
Previous CABG	0 (0%)	1 (5%)	.25
LM disease	1 (5%)	2 (10%)	.5
Multivessel disease	16 (80%)	19 (95%)	.26
EF < 50%	2 (10%)	6 (30%)	.28
Multi-lesion PCI	15 (75%)	19 (95%)	.077
New oral antiplatelet agents	3 (15%)	1 (5%)	.48
SYNTAX observer A	25.8 ± 15.7	24.4 ± 9.3	.73
SYNTAX observer B	26.8 ± 17.2	24.4 ± 11.8	.61

BMI, body mass index; CABG, coronary artery bypass graft surgery; DM, diabetes mellitus; EF, ejection fraction; LM, left main coronary artery; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RA, rotational atherectomy; STEMI, ST-segment elevation myocardial infarction.

defined as any plaque of at least 3 contiguous pixels with a density > 130 Hounsfield units. Per-lesion calcium scores were estimated by multiplying the target lesion area by a density factor derived from the maximal Hounsfield units within this area, and as described by Agatston.[6] The Bypass Angioplasty Revascularization Investigation (BARI) nomenclature endorsed by 2018 ESC/EACTS Guidelines on myocardial revascularization was used to describe the specific anatomical location of a given coronary lesion.[7,8]

PCI

According to the previously designed protocol, PCI was performed after MSCT, and all operators were blinded to the study results. Femoral access was considered the preferred artery approach, 7-8 F guiding catheters were used, and intravenous heparin was administered to maintain an activated clotting time ≥ 250 ms. All patients received dual antiplatelet therapy with aspirin and a $P2Y_{12}$ inhibitor (clopidogrel, ticagrelor, or prasugrel) according to the recommendations established by the clinical practice guidelines. Hydrophilic wires were used to cross the target lesion and predilation with a semi-compliant balloon up to 16 atm (burst rupture pressure) was performed. Non-compliant balloons were not used as most of them had worse crossing profile than semi-compliant at the time of our study. A specific balloon catheter of 15-20 mm in length was selected to meet a ratio of 0.8-1 with the reference diameter vessel by visual estimation. When the balloon did not cross the lesion, it was considered non-crossable. If the ratio between the minimal balloon diameter at 16 atm and the nominal balloon diameter was less than 80%, then the lesion was considered non-dilatable. It is important to explain that currently there is not such a thing as a clear-cut definition of non-dilatable coronary lesions. All non-crossable and non-dilatable lesions underwent RA, and the remaining ones were treated with conventional PCI. Therefore, 2 groups were established, and pre-specified variables were compared (figure 1). Routine use of intravascular ultrasound (IVUS) was not performed in this study due to the difficulties experienced when crossing these types of lesions.

Rotablation was performed using the Rotablator (Boston Scientific Corporation; Natick, MA, United States) and burr sizes from 1.25-2.5 mm. The burr size was selected to reach a burr/vessel ratio of 0.7. The recommended burr speed was 165 000-200 000 rpm with each sequence being less than 15 seconds, and care was taken to prevent any drops in the rotational speed > 5000 rpm. Temporary pacing was used in cases of rotablation of right coronary artery and dominant left circumflex.

Angiographic success was defined as adequate release and expansion of the stent with a residual stenosis of less than 20% of the

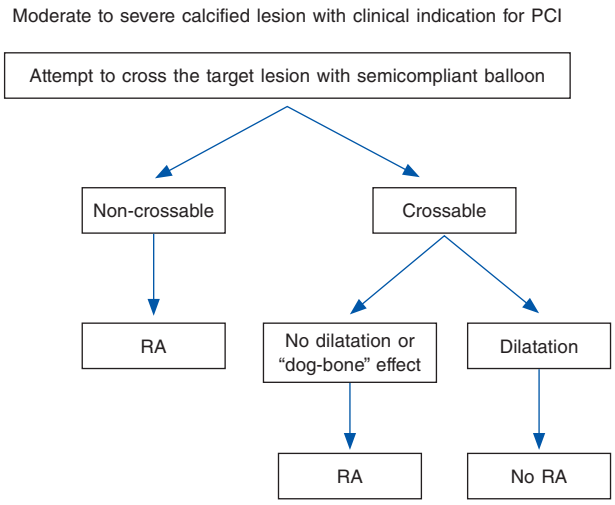

Figure 1. Study revascularization protocol. Lesions were considered *non-crossable* if *a* semicompliant dilatation balloon could not pass through them. If the ratio between the minimal balloon diameter at 16 atm and the nominal balloon diameter was less than 80%, the lesion was considered non-dilatable. All non-crossable and non-dilatable lesions underwent rotational atherectomy, and the remaining ones were treated through conventional percutaneous coronary intervention. RA, rotational atherectomy.

target lesion in the presence of Thrombolysis in Myocardial Infarction (TIMI) flow grade 3; non-success was defined as an non-crossable injury or loss of the stent and other complications like dissection, perforation or no reflow.

Follow-up and endpoints

Troponin I levels were obtained 8-10 hours after the intervention and an ECG was performed in all patients the day after the procedure. The primary endpoint was defined as the need to perform RA during the revascularization of target lesions. Secondary endpoints included the incidence of cardiac and non-cardiac events during the index hospitalization and long-term follow up. Follow-up data were collected by phone or using central databases. Death was defined as all-cause mortality. Myocardial infarction was defined as chest pain or other clinical data consistent with myocardial ischemia, new pathologic Q waves in 2 or more contiguous leads or elevated troponin levels 5 times the normal values after the procedure. Target vessel revascularization was defined as either repeated percutaneous or surgical revascularization of the treated vessel, and target lesion revascularization as any reintervention anywhere within the stent implanted during the index procedure, or on the 5 mm proximal or distal edges of the stents. Stent thrombosis was defined following the criteria developed by the Academic Research Consortium.[9]

Statistical analysis

Categorical variables were expressed as absolute and relative frequencies and compared using the Chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation or, when not normally distributed, as median and interquartile range. The differences among the continuous variables were analyzed using the Student t-test or the Kruskal-Wallis method, respectively. The level of inter-observer agreement was assessed using the Kappa and Phi coefficients. Forward stepwise logistic regression analysis was used to select candidate variables that improved the prediction of RA during PCI, with a statistically significant *P* value of .05. Receiver operating characteristic (ROC) curve analysis was performed to estimate the sensibility and specificity of the different cut-off points provided by the variables obtained through logistic regression.

Table 2. Coronary artery calcium analysis using Agatston score

	RA Group	PCI Group	*P*
Total Agatston score	3772.0 ± 2154.7	3040.4 ± 1693.8	.240
Per-vessel Agatston score	1628.5 ± 1142.8	833.2 ± 466.0	.008
Per-lesion Agatston score	864.1 ± 471.0	458.4 ± 360.3	.004

PCI, percutaneous coronary intervention; RA, rotational atherectomy.

RESULTS

Baseline clinical and angiographic characteristics

A total of 40 patients (77.5 % male, 72 ± 10.3 years) were included in the study. The most common indications for index coronary angiography were non-ST-segment elevation acute coronary syndromes (50%) and stable angina with a positive stress test (40%).

The baseline clinical characteristics are shown in table 1. There were no significant differences in the demographic characteristics or antithrombotic regimens between both arms, although there was a trend towards a higher rate of dyslipidemia in the PCI group (P = .077) and worse renal function in the RA group (P = .05).

The Syntax score was high in both treatment groups, without any significant differences between them and a good correlation between the 2 observers (Phi coefficient 0.83, P = .001).

Multislice cardiac computerized tomography

Agatston score was over 3000 in both arms, with no statistically significant differences (P = .24). However, the per-vessel and per-lesion Agatston scores were significantly higher in the RA group (table 2).

Regarding the anatomical distribution of calcium, the vessel with a higher Agatston score was the right coronary artery, showing homogeneous calcification between the proximal and distal segments. The left anterior descending artery was the second most calcified blood vessel, especially at its proximal and middle segments. The circumflex artery had the lowest Agatston score.

Procedural details and outcomes

Procedural details are shown in table 3. Percutaneous access occurred through the femoral artery in 37 patients (92.5%). In 29 patients (72.5%), the target lesion could be crossed by the dilation balloon. Among these 29 crossable lesions, 9 (31%) showed the "dog bone" effect during balloon inflation and could not be dilated. Therefore, according to the study protocol, 20 patients (50%) underwent conventional PCI and the other 20 (50%) RA.

The mean balloon size and length was similar in both arms. Among patients undergoing RA, a single burr was used in most lesions

Table 3. Angiographic and procedural characteristics

	RA Group	PCI Group	*P*
Location			.17
LMCA	0	1	
Proximal LAD	10	6	
Mid LAD	2	8	
Proximal LCx	3	4	
Proximal RCA	2	1	
Mid RCA	2	0	
Ramus Intermedius	1	0	
RVD (mm)	2.96 ± 0.43	2.91 ± 0.26	.68
Lesion length (mm)	44.85 ± 17.84	41.25 ± 24.13	.59
Diameter stenosis, %	79.2 ± 7.9	73.0 ± 9.2	.028
Bifurcation	6 (46.2%)	7 (53.8%)	.73
Maximum burr size (mm)	1.45 ± 0.15		
No. of stents/lesion	1.84 ± 0.60	2.05 ± 0.89	.40
Contrast media (mL)	312.0 ± 96.7	239.0 ± 66.5	.018
Contrast-induced nephropathy	4	0	.035
Dissections	2	2	.36
Perforations	1	0	.56
Intraprocedural major complications	0	0	> .99
Angiographic success	90%	100%	.14
Death	0	0	> .99
Target vessel re-PCI	1	1	> .90
Myocardial infarction	1	0	.31
Access site complications	2	0	.34

LAD, left anterior descending artery; LCx, left circumflex artery; LMCA, left main coronary artery; PCI, percutaneous coronary intervention; RA, rotational atherectomy; RCA, right coronary artery; RVD, reference vessel diameter.

(95%) with a mean burr size of 1.45 ± 0.15 mm. In the entire study population, the most frequently treated artery was the left anterior descending artery (65%); 32.5% of the target lesions were bifurcations; 35 patients (87.5%) had multivessel disease, and 34 (85%) required intervention in more than one major coronary artery. No differences were seen on the target lesion treated no in the number of bifurcation lesions between both groups.

Angiographic success rate was 90% in the RA arm and 100% in the PCI arm, without any significant differences between groups. Coronary dissections, perforations, and no-/slow-flow phenomena were rare and occurred equally in both groups. A significantly larger contrast volume was used in the RA group compared to conventional PCI group.

Stepwise logistic regression analysis showed that creatinine and per-lesion Agatston were the only predictors of RA. For every 0.1mg/dL increase in creatinine level, the probability of RA increased 48%. On the other hand, every 100 point increment in per-lesion Agatston score increased the probability of RA in 22%. Using the optimal cut-off value from ROC analysis (figure 2A), a per-lesion Agatston score of 383 resulted in a sensitivity of 89.5% and specificity of 60% (area under the curve, 0.79). ROC curve for serum creatinine level (figure 2B) showed a sensitivity of 75% and a specificity of 65% for an optimal cut-off point of 1.02 mg/dL (area under the curve, 0.75). Given the association of both variables with the use of RA, we created a combined index of creatinine (Cre) and per-lesion Agatston score (CAC-Cre index), obtained by multiplying the creatinine levels and the per-lesion Agatston score. The ROC analysis of CAC-Cre index (figure 2C) demonstrated better area under the curve (0.86), being 622.79 the value with the best sensitivity (78.9%) and specificity (80%).

In-hospital outcomes and long-term follow-up

There were no deaths during hospitalization. Two patients (1 in the RA group and 1 in the PCI group) underwent target vessel revascularization during the index admission. Only 1 patient, included in the RA group, experienced a protocol-defined MI. Complications in the access site were numerically higher in the RA group, without any significant differences. One patient of the PCI group required one intra-aortic balloon pump. On the other hand, the RA group showed a higher incidence of contrast-induced nephropathy (P = .035), possibly due to worse baseline renal function.

There were no differences between the 2 treatment groups regarding major cardiac events at the end of the follow up (4.1 ± 2.2 years) (table 4); with an overall mortality of 12 patients (30%) and 7 cardiovascular deaths (58.3%). Other cardiovascular events such as myocardial infarctions, target-vessel revascularizations and non-target vessel revascularizations, were statistically not-significant. None of the baseline clinical or angiographic variables included in the analysis was associated with the occurrence of major events at follow-up.

Regarding the analysis of coronary calcium using the MSCT, a statistically significant correlation was observed between long-term mortality and the total Agatston score (P = .005).

DISCUSSION

Severe coronary artery calcification remains a major challenge in contemporary interventional cardiology. It reduces the chances of angiographic success, and significantly increases the rate of procedural complications.[10] The stent underexpansion or asymmetric expansion and malapposition are frequently observed in very calcified plaques; this results in a significantly greater incidence of restenosis and stent thrombosis.[11] It is in this context that RA may be useful.[12,13]

Table 4. Major adverse cardiac events during follow-up

	RA Group	PCI Group	*P*
Death	6 (30%)	6 (30%)	.59
MI	3 (15%)	5 (25%)	.34
TLR	1 (5%)	3 (15%)	.3
NTLR	4 (20%)	5 (25%)	.5

MI, myocardial infarction; NTLR, non-target lession revascularization; PCI, percutaneous coronary intervention; RA, rotational atherectomy; TLR, target lesion revascularization.

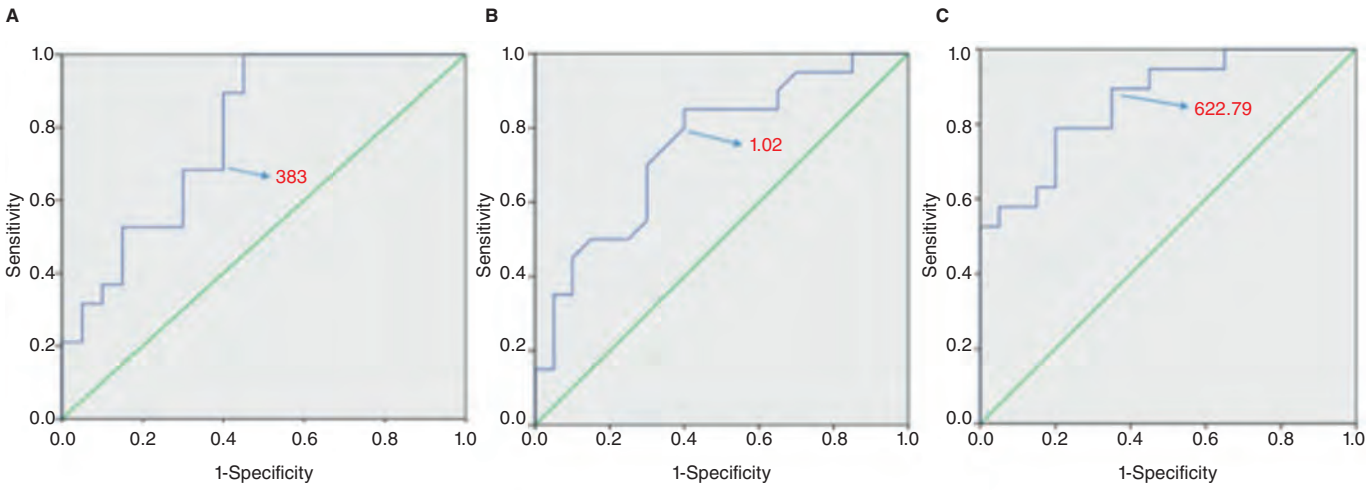

Figure 2. Receiver operating characteristic curve (ROC) for predicting rotablation based on the per-lesion Agatston score **(A)**, the serum creatinine levels **(B)** and the CAC-Cre index **(C)**. The optimal thresholds for predicting rotablation were 383 per-lesion Agatston points, creatinine levels of 1.02 mg/dL, and a 622.79 CAC-Cre index, respectively.

In order to implement the most appropriate revascularization strategy, there is a growing interest in the non-invasive assessment of complex coronary lesions that may benefit from plaque modification techniques.[15,16] If we were able to anticipate what patients will require elective RA, we would not have to use this technique as a bailout strategy, thus reducing procedural time, use of contrast media, and the number of ischemic complications.

Fluoroscopy is not useful to adequately quantify coronary calcium, because of its limited sensitivity and significant intra- and interobserver variability, and it has not proven useful either to anticipate the need for RA. Intravascular ultrasound improves the assessment of coronary plaques, providing an accurate evaluation of the amount of calcium in the arterial wall.[17] However, it cannot adequately characterize calcium itself, limiting its ability to anticipate the response of a given plaque to balloon catheter dilatation. Another limitation of intravascular ultrasound is the inability to cross many complex lesions with the ultrasound catheter. Although some operators use this situation as a criterion for using RA, there is no clinical evidence that supports such a practice.

In this study we have seen that the Agatston score improves the identification of patients who would benefit from a plaque modification strategy with elective RA. The Agatston score analysis is a sensitive, reproducible and widely available technique that may improve the interventional management of patients with complex coronary lesions. As far as we know, there is only another study that has tested this hypothesis, although with a different methodology. Sekimoto et al.[18] studied patients with chronic stable angina who underwent non-invasive angiography and coronary calcium quantification by CT prior to cardiac catheterization. In this study, the decision to perform RA was entirely left to the discretion of the interventional cardiologist.

Our work tried to investigate the use of these parameters both in stable ischemic heart disease and patients after an acute coronary syndrome, selecting a population with significant coronary calcification and high pre-test chances to have calcified circumferential lesions,[17] that may perhaps be better treated with RA as the first-line proactive therapy.

Also, our study was designed in such a way that the decision to perform RA was not left at the discretion of the operator, but dictated by the formal prospective protocol. Only non-crossable or non-dilatable lesions with a balloon catheter were treated with RA, which is strictly in accordance with the clinical practice guidelines. This strategy also limits the disparity of criteria among different operators, providing a greater consistency to the study results.

We decided not to perform CT angiography because of its limitations in adequately characterizing the degree of stenosis in patients with significant calcification and also to avoid the use of unnecessary radiation and contrast. Regarding the Agatston calcium score, we selected 3 parameters: global, per-treated vessel and per-lesion or segment. In our study that included patients with complex coronary anatomy, global Agatston values were above 3000 in both treatment arms, with no significant differences between the 2 groups. As in the Japanese study,[18] significantly higher values of per-vessel and per-lesion Agatston score were observed in patients who underwent rotational atherectomy. After logistic regression analysis, only the per-lesion score turned out to be an independent predictor of the need for RA. A per-lesion Agatstson score of 383 was the optimal cut-off value determined by the ROC analysis, relatively close to that described by Sekimoto et al.[18] An analytical variable, serum creatinine, also turned out to be an independent predictor of RA (chronic renal failure was also significantly higher in the AR group, indicative of a clear clinical association between chronic renal failure and the percentage of intracoronary calcium; something already confirmed in the past). However, ROC curve analysis showed that its use resulted in an optimal classification of the patients. Additionally, we combined both predictors (per-lesion Agatston and serum creatinine) to create an index that would improve the prediction of RA in our patients, being 622.79 the value with the best sensitivity and specificity rate. Therefore, the CAC-Cre index may become useful in the decision-making process at the the cath lab.

Lesion length is one of the characteristics included in the Syntax score that increases complexity during PCI. Sekimoto et al. found that the length of the lesion was significantly associated with the use of RA during the revascularization procedure. In our series, in which the decision to perform rotablation was made following a strict protocol, we found no significant correlations between lesion length and the need for RA. These results are consistent with the findings of Dill et al., who did not observe a significant benefit from routine RA compared to simple angioplasty in patients with complex coronary disease and longer lesions.[19]

Baseline characteristics were well balanced between both treatment arms, both clinically and in terms of the complexity reflected in the Syntax score. The population included is representative of a subset of patients with severe coronary artery disease who are eligible for PCI in contemporary cardiology centers. In this group, RA showed good angiographic results, with no significant differences between groups during follow-up. Long term incidence of major adverse cardiovascular events was high, but similar to that described by other groups in patients with a similar risk profile.[20,21]

Limitations

This is an observational, non-randomized protocol with the corresponding limitations of its specific study design. The number of patients included was small, but provided useful information to plan interventions of complex lesions. Defining a lesion as non-dilatable or non-crossable may have a significant component of operator-dependency, and currently there is not such a thing as a clear-cut definition of non-dilatable coronary lesions. Thus, our protocol was designed to be straightforward in order to follow the actual clinical practice guidelines and reduce the inter-operator variability. On the other hand, although the Agatston calcium score is a common technique used in cardiac imaging units all over the world, the per-vessel and per-lesion assessment may require additional time and experienced staff. Selection bias may occur in patients without a CT study during the recruitment period. Also, the fact that this technique is not an indication after performing a diagnostic angiography involves a low use of this technique in the routine clinical practice.

CONCLUSIONS

Coronary artery calcification analysis using Agatston coronary calcium score is a simple technique that improves the non-invasive assessment of complex coronary plaques prior to PCI. The per-lesion Agatston score and the serum creatinine levels may be useful indicators to anticipate the need for elective rotational atherectomy during PCI. A new parameter created by combining both variables, the CAC-Cre index, improved even more the prediction of RA during PCI. A prospective study is needed to validate this index.

CONFLICTS OF INTEREST

R. Moreno is associate editor of *REC: Interventional Cardiology*. The journal's editorial procedure to ensure impartial handling of the manuscript has been followed. No other conflicts of interest were declared by the authors.

WHAT IS KNOWN ABOUT THE TOPIC?

- The percutaneous treatment of moderate-to-severely calcified coronary lesions remains a challenge for contemporary interventional cardiologists since choosing the wrong management strategy may lead to severe complications.
- RA is a useful technique that may improve outcomes in non-crossable or non-dilatable coronary lesions, yet its results are not optimal when used as a bailout strategy.
- The MSCT-determined Agatston score is the most useful technique for the quantitative assessment of coronary calcium. There is limited information on its role as a predictive tool for the assessment of a particular coronary plaque as non-crossable or non-dilatable.
- To our knowledge, the combination of a clinical variable such as creatinine levels with a CAC variable to create an index to anticipate the need of RA has not previously been reported.

WHAT DOES THIS STUDY ADD?

- In this study we have seen that the Agatston score improves the identification of patients who would benefit from a plaque modification strategy with elective RA.
- A per-lesion Agatstson score of 383 and the serum creatinine levels are independent predictors of RA. We combined both predictors to create an index that improved the prediction of RA in our patients (CAC-Crex index), being 622.79 the value with the best sensitivity and specificity rate.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M19000037.

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Original article

Procedural and clinical benefits of selective thrombus aspiration in primary PCI. Insights from the TAPER Registry

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ABSTRACT

Introduction and objectives: After the results of several randomized trials, routine thrombus aspiration (TA) has remained out of the spotlight after not improving the prognosis of patients with ST-segment elevation myocardial infarction and even increasing their complications. The goal here was to assess the impact of selective TA during primary percutaneous coronary intervention (pPCI), its safety and clinical benefits at 1-year follow-up.
Methods: The TAPER registry (efficacy and safety of selective Thrombus Aspiration in Real clinical Practice) retrospectively included patients with ST-segment elevation myocardial infarction treated with pPCI. The clinical and procedural characteristics and the composite endpoint of cardiovascular mortality, non-fatal myocardial infarction, stent thrombosis, target lesion revascularization or stroke were evaluated after at 1-year follow-up.
Results: 687 patients (76.9% males, 64 ± 12 years) were analyzed. The TA was performed in 40.3% of cases (in 89.9% as the initial strategy and in 10.1% as the bailout strategy) and it was successful in 93.8% of them. The most important predictor of TA use was a higher initial Thrombolysis in Myocardial Infarction (TIMI) thrombus grade (OR, 3.2; 95%CI, 2.5-3.9; $P < .0001$). TA achieved a significant improvement of TIMI-flow (2.4 points) and a significant reduction of the TIMI thrombus grade (2.6 points). At 1-year follow-up, no stroke was observed in the TA-group and the rate of the composite endpoint (cardiovascular mortality, non-fatal myocardial infarction, stent thrombosis, target lesion revascularization or stroke) was similar in both groups (TA-group 8% vs non-TA-group 5.7%; $P = .24$).
Conclusions: Selective TA is frequently used in the current clinical practice with a high success rate and a low rate of associated complications. It significantly reduces thrombotic burden and improves coronary flow. At 1-year follow-up, a similar rate of adverse events was observed regardless of the use of TA.

Keywords: Thrombus aspiration. Primary PCI. STEMI.

Beneficios clínicos y angiográficos de la tromboaspiración selectiva en la angioplastia primaria. Resultados del registro TAPER

RESUMEN

Introducción y objetivos: Tras los resultados de varios estudios aleatorizados, la tromboaspiración (TA) sistemática ha sido relegada a un segundo plano por no mejorar el pronóstico de los pacientes con infarto agudo de miocardio con elevación del segmento ST e incluso aumentar sus complicaciones. El objetivo de este trabajo fue evaluar el impacto de la TA selectiva durante la angioplastia primaria (ICPp), su seguridad y sus beneficios clínicos tras 1 año de seguimiento.
Métodos: El registro TAPER (eficacia y seguridad de la tromboaspiración selectiva en la práctica clínica real) incluyó retrospectivamente pacientes con infarto de miocardio con elevación del segmento ST tratados con ICPp. Se evaluaron las características clínicas y de los procedimientos, así como la presentación del evento combinado de muerte cardiovascular, infarto de miocardio no fatal, trombosis de *stent*, necesidad de revascularización de la lesión tratada o ictus tras 1 año de seguimiento.
Resultados: Se analizaron 687 pacientes (76,9% varones, 64 ± 12 años). La TA se realizó en el 40,3% de los casos (89,9% como estrategia inicial y 10,1% como rescate) y fue exitosa en el 93,8%. El predictor más importante de uso de TA fue un alto grado de

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trombo inicial según la escala TIMI *(Thrombolysis in Myocardial Infarction)* (*odds ratio* = 3,2; intervalo de confianza del 95%, 2,5-3,9; p < 0,0001). La TA consiguió una mejora significativa del flujo de 2,4 puntos en la escala TIMI de flujo y una reducción significativa del grado de trombo de 2,6 puntos en la escala TIMI de trombo. En 1 año de seguimiento no se observó ningún ictus en el grupo de TA y la tasa del evento combinado fue similar en ambos grupos (grupo de TA 8% y grupo de no-TA 5,7%; p = 0,24).
Conclusiones: La TA selectiva se usa con frecuencia en la práctica clínica actual, con una alta tasa de éxito y pocas complicaciones asociadas. La TA selectiva reduce significativamente la carga de trombo y mejora el flujo coronario. Tras 1 año de seguimiento, se observó una tasa similar de eventos adversos en los pacientes a quienes se realizó ICPp con independencia del uso de TA.

Palabras clave: Tromboaspiración. Angioplastia primaria. IAMCEST.

Abbreviations

pPCI: primary percutaneous coronary intervention. **TA:** thrombus aspiration.

INTRODUCTION

Primary percutaneous coronary intervention (pPCI) is the preferred treatment for the management of ST-segment elevation myocardial infarction.[1] However, one of its limitations is the possibility of distal embolization of thrombus and failure to restore flow at the microvascular level, which is associated with a significantly higher mortality rate.[2] Thrombus aspiration (TA) was thought to be a simple method to remove thrombus before stent deployment, thereby reducing distal embolization and improving outcomes.[3]

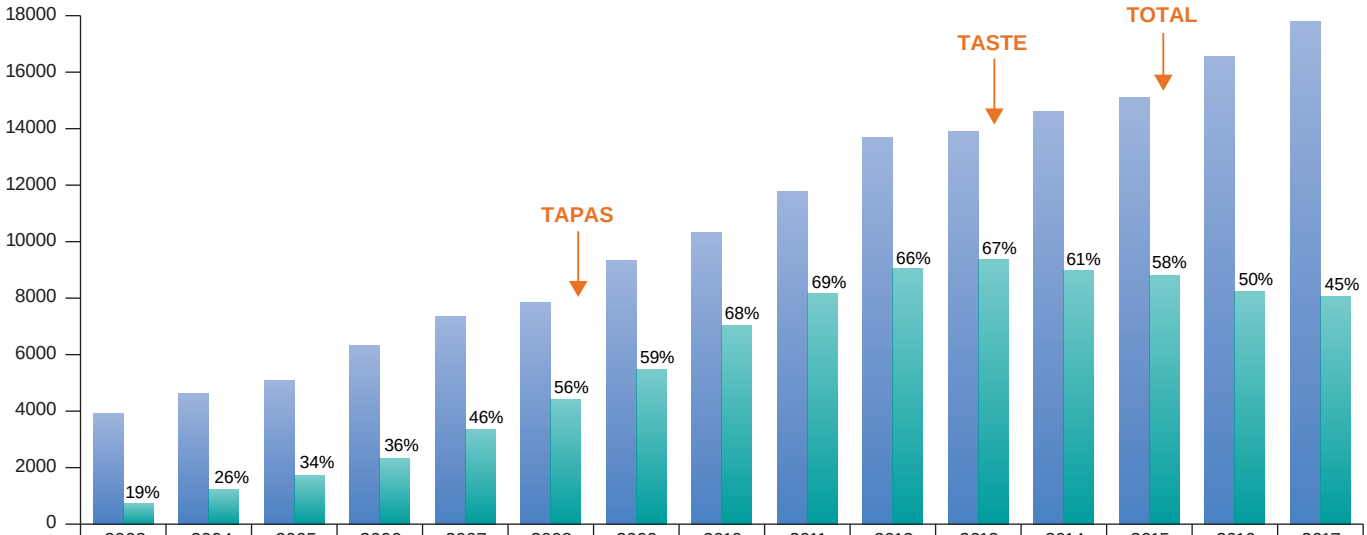
After the promising results of the TAPAS trial,[4,5] TA was included in the routine practice and was probably overused.[6] However, the results from the TASTE[8] and TOTAL[9] clinical trials have brought uncertainty to the clinical benefits of TA. Additionally, possible harm from an increased risk of stroke has been suggested.[9] Subsequently, guidelines have downgraded the indication for routine TA from IIa[10-12] to III,[13,14] resulting in a progressive reduction in the use of TA (figure 1).[4,7,9,15]

In addition to the fact that the above-mentioned clinical trials may not reflect the actual clinical practice,[6] we should be consider that these recommendations apply for routine TA and not for selective TA, where the operator performs the technique in cases where the expected benefit is higher. Although selective TA may be more indicative of the common practice, we do not have actual data on its application. For this reason, we designed the TAPER registry (efficacy and safety of selective Thrombus Aspiration in Real clinical Practice) in an attempt to analyze the procedural advantages of selective TA during pPCI, its safety and clinical benefit at 1-year of follow-up.

METHODS

Patients and study design

The TAPER registry retrospectively included patients with ST-segment elevation myocardial infarction treated with pPCI in 4 high-volume centres of different countries (A, B, C, D) on a 24/7 program.



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
pPCI	3900	4640	5101	6316	7358	7837	9334	10339	11766	13690	13890	14600	15089	16554	17784
TA	743	1225	1732	2308	3353	4427	5481	7032	8171	9041	9370	8981	8813	8235	8045

Figure 1. Evolution of pPCI and TA over the last 15 years: Evolution of primary percutaneous coronary intervention and TA in Spain over the last 15 years[15] in relation to the publication of the main TA trials.[4,7,9] pPCI, primary percutaneous coronary intervention; TA, thrombus aspiration.

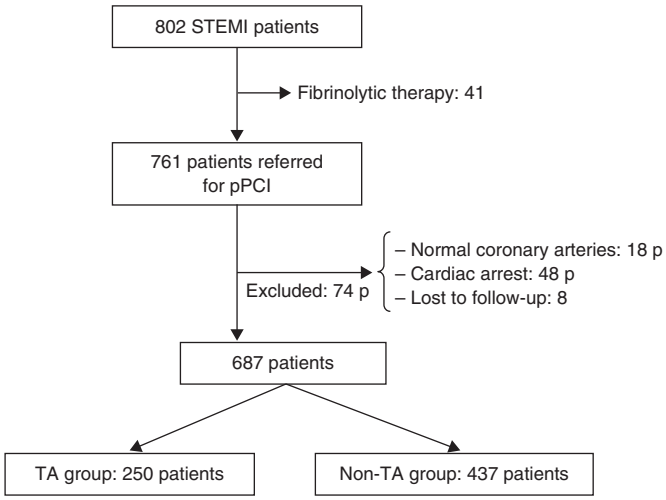


Figure 2. Study flowchart. P, patients; pPCI, primary percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TA, thrombus aspiration.

These centers serve communities of 615 000, 400 000, 450 000, and 350 000 people, respectively.

Consecutive patients with ST-segment elevation myocardial infarction who were referred to undergo pPCI within 12 hours after symptoms onset in the period between January 2015 and December 2016 were included. Those who had received fibrinolytic therapy were not eligible.

We excluded those patients who did not have an evident culprit coronary lesion, those who presented with cardiac arrest and those who were lost to follow-up. Patients with contraindications to antiplatelet therapy were also excluded (figure 2).

The TA group was defined as those patients in whom the TA was performed as an initial strategy and non-TA group as those patients in whom the TA was not performed or it was performed as a bailout strategy after balloon dilatation or stent implantation.

Both the clinical and procedural characteristics were analyzed and a combined endpoint of cardiovascular mortality, non-fatal myocardial infarction related to the treated lesion, stent thrombosis, target lesion revascularization or stroke was evaluated at 1-year follow-up.

Study procedures

Patients received antiplatelet and anticoagulant treatment according to the clinical practice guidelines.[16] The addition of IIb/IIIa glycoprotein inhibitors was left to the discretion of the operator. The use of TA and other technical details of the pPCI were left at the discretion of the interventional cardiologist. TA was performed using a standard technique.[9]

Angiographic assessment

The angiographic analysis was performed by 4 experienced interventional cardiologists. After defining the culprit lesion in the initial coronary angiogram, the distal flow of the culprit vessel was assessed using the Thrombolysis in Myocardial Infarction (TIMI) grade score.[17] Once the culprit lesion had been crossed with a coronary guidewire, the thrombotic burden was defined according to the TIMI-thrombus scale.[18] Both the TIMI-flow scale and the TIMI-thrombus scale were reassessed after the TA. The presence of no-reflow phenomenon and thrombus distal embolization were also evaluated.

Follow-up and clinical endpoints definitions

The follow-up of the patients was carried out through telephone calls and in-hospital clinical records of the visits to the cardiology department after the initial admission.

The occurrence of major acute cardiovascular events (MACE) [cardiovascular mortality, myocardial infarction related to the treated lesion, stent thrombosis or need for revascularization of the treated lesion or stroke] at 1-year follow-up was established as the primary endpoint. The secondary endpoints were the independent analysis of each individual event of the composite endpoint.

All deaths were considered cardiac unless another specific cause was documented. Myocardial infarction was defined following the actual recommendations[19] and only those related to the treated lesion, whether periprocedural or at follow-up, were taken into consideration. Target lesion revascularization or stent thrombosis was defined according to the Academic Research Consortium criteria.[20]

The angiographic success was defined as final TIMI 3 distal flow with less than 20% of vessel stenosis and no immediate mechanical complications. TA was considered successful if an improvement of TIMI-flow ≥ 1 grades or a reduction of TIMI-thrombus scale ≥ 1 grades were achieved, without any immediate complications related to the technique.

Statistical analysis

Quantitative variables following a normal distribution were expressed as mean ± standard deviation. Those that did not follow were described by the median [range]. Qualitative variables were expressed as absolute and relative frequencies of their categories.

P levels < .05 were considered statistically significant and the 95% confidence interval (95%CI) of the target analysis variables was estimated. When it comes to the bivariate analysis, the Student *t* test or the non-parametric Mann-Whitney *U* test were used for mean comparison purposes and the chi-square test or Fisher's exact test were used to compare qualitative variables.

For the multivariate analysis, logistic regression was used. Variables were considered as potential predictors of risk in the multivariate model when they showed a statistically significant association in the univariate analysis. The SPSS statistical package software version 20 (Armonk, NY: IBM Corp), was used for calculations.

RESULTS

Out of the 761 patients initially screened, 74 were excluded (18 patients did not have any evident culprit coronary lesions, 48 patients presented with cardiac arrest, and 8 patients were lost to follow-up). The remaining 687 patients (64.1 ± 12.2 years; 76.9% male) were finally analyzed. The baseline characteristics are shown on table 1.

Procedural characteristics

In the overall cohort, the culprit lesion was more frequently located at the left anterior descending coronary artery (45.6%), followed by

Table 1. Baseline characteristics

	TA group N = 250	Non-TA group N = 437	*P*
Age (y)	63.6 ± 12.6	64.4 ± 12.1	.46
Male	208 (83.2%)	320 (73.2%)	.003
BMI	27.2 ± 6.4	26.6 ± 5.8	.23
Current smoker	105 (42%)	140 (32%)	.012
Diabetes mellitus	44 (17.6%)	80 (18.3%)	.86
Dyslipidemia	74 (29.6%)	103 (23.6%)	.07
Hypertension	114 (45.6%)	195 (44.6%)	.68
LVEF	48.7 ± 10.7	49.7 ± 10.4	.27
Previous PCI	27 (10.8%)	37 (8.5%)	.29
Previous CABG	3 (1.2%)	5 (1.1%)	.93
Chronic kidney disease	13 (5.2%)	13 (2.9%)	.14

BMI, body mass index; CABG, coronary artery bypass grafting; LVEF, left ventricle ejection fraction; PCI, percutaneous coronary intervention; TA, thrombus aspiration.
Data are expressed as no. (%) or mean ± standard deviation.

the right coronary artery (36.9%). Forty-eight-point-one per cent of patients had multivessel disease. The initial TIMI-flow was 0-1 in 72.7% of cases and the TIMI-thrombus grade was ≥ 3 in 61.6% of the cases.

The TA was performed in 40.3% of cases. In 89.9%, the TA was the initial strategy after crossing the culprit lesion with the coronary guidewire, whereas in 10.1% of the cases it was performed as a bailout strategy (figure 3). Procedural characteristics are shown on table 2.

Predictors of use of thrombus aspiration

There were significant differences in the use of TA rates among the different centers (A = 63.7%; B = 32.9%; C = 16.9%; D = 15.7%; $P < .0001$). The TA was more frequently used as the initial strategy in male patients (40.9% vs 26.4%; $P = .003$), in current smokers (47.7% vs 36.1%; $P = .012$), and when the culprit lesion was the thrombosis of a former stent (66.7% vs 36%; $P = .004$). The rate of TA was also different when it comes to the culprit artery (left anterior descending coronary artery, 31.9%; left circumflex coronary artery, 29.7%; right coronary artery, 43.5%; $P = .01$). Also, the patients from the non-TA group were treated more often with ticagrelor or prasugrel compared to clopidogrel ($P < .0001$) and received more frequently drug-eluting stents (TA group, 68% vs non-TA group, 75.3%; $P = .04$). In the patients from the TA-group, the initial TIMI-flow was significantly lower (0.3 ± 0.8 vs 1.1 ± 1.3; $P < .0001$) and the initial TIMI-thrombus grade was higher (4.3 ± 0.9 vs 2.5 ± 1.4; $P < .0001$).

In the multivariate analysis, we included those variables that showed a statistically significant association with TA in the univariate analysis: gender, current smoking habit, culprit artery, $P2Y_{12}$ inhibitor, initial TIMI-flow, initial TIMI-thrombus grade, initial stent thrombosis (as culprit lesion), center and type of stent. The strongest independent predictor for the use of TA as the initial strategy was a higher initial TIMI-thrombus grade (odds ratio [OR], 3.2; 95%CI, 2.5-3.9; $P < .0001$). The performance of the pPCI in center A (OR, 20.7; 95%CI, 10-42.5; $P < .0001$) or B (OR, 3.3; 95%CI, 1.4-7.5; $P = .005$) was also an independent predictor of TA (compared to center D; the center where the TA was less frequently used). Culprit lesions located at the right coronary artery (OR, 2; 95%CI, 1.008-3.9; $P = .047$) were also identified as predictors for the use of TA as the initial strategy.

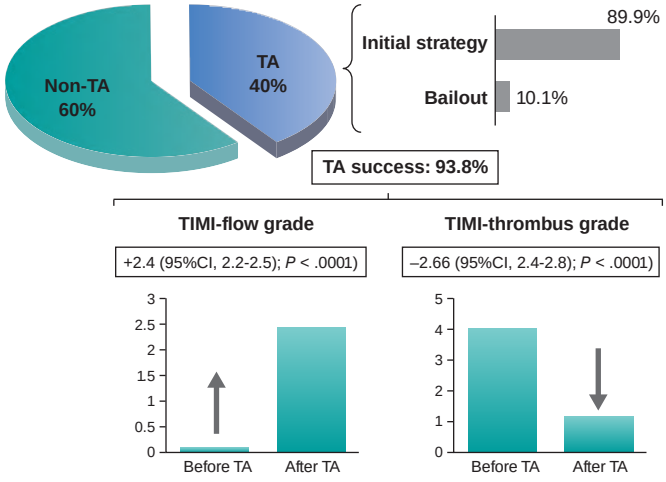


Figure 3. Selective TA performance and beneficial effects during primary percutaneous coronary intervention. Percentage of cases in which TA was used (as an initial or bailout strategy) and TA success rate by improving TIMI-flow or TIMI-thrombus grade. TA, thrombus aspiration; TIMI, Thrombolysis in Myocardial Infarction.

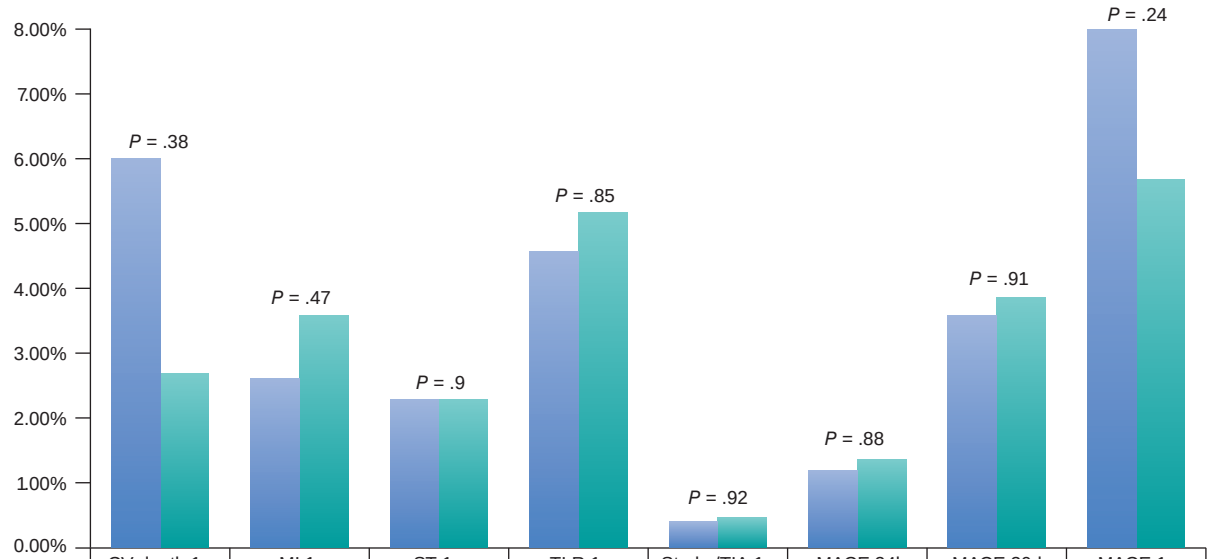
Angiographic results after thrombus aspiration

When TA was performed as initial strategy, a significant improvement of TIMI-flow (2.4; 95%CI, 2.2-2.5; $P < .0001$) and a significant reduction of TIMI-thrombus grade [2.6; 95%CI, 2.4-2.8; $P < .0001$] were observed (figure 3). There were no significant differences between both groups in the occurrence of no-reflow phenomenon or distal embolization. The rate of direct stenting was twice as frequent in the TA group. Similarly, the rate of procedural success was high and similar in both groups (TA group, 95.2% vs non-TA group, 92.4%; $P = .16$) (table 2).

Table 2. Angiographic and procedural characteristics

	TA group n = 250	Non-TA group n = 437	*P*
Culprit artery			
LM	5 (2%)	2 (0.5%)	
LAD	98 (39.2%)	209 (47.8%)	.01
LCx	30 (12%)	71 (16.2%)	
RCA	114 (45.6%)	148 (33.8%)	
Other	3 (1.2%)	1 (0.2%)	
Multivessel disease	107 (42.8%)	221 (50.6%)	.08
$P2Y_{12}$ inhibitor			
Clopidogrel	185 (74%)	272 (62.2%)	< .0001
Prasugrel	15 (6%)	29 (6.6%)	
Ticagrelor	37 (14.8%)	119 (27.2%)	
Anticoagulation			
UFH	245 (96%)	433 (99%)	.69
Bivalirudin	2 (0.8%)	2 (0.45%)	
Enoxaparin	0 (0%)	1 (0.22%)	
Glycoprotein IIb/IIIa inhibitor			
Abciximab	91 (36.4%)	120 (27.5%)	.13
Eptifibatide	15 (6%)	18 (4.1%)	
Ventricular assist device	11 (4.4%)	12 (2.7%)	.24
Initial TIMI-flow	0.3 ± 0.8	1.1 ± 1.3	< .0001
Initial TIMI-flow 0-1	228 (91.2%)	271 (62%)	< .0001
Initial TIMI-thrombus grade	4.8 ± 0.9	2.5 ± 1.4	< .0001
Initial TIMI-thrombus grade ≥ 3	233 (93.2%)	191 (43.7%)	< .0001
Initial stent thrombosis (as culprit lesion)	14 (5.6%)	7 (1.6%)	.004
Bifurcation (at the culprit lesion)	62 (24.8%)	108 (24.7%)	.8
DTB time (minutes)	101 ± 55	102 ± 83	.8
TA device			
Medtronic Export	134 (53.6%)	NA	
Terumo Eliminate	96 (38.4%)	NA	
Hexacath Recover	20 (8%)	NA	
Direct stenting	178 (71.2%)	144 (32.9%)	< .0001
Type of stent			
Bare metal	80 (32%)	108 (24.7%)	.04
Drug-eluting	170 (68%)	329 (75.3%)	
Stent length (mm)	29 ± 13.8	27.8 ± 14.8	.29
Stent diameter (mm)	3.3 ± 0.7	3.4 ± 2.2	.8
Post-dilatation	43 (17.2%)	82 (18.8%)	.47
No reflow	24 (9.6%)	31 (7.1%)	.24
Distal embolization	4 (1.6%)	7 (1.6%)	.97
Angiographic success	238 (95.2%)	404 (92.4%)	.16

DTB, door-to-balloon time; LAD, left anterior descending coronary artery; LCx, left circumflex artery; LM, left main coronary artery; RCA, right coronary artery; TA, thrombus aspiration; TIMI, Thrombolysis in Myocardial Infarction.
Data are expressed as no. (%) or mean ± standard deviation.



	CV death 1y	MI 1y	ST 1y	TLR 1y	Stroke/TIA 1y	MACE 24h	MACE 30d	MACE 1y
TA as initial strategy	6.00%	2.70%	2.30%	4.60%	0.40%	120%	3.60%	8.00%
Non-TA as initial strategy	4.10%	3.60%	2.30%	5.20%	0.46%	137%	3.89%	5.72%

Figure 4. MACE at follow-up. CV, cardiovascular; MACE, major acute cardiovascular events; MI, myocardial infarction; ST, stent thrombosis; TA, thrombus aspiration; TIA, transient ischemic attack; TLR, target lesion revascularization.

Adverse events at follow-up

After a 1-year follow-up, there were no significant differences in terms of the overall rate of MACE between both groups (TA group, 8% vs non-TA group, 5.7%; $P = .24$). Also, no differences were seen in any of the individual adverse events: cardiovascular mortality (TA group, 5.2% vs non-TA group, 3.9%, $P = .38$), myocardial infarction (TA group, 2.4% vs non-TA group, 3.4%; $P = .47$), stent thrombosis (TA group, 2.4% vs non-TA group, 2.3%, $P = .9$) or target lesion revascularization (TA group, 4.4% vs non-TA group, 4.8%; $P = .85$). The incidence of cerebral ischemic events was similar in both groups (TA group, 0.4% vs non-TA group, 0.46%; $P = .92$). One patient only was diagnosed with transient ischemic attack in the TA group that occurred > 30 days after the pPCI. None of the patients of this group suffered a stroke during follow-up. In the non-TA group, two patients suffered a stroke (one was a ischemic stroke 24 hours after the pPCI and the other one was a hemorrhagic stroke that occurred 3 months after the procedure in a patient treated with triple therapy due to atrial fibrillation). There were no differences in the rate of MACE during the first 24 hours after pPCI (TA group, 1.2% vs non-TA group, 1.4%; $P = .88$) or at the 1-month follow-up (TA group, 3.6% vs non-TA group, 3.9%; $P = .9$) (figure 4).

DISCUSSION

The main findings of this study are: a) TA is frequently used during pPCI (40.3%), mainly as an initial strategy, with significant differences between the different centers; b) A higher initial TIMI-thrombus grade is the most important predictor for the use of TA; c) TA has a high technical success rate, leading to a significant reduction of the thrombus burden and an improvement of TIMI-flow, facilitating pPCI by allowing more frequently direct stenting; d) TA was not associated with higher rates of cerebrovascular events; and e) The TA was not associated with any differences in the occurrence of MACE during acute phase or at the 1-year follow-up.

The present study analyzes the efficacy and safety of selective TA in the real clinical practice. And this is remarkable for 2 reasons: the most important TA studies[4,7,9] assessed the routine use of this technique. Performing routine TAs during pPCI is not the standard in clinical practice, where TA is selectively performed in scenarios where it is expected that this technique will be more effective. Also, some of these trials may have a non-negligible sample selection bias[6,7,9] that may not reflect the actual clinical practice. In our study, the average rate of TA use was around 40.3%. This rate was similar in other nationwide registries.[15] The most important predictor for the use of TA was a high initial thrombotic burden.

A key finding of this registry is that TA is effective when it comes to facilitating the pPCI. Unlike other studies, we specifically described thrombotic burden reductions and coronary flow improvements after the TA which, in our opinion, are the most representative effects of the utility of this technique. TA success was achieved in 93.8% of the cases. Since this was not a randomized study, it is not easy to analyze the reduction of no-reflow or the rate of distal embolization with TA. This is so because while trying to reflect real practice TA was used at the discretion of the operator and consequently the TA-group had a higher initial thrombus grade (approximately twice as much) compared to the non-TA group (table 2). It is precisely in patients with a higher thrombotic burden where we can expect higher no-reflow or distal embolization rates. However, probably due to this initial TA that allowed significant reductions of the TIMI-thrombus grade, there were no differences in the rates of no-reflow or distal embolization with the non-TA group that had a lower initial thrombus grade.

Also, patients who underwent TA as an initial strategy had a more than two-fold increase in the rate of direct-stenting compared to those treated conventionally. Beyond the potential economic benefit, direct stenting could be associated with clinical benefits.[21]

As our study suggests it is possible that the greatest benefit of TA occurs when performed selectively in patients with a higher thrombotic burden. This idea has been suggested in a meta-analysis including the most important TA studies.[3] These results must be interpreted with caution since a significant percentage of patients who underwent routine TA did not have significant thrombotic loads. In the TAPAS trial, angiographic thrombi were not observed

in 51.4% of cases,[4] which also happened in 35% of patients included in the TASTE trial.[7] The TOTAL study showed that in up to 90% of patients the thrombus scale ≥ 3.[9] Nevertheless, the thrombotic burden was assessed before crossing the culprit lesion with the coronary guidewire which probably lead to overestimating the TIMI-thrombus scale[18] as 65% of patients showed TIMI 0 flow. In our own opinion this limits the conclusions drawn from this trial and subsequent subanalyses.[22]

Beyond the effectiveness of TA, our results support the safety of the technique. The TOTAL study[9] described a slight increase in the rate of TA-related strokes. This fact was not consistent with previous trials and ignited and ongoing controversy that still goes on. In our study, there were no significant differences in the stroke rate between both groups. These data are similar to those from the TASTE[7,8] or INFUSE-AMI trial.[23] On this regard, TA-related strokes would initially be of ischemic nature, appear during the procedure, and would be evident during the first 24 hours. It is unlikely that hemorrhagic or ischemic strokes occurring > 24 hours after the procedure would have anything to do with this technique.[24] In the TOTAL trial,[9] the rate of ischemic strokes during the first 48 hours after the procedure was low and did not significantly differ between arms. Also, in the on-treatment and per-protocol analyses the rate of all-cause stroke at 30 days was no significantly different between groups.

Similar to the TA trials most recently published,[7,9] we did not find a significant prognostic benefit associated with TA during the acute phase or at the 1-year follow-up. Despite having repeatedly demonstrated that TA improves reperfusion parameters,[4,9] the lack of an association with any prognostic benefits somehow makes sense. First because it is unlikely that a technical tool, designed to facilitate pPCI, can reduce mortality. Secondly, because the low rate of events described (reported in our cohort as in previous studies) make it difficult for an individual therapy to prove significant reductions of mortality rate. Finally, because mortality depends on many more factors that were not analyzed in our study or in these trials.[25]

Limitations

This is a retrospective, observational study, with the natural limitations of this design. The exclusion of patients who had a cardiac arrest or underwent bailout PCIs may be indicative of selection bias.

The quantification of thrombotic load according to the previously validated TIMI-thrombus scale may not be accurate due to the design of this tool. We have maintained this classification because it is the most widely used in this setting. However, the degree of thrombus before the TA was assessed after crossing the culprit lesion with the angioplasty guidewire in order to reduce the number of cases with initial TIMI-flow = 0 in which it is impossible to assess the initial TIMI-thrombus grade.

We decided to define TA success when achieving improvements of TIMI-flow grade ≥ 1 or reductions of TIMI-thrombus scale grades ≥ 1 without any immediate complications associated with the technique. However, other parameters of microvascular reperfusion such as the ST-segment elevation resolution or the myocardial blush grade were not measured.

The angiographic coronary flow data are not described after the alternative strategy to perform TA in the non-TA group. This can be a limitation since the immediate results cannot be compared to the TA group. Also, the angiographic analysis was not conducted by an independent core-lab that would have added validity to the results.

The high heterogeneity of the operators involved may have influenced the results seen due to their individual preferences in relation to TA. However, we believe that this may play a favorable role in the external validation of our findings.

CONCLUSIONS

Despite being recently discredited, TA is frequently used in current clinical practice during the pPCI, basically as an initial strategy. A higher initial TIMI-thrombus grade is the most important predictor for the use of selective TA. Selective TA facilitate pPCI by reducing thrombotic burden and improving coronary flow. Selective TA is not associated with with a reduction of MACE neither during the acute phase or at the 1-year follow-up. There is no association of TA with a higher stroke rate.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

WHAT IS KNOWN ABOUT THE TOPIC?

- Following the results of several randomized trials, routine TA has remained out of the spotlight after not improving the prognosis of patients with ST-segment elevation myocardial infarction and even increasing their complications.
- Although selective TA may reflect better common practice, we do not have enough data on its implementation.

WHAT DOES THIS STUDY ADD?

- Selective TA is still frequently used in current clinical practice during pPCI, mainly as an initial strategy.
- A higher initial TIMI-thrombus grade is the most important predictor for the use of TA.
- It facilitates pPCI by reducing thrombotic burden and improving coronary flow.
- Selective TA is not associated with a reduction of MACE at 1-year follow-up. There is no association between TA and a higher stroke rate.

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Review article

Update on percutaneous coronary intervention in the management of chronic total occlusions

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ABSTRACT

The management of chronic total coronary occlusions (CTO) is still today one of the greatest challenges of cardiology. The complexity of the angioplasty procedure of a CTO added to its controversial clinical benefits has generated certain skepticism in the community of cardiologists when developing CTO intervention programs at the catheterization laboratory. However, the evidence from observational studies indicates that if the intervention is successful it can significantly increase the patient's quality of life, improve the left ventricular function, reduce the need for a subsequent coronary artery bypass graft, and possibly improve survival. Several factors must be taken into consideration in the selection of patients elective for an intervention, including the extent of ischemia surrounding the occlusion, the myocardial viability, the coronary location of the CTO, and the chances of being successful with the procedure. This review provides a general description of the anatomy and histopathology of the CTOs, the evidence surrounding the clinical benefit of these procedures, the use of useful scoring systems to assess more objectively the probability of success, and a summary of the latest techniques available today to perform this procedure.

Keywords: Coronary artery disease. Chronic total coronary occlusion. Percutaneous coronary intervention. Stable ischemic heart disease.

Actualización del intervencionismo percutáneo en la oclusión total crónica

RESUMEN

El tratamiento de la oclusión total coronaria (OTC) sigue siendo uno de los grandes retos de la cardiología. La complejidad del procedimiento de angioplastia de una OTC, unida a cierta controversia en cuanto al beneficio clínico, han generado resistencias en la comunidad de cardiólogos para desarrollar programas de intervención coronaria en los laboratorios de hemodinámica. Sin embargo, la evidencia proveniente de estudios observacionales indica que el intervencionismo con éxito puede aumentar de manera significativa la calidad de vida del paciente, mejorar la función ventricular izquierda, reducir la necesidad de una posterior cirugía y, posiblemente, prolongar la supervivencia. Deben tenerse en cuenta varios factores en la selección de los pacientes para el intervencionismo, como la extensión de la isquemia que rodea a la oclusión, la viabilidad miocárdica, la ubicación coronaria de la OTC y la probabilidad de éxito del procedimiento. Esta revisión proporciona una descripción general de la anatomía y de la histopatología de las OTC, la evidencia sobre el beneficio clínico del intervencionismo, el uso de sistemas de puntuación que pueden ser útiles para evaluar de forma más objetiva la probabilidad de éxito, y un resumen de las técnicas actuales para la realización del procedimiento.

Palabras clave: Enfermedad arterial coronaria. Oclusión total crónica. Intervención coronaria percutánea. Cardiopatía isquémica estable.

Abbreviations

CAD: coronary artery disease. **CTO:** chronic total coronary occlusion. **DLM:** dual lumen micro-catheter. **IVUS:** intravascular ultrasound. **MACE:** major adverse cardiovascular event. **PCI:** percutaneous coronary intervention.

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INTRODUCTION

Treating patients with chronic total coronary occlusions (CTO) is one of the toughest challenges in the management of coronary artery disease (CAD). Nowadays, the indications for prescribing percutaneous coronary interventions (PCI) in patients with CTOs and the possible impact of revascularization on final prognosis are controversial. No wonder that many interventional cardiologists try to avoid these potentially expensive and long procedures with a significant exposure to radiation. The complexity and lack of familiarity with the new devices and techniques often leads to failed attempts and abandoning this intervention prematurely. However, there are techniques currently available with high rates of success.

That is why in this review we urge the community of interventional cardiologists to promote clinical excellence by teaching coronary disocclusion through learning curves and promoting research and technological advances in this field.[1]

DEFINITION, EPIDEMIOLOGY, AND CLINICAL SIGNS

Definition

The current consensus establishes the definition of a true CTO as the presence of TIMI (Thrombolysis In Myocardial Infarction) grade-0 flow in the occluded segment with an estimate duration of over 3 months. The duration of an occlusion is difficult to determine with absolute certainty. That is why it is often established after carefully assessing the clinical history and the heart disease symptoms over the previous 3 months.

An important aspect is the process of neovascularization that happens all through the occlusive lesion and on the vessel wall. Neoangiogenesis grows with the time of occlusion. In CTO durations < 1 year, the formation of new blood capillaries is predominantly adventitial. In CTO durations > 1 year, there is usually a rich network of new blood vessels running through the adventitial layer of the vessel wall towards the intima forming the bridging collaterals. The process of new vascular formation can promote the formation of relatively long capillary blood vessels called microchannels that run through the body of the occlusion partially recanalizing the distal lumen (figure 1A). Their presence is important because an angioplasty guidewire with hydrophilic coating can run through them and reach the distal lumen. Also, microchannels can connect to the vasa vasorum of the adventitial layer creating an extraluminal collateral pathway to the distal lumen with the typical appearance of caput medusae (figure 1B). This is typical of complex CTOs of long duration. In general, the toughness and density of the fibrocalcific material and the complexity of the CTO are related to the duration of the occlusion.[2]

Another key anatomic component of CTOs is collateral circulation that supplies blood flow to the occluded territory. It can be epicardial or intramyocardial and it originates at the homolateral or contralateral coronary territory. When it is present before the CTO occurs, it supplies enough blood flow to maintain the viability of the myocardium irrigated by the occluded artery. However, this is often insufficient to prevent the appearance of exercise-induced angina pectoris or ischemia. Collateral circulation does not require myocardial viability to develop. That is why it is important to emphasize that the disocclusion of a CTO should not be based on the presence, amount or quality of collateral circulation.[3,4]

Epidemiology

According to data obtained from the HLBI Dynamic Registry[5] between 1997 and 1999, CTOs are more prevalent in the right coronary artery and less prevalent in the circumflex artery. In this series, the percentage of patients who underwent PCIs due to their CTOs was 15.6%. According to data from the EuroCTO Club, in 28 283 patients, 12% of the PCIs were performed on CTOs. The prevalence of the CTOs reported ranges from 16% to 50% in patients with clinically significant CAD but in general it is around 18% to 20%.[6,7]

Clinical signs

Patients with CTOs have a more unfavorable profile of cardiovascular risk compared to those without CTOs.[6] The clinical presentation of a CTO is varied: stable angina, silent ischemia, ischemia-related heart failure, early-onset angina or as an incidental finding in patients undergoing primary PCIs due to acute occlusion in a different culprit vessel.

In stable CAD, the goal of revascularizing a CTO is to improve symptoms and prognosis by assessing the presence of symptoms, viability or ischemia. For this reason, in asymptomatic patients with CTOs, the ischemic load should be assessed before considering a PCI.[8] In patients with confirmed prior myocardial infarction and segmental contraction abnormalities, it is advisable to conduct a non-invasive study before the treatment to establish

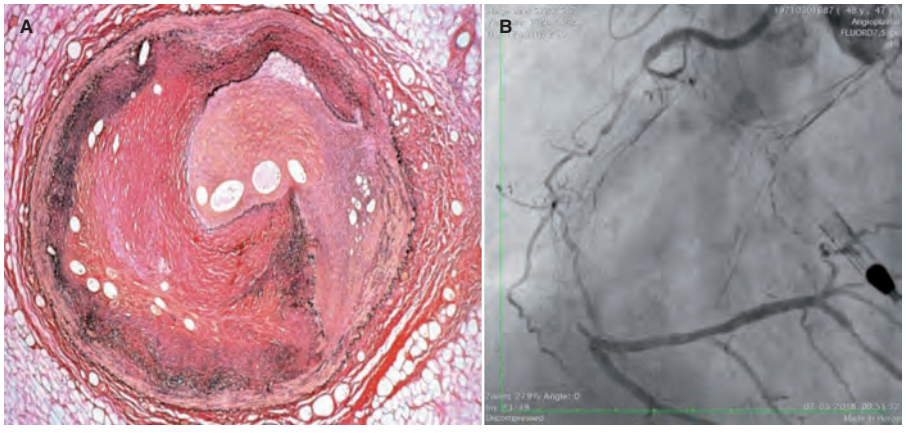

Figure 1. A: presence of microchannels inside the vessel lumen surrounded by significant fibrosis. **B:** typical caput medusae extraluminal neovascularization.

the presence of ischemia or viability in the territory of the occluded artery.

BENEFIT OF CORONARY INTERVENTIONS WHEN TREATING CHRONIC TOTAL CORONARY OCCLUSIONS

Several studies have documented that the successful treatment of a CTO leads to the clinical improvement of angina pectoris[9], the normalization of functional tests, an improved left ventricular function, and less coronary revascularization surgeries.[10,11] It has also been reported that the recanalization of a CTO contributes to the electric stabilization of the myocardial segment and improves clinical tolerance to future coronary events in the non-occluded territory.[12]

Yet despite this, many patients with single-vessel CAD chronically occluded are only treated with drugs, regardless of the severity of the symptoms and level of ischemia. The presence of a CTO in patients with multivessel disease is a classic indication for surgery. In the randomized SYNTAX trial[13] (surgery versus PCI in multivessel disease), 27% of the patients of each group had at least 1 CTO and in general they were more complex patients and with higher SYNTAX scores. Occluded vessels were revascularized in only 68.1% of the patients randomized to surgery, and the rate of success of percutaneous revascularization in patients undergoing PCI was 49.4%. This lead to complete revascularization in 49.6% of surgical cases and 35.8% of PCI cases. This means that the strongest reason for having a SYNTAX score > 32 —the presence of a CTO— is not necessarily indicative that this CTO should be surgically revascularized as it actually happened in 31.9% of the cases. Patients with incomplete revascularizations had a significantly larger number of the composite endpoints of death, infarction or stroke.

Regarding the benefit of interventional procedures, the clinical evidence from randomized clinical trials and observational studies varies. Overall, randomized trials have limitations such as slow recruitment rates that give rise to insufficient and inadequately powered samples with a high rate of crossing among the study groups. Similarly, patients are subject to selection bias since it is unacceptable to randomize patients with a great ischemic load who may benefit from interventional procedures. For this reason, the most favorable data on interventional procedures come from observational studies that have become an essential tool in the overall assessment of the benefits of revascularization.

Randomized clinical trials

The EuroCTO trial proved that interventional procedures on a CTO improve health, the frequency of angina, the level of physical limitations, and the quality of life of patients with stable angina.[14]

However, the EXPLORE trial[15] showed no differences in the left ventricular function in patients with ST-segment elevation myocardial infarction undergoing early interventional procedures of their CTOs compared to the optimal medical treatment. The DECISION-CTO[16] showed similar rates of death, infarction, stroke or target lesion revascularization at 3 years in groups undergoing interventional procedures and receiving drugs in patients with acute coronary syndrome or stable angina.[15,16]

The recently published REVASC trial[17] did not show any improvement either in the regional myocardial function at 6 months assessed though MRI in the CTOs of patients consecutively treated with PCI compared to the optimal medical treatment. Nevertheless, the annual rate of major adverse cardiovascular events (MACE) was significantly lower in the PCI group.[17]

Table 1 shows the results of randomized clinical trials on most relevant CTOs.

Observational studies

Several observational studies have compared the results of PCI and medical treatment. Tomasello et al.[18] examined the long-term results of 1777 patients with CTOs from the Italian CTO registry based on the treatment strategy: PCI (43.7%), medical treatment (46.5%) or surgery (9.8%). At the 1-year follow-up, medical treatment was associated with a higher rate of MACE (7.6% vs 1.7%; $P < .001$),

Table 1. Results of randomized clinical trials on the most relevant chronic total coronary occlusions

	DECISION-CTO[16]	EuroCTO[14]	EXPLORE[15]	REVASC[17]
Patients	834	407	304	205
Study period	2010-2016	2012-2015	2007-2015	2007-2015
Comparison	CTO PCI vs OMT	CTO PCI vs OMT	CTO PCI vs OMT in STEMI	CTO PCI vs OMT
Primary endpoint	Death, infarction, stroke, TVR	Clinical state and quality of life	LVEF, LVEDV	Segmental thickening CTO territory through MRI. MACE: NS
Rate of crossing (%)	18.1	7.3		
J-CTO score	2.2 ± 1.2	1.82 ± 1.07	2 ± 1	2 ± 1
Rate of success (%)	91.1	86.3	73	99
Follow-up	3 years	12 months	4 months	12 months
MACE (%)	19.0 (OMT) vs 21.4 (PCI); P = NS	6.7 (OMT) vs 5.2 (PCI); P = NS	5.4 (OMT) vs 2.6 (PCI); P = NS	16.3 (OMT) vs 5.9 (PCI); P = .02
Conclusion	No improvement in primary endpoint	Improvement in clinical signs and quality of life	No improvement in LVEF or LVEDV	No improvement in segmental thickening

CTO, chronic total coronary occlusions; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular event; MRI, magnetic resonance imaging; NS, not significant; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TVR, target vessel revascularization.

cardiovascular mortality (4.4% vs 1.5%; $P = .002$), acute myocardial infarction (2.9% vs 1.1%), and rehospitalization (4.4% vs 2.3%; $P = .04$). Jang et al.[19] compared the long-term results of different treatment strategies in 738 patients with, at least, 1 occlusive lesion and well-developed collaterals. The 42-month mean follow-up showed that the incidence of cardiovascular mortality (hazard ratio [HR], 0.27; 95% confidence interval [95%CI], 0.09-0.80; $P = .029$) and MACE (HR, 0.44; 95%CI, 0.23-0.82; $P = .01$) in patients who underwent coronary revascularizations was lower.

Several small observational studies have explored the possible effect the PCI has on CTOs through several secondary endpoints like depression, the capacity of performing physical activities, and the risk of ventricular arrhythmias with favorable results for the PCI.[12,20,21]

Similarly, other studies have compared successfully recanalized CTOs with failed ones. A meta-analysis of 25 studies compared successful (71%) with failed procedures (29%) performed from 1990 through 2014 in 28 486 patients. The 3.11-year mean follow-up showed that success was associated with a lower mortality rate (odds ratio [OR], 0.52; 95%CI, 0.43-0.63), less residual angina (OR, 0.38; 95%CI, 0.24-0.60), lower risk of stroke (OR, 0.72; 95%CI, 0.60-0.88), and less need for further coronary revascularization surgeries (OR, 0.18; 95%CI, 0.14-0.22).[22] Tsai et al.[23] examined the interventional attempts on the CTOs of 2394 patients from 79 centers between 2007 and 2013. The success of the PCI was associated with a lower risk-adjusted mortality rate and referral to coronary revascularization at 2 years.

The OPEN CTO registry[24] used the Seattle Angina Questionnaire in 1000 consecutive patients undergoing a hybrid strategy. According to the questionnaire, at the 1-month follow-up the quality of life improved (from 49.4 ± 0.9 to 75.0 ± 0.7; $P < .01$) with a simultaneous reduction of symptoms.

It should be mentioned that the location of the CTO in the coronary tree can be important for patient's survival. In a study of 2608 patients, the PCI of the CTO benefited the survival of patients with occlusions in their anterior descending artery only (88.9% vs 80.2%; $P < .001$).[25]

Lastly, a meta-analysis that studied these 4 randomized trials and 3 observational studies found no differences in the primary composite endpoint studied (cardiovascular mortality, myocardial infarction and coronary reinterventions). The independent analysis of each component showed that the interventional procedure had better results on cardiovascular mortality (OR, 0.52; 95%CI, 0.33-0.81; $P < .01$) basically at the expense of the favorable results of observational studies.[26]

FACTORS IMPACTING SUCCESS

Added to clinical factors such as the extent of ischemia surrounding the occlusion, myocardial viability, and the location of the CTO, the probability of success of the procedure when recanalizing an occlusion should also be taken into consideration.

Prerequisites to perform interventional procedures on CTOs

To optimize the chances of success and overcome the differences in the rates of success achieved by different registries (54% to 80%) and experienced centers (85% to 90%), new machines and techniques should probably be developed, as well as training, continuing medical education programs, and live-case demonstrations.[27] The best case-scenario would be that each center training interventional cardiologists implemented CTO disocclusion programs to provide enough theoretical knowledge for the right selection of patients and CTOs; as well as having practical experience to increase the chances of success and avoid the most common mistakes.[28]

Predictors of success and failure

Numerous predictors of success and failure have been reported in the recanalization of CTOs although, in general, there is wide consensus among the studies.

A meta-analysis reviewed the angiographic and demographic predictors of clinical and technical success.[29] Among the demographic variables, it has been shown that prior infarctions and PCIs, coronary revascularization surgeries, strokes, and peripheral vascular disease are associated with a reduction of at least 20% of success probability. The angiographic variables associated with lower chances of success were the presence of bridging collaterals, moderate-to-severe calcifications, vessel angulations > 45º, vessel tortuosity, presence of blunt stumps, ostial occlusive lesions, and CTOs in vessels other than the anterior descending artery.[29]

Scoring systems in the interventional procedures of a CTO

Over the last few years numerous scoring systems have been developed to predict the chances of technical success in disocclusion procedures.

Scoring systems are considered very useful for several reasons: *a)* they quantify the chances of success and complications; *b)* they optimize the selection of cases; *c)* they study and plan how the CTO should be accessed; and *d)* they contribute to standardize the complexity of the lesions and compare the results.[30]

The J-CTO scoring system[31] assigns 1 point to every independent predictor of crossing the occlusive lesion within 30 minutes after starting the procedure. The total value was used to develop a model to categorize all lesions into 4 groups depending on the difficulty of the procedure: easy (score = 0), intermediate (score = 1), difficult (score = 2) or extremely difficult (score = 3-5). In our own opinion, high J-CTO scores do not mean that we should not perform an interventional procedure but that the patient should be referred to an experienced center for revascularization surgery.[31]

The ORA scoring system is more appropriate for experienced interventional cardiologists used to hybrid and retrograde procedures.[32] The CL[33] is more suitable for operators who use the antegrade access only, and the PROGRESS CTO system[34] is suitable for hybrid procedures of disocclusion.

Table 2 shows some of the most common scoring systems used today.

Diagnostic study of a CTO

The rate of success is associated with a good diagnostic study to determine the vessel architecture in the occlusion region. It is important to locate the occlusion proximal edge and see if there are microchannels or proximity collaterals, but we do not need to use more than 15 images per second; however, at times it is necessary to increase the volume and pressure of contrast injection. The catheters should be perfectly placed inside the coronary ostia to avoid losing contrast through the aorta. Contralateral injections are also crucial (sometimes collateral circulation is homolateral) to see the occlusion final edge, the anatomy of the

Table 2. Most common scoring systems used today

Variable	J-CTO[31]	ORA[32]	CL[33]	PROGRESS[34]
No. of cases	494	1073	1657	781
Primary endpoint	Guidewire crossing < 30 min	Technical success	Technical success	Technical success
Age, years	–	+ (≥ 75)	–	–
Prior coronary revascularization surgery	–	–	+	–
Prior failure	+	–	–	–
Proximal capsule	+ (blunt)	+ (ostial)	+ (blunt)	+ (ambiguous)
Tortuosity	+ (> 45° intralesional)	–	–	+ (moderate/proximal)
Calcification	+	–	+ (serious)	–
Lesion length	+ (≥ 20 mm)	–	+ (≥ 20 mm)	–
Target vessel	–	–	+ (if target vessel different from anterior descending artery)	+ (if the target vessel is the circumflex artery)
Collaterals	–	+ (Rentrop < 2)	–	+ (non-accessible)
Other	–	–	Prior infarction	–

distal bed, make correct assessments of the collaterals, and determine whether the retrograde interventional procedure is possible.

Table 3 shows the basic projections for the right assessment of occluded segments (estimate values).

There is a special situation when the anterior descending artery receives collateral circulation through Viuessens' arterial ring[35] where the right conus artery may anastomose with the left conus artery that exits the proximal or medial segment of the anterior descending artery. There are times when this conus artery exits an independent ostium of the right coronary artery and needs to be cannulated using a mammary artery catheter with a specifically curved tip or a hockey stick design. It is advisable to perform a coronary CT scan to evaluate the architecture of the occlusion in patients undergoing aortocoronary revascularization surgery, with high J-CTO scores or aorto-ostial occlusions.

TECHNIQUE AND METHOD OF INTERVENTIONAL PROCEDURE

General aspects

Although there is a tendency to perform minimalist interventional procedures, when the values of the scoring scales are high it is recommended to following these patterns:

- *Antegrade access.* It is advisable to use 8-Fr guide catheters preferably with maximum internal lumen. Extra back up curves should be used in the left coronary artery. In right coronary artery occlusions, the 8-Fr Amplatz Left 1 guidewire with side holes should be used. These catheters should be used with both hands with a Teflon coated 0.035-8 in-guidewire inside to avoid sudden moves and prevent ostial dissections. Depending on the anatomy of the left coronary artery, there are times when a 3.5 Judkins Left catheter should be used. When treating the right coronary artery, a 3.5-4 multipurpose Judkins Left (vertical exits) or an Amplatz Left 2 (elongated aortas) catheter should be used.

- *Retrograde access.* When only injecting contrast, radial access with a 5-Fr or 6-Fr guide catheter can be used. It is advisable to use a guide catheter to insert an angioplasty guidewire inside the coronary artery and stabilize the catheter; this improves the quality of contrast injections and prevents problems due to possible ostial dissections. If collaterals are eligible for an intervention, the 7-Fr or 8-Fr extra back-up guide catheters can be used in the left coronary artery and the Amplatz Left 1 in the right coronary artery. Contralateral guide catheters should not have lateral holes to avoid losing contrast towards the aorta.

Hybrid algorithm and Asia-Pacific algorithm

Until the arrival of the hybrid algorithm[36] there were no defined guidelines on how to access a CTO. This algorithm promotes a dual coronary injection for careful anatomy assessment and to determine the best strategy to treat the CTO by using the antegrade and retrograde accesses, dissection, and re-entry. When the level of difficulty of the CTO is low, the rate of success is high with the antegrade access. With more difficult anatomies, conventional

Table 3. Best projections to see different occluded segments in coronary arteries

Artery	Anterior descending	Anterior descending	Circumflex	Right coronary	Right coronary
Segment	Middle	Ostium	Proximal-medial	Proximal-medial	Distal
Projection	AP 0°, cranial 30°-40°	LAO 30°, caudate 30°	AP 0°, caudate 30°-40°	LAO 90°	AP 0°, cranial 30°-40°, LAO 30°, cranial 30°

AP, anteroposterior; LAO, left anterior oblique.

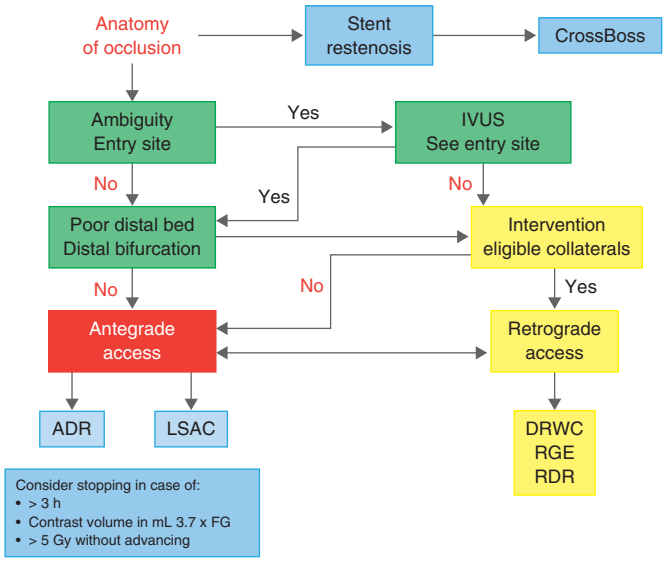

Figure 2. Modified algorithm (Asia-Pacific) to approach occlusions. ADR, antegrade dissection/re-entry; DRWC, direct retrograde wire crossing; GF, glomerular filtration; IVUS, intravascular ultrasound; LSAC, limited subintimal antegrade access; RDR, retrograde dissection/re-entry; RGE, retrograde guidewire escalation.

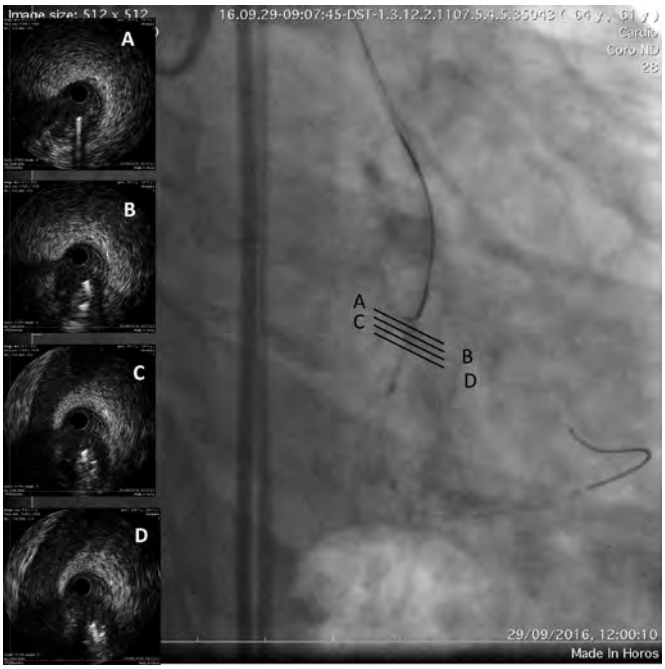

Figure 3. The occluded vessel is at the 6 o'clock position approximately (**A**) as the guidewire is moving towards the occlusion (**B**, **C** and **D**).

techniques have a lower rate of success and it is necessary to use the retrograde access or specific techniques of dissection and re-entry. This algorithm assesses the presence of ambiguous stumps, lengths > 20 mm, and the quality of the distal bed to make decisions about the access. The rate of success of this algorithm is 87%; antegrade access, 52%; retrograde access, 27%; and dissection and re-entry, 21%.

The Asia-Pacific algorithm[37] integrates all techniques of coronary interventions on CTOs and establishes the strategy based on the anatomical findings. It also assesses the need to terminate a procedure (figure 2).

The Asia-Pacific algorithm takes into consideration the vessel architecture in the occlusion region; that is why a good bilateral injection is required to see the coronary arteries, even a coronary CT scan when necessary. Three basic parameters of the coronary anatomy are established (lengths > 20 mm do not determine the approach):

- The ambiguity of the entry site.
- The characteristics of the distal bed with respect to the occlusion site, assessing the quality of the distal bed and whether the CTO ends in a large bifurcation.
- The presence of collaterals suitable for the retrograde access.

This algorithm also takes into consideration other factors like vessel tortuosity in the occlusion site, calcification, prior failed attempts, possible microchannels, and regions of reference (stents, calcium, contrast) to decide the strategy.

Antegrade access

Intravascular ultrasound

The intravascular ultrasound (IVUS) is useful when the entry site is ambiguous and there are no references to position the guidewire.

A lateral branch is required to place the guidewire and IVUS. In these cases, the Slipstream technique[38] is very useful. It consists in placing a dual-lumen micro-catheter (DLM) behind the IVUS above the branch guidewire. This increases tremendously the strength exerted with the guidewire that exits the DML lateral port providing better torque and grip (figure 3). The IVUS shows where the occlusion of the vessel is in order to navigate the guidewire (of high-gram, directivity, and torque-response) towards that point (figure 4).

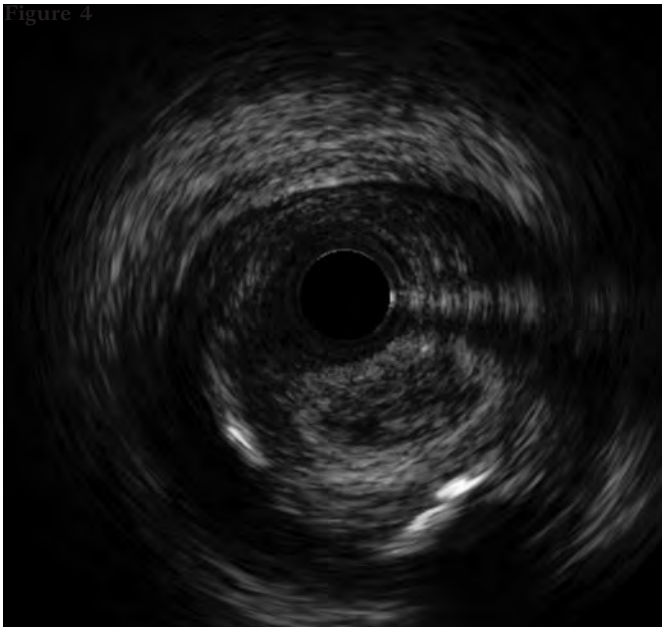

Figure 4. The catheter of intravascular ultrasound in the subintimal space is between the 9 and 12 o'clock positions and true lumen between the 3 and 9 o'clock positions.

Table 4. Move and direction of angioplasty guidewires

Artery	Clockwise	Counterclockwise
Left main coronary artery	Towards the circumflex artery	Towards the anterior descending artery
Anterior descending artery	Towards diagonal branches	Towards septal branches
Circumflex artery	Towards the main circumflex artery	Towards marginal branches
Right coronary artery	Towards the right coronary and posterolateral branches	Towards the acute marginal and posterior descending branches

Guidewire escalation

It is essential to use a microcatheter that navigates well. It should be flexible enough and it should not condition the direction of the guidewire inside the vessel architecture.

Chosing the guidewire is at the operator's discretion. It is advisable to check the occlusion proximal edge since the degree of toughness of the plaque is unknown and can be variable. Starting with high-gram or high penetration power or polymer-coated guidewires can make us lose perception of the true characteristics of the CTO. The main problem is when the guidewire advances towards the subintimal space limiting the possibilities of successful recanalization; this happens because the plaque is tougher than the guidewire, which conditions the selection of higher-gram guidewires.

Dual-lumen microcatheters

The actual way of re-entry from the subintimal space to the distal true lumen is using a DLM. If a guidewire advances towards the subintimal space it is essential to stop moving it and not inject contrast to avoid the formation of hematomas that would limit distal re-entry. It should be used in such a way to allow the insertion of another higher-gram guidewire through the lateral port to penetrate the occlusion, increase the strength of the guidewire, and reach the distal bed.

Like Tanaka et al.[39] explain, this technique requires the 3D control of the guidewire inside the vessel architecture through specific turns depending on the arterial segment we are treating. The 90°-180° rotation turns are shown on table 4.

Dissection and re-entry with specific devices

Inside the hybrid algorithm[36] when the CTOs show ambiguous stumps, lengths > 20 mm, and it is impossible to use the retrograde access, the dissection/re-entry technique that can be used. It is done using a specific device to achieve an easy and effective re-entry of subintimal space into the true lumen using the Stingray LP balloon with its specific guidewire (Boston Scientific, Nattick, Massachusetts, United States).

Until recently, this dissection/re-entry technique was conventionally performed using the CrossBoss and Stingray catheters. Nowadays there are times than the CrossBoss catheter is not even necessary. The 135-cm Corsair (ASAHI Intec, Nagoya, Japan) or Turnpike (Teleflex Inc, Wayne, PA, United States) catheters can be used to advance the guidewire with the microcatheter to a point where it cannot advance anymore. Once it has reached this point in the subintimal position, it is changed for the Stingray LP balloon that is inflated at 4 atm in the subintimal space. Through the 2 lateral ports situated at 180° from one another, the distal true lumen is re-entered with a rigid guidewire (Stingray wire, Hornet 14, Confianza Pro 12) using the stick and swap or multiple fenestration techniques. Then distal canalization occurs using a polymeric Pilot 200 (Abbott Santa Clara, CA, United States) or Gladius Mongo guidewire (ASAHI Intecc, Nagoya, Japan).

Retrograde access

Retrograde access depends on the distal region histological characteristics since the degree of toughness is lower compared to the proximal region[40] because it is not exposed to the system direct arterial pressure.

Retrograde access routes

The native collateral channels or coronary artery bypass grafting are the access routes. Collateral branches are located in the septal, epicardial or intramyocardial regions. The most important limitation when crossing them is vessel tortuosity. A collateral branch can be approached if it can be crossed without causing perforations. Werner's classification[41] is the most widely used today: CC0, no continuous connection between donor and receiver; CC1, threadlike continuous connections (estimate diameter of 0.3 mm); and CC2, side-branch like connection along the entire route (estimate diameter of 0.4 mm).

There are added risks when crossing a collateral: tears, dissections, and occlusions. However, the septal branches (usually more numerous) have the lowest risk and are used 68% of the times;[42] if they tear, the tear can be contained or fistulized to the ventricular cavity. There are invisible branches that can be easily crossed. The best projection to study them is the right anterior oblique branch at 0° or 30° of cranial angulation. Usually the septal branches go from the anterior descending to the posterior descending artery. It is easier to cross from the anterior descending to the posterior descending artery using the septal branch exit angulation. Sometimes very proximal septal branches connect to the posterolateral artery, and the distal ones connect to the branches that run through the right ventricular free wall.

Epicardial branches connect the anterior descending to the posterior descending artery at apical level, from the posterolateral to the obtuse marginal artery or from the obtuse marginal to the diagonal branches. Crossing them brings the added risk of tear with pericardial tamponade as it happens with the collaterals of the atrioventricular region.

Intramyocardial collaterals are found between the obtuse marginal and the posterolateral artery, and between the obtuse marginal and the posterior descending artery.

The preferred catheters are the Corsair, Turnpike, Mamba Flex (Boston Scientific Natick, Massachusetts, United States) or the Teleport (OrbusNeich, Hong Kong) built with several internal meshes to facilitate fracture-free rotations. The guidewire of

choice to cross a collateral is the SION or SION black (ASAHI). In cases of major collateral tortuosity, the guidewire of choice is the SUOH03 (ASAHI).

Guidewire escalation

Retrograde access allows advancing towards the CTO with the same guidewire that passed the collateral except if it was with a SUOH03. Once the CTO has been reached, it is possible to study the toughness of the plaque and establish guidewire escalation.[41] In 40% of the cases direct recanalization is possible with guidewire escalation: sometimes using a more rigid guidewire for penetration control or quick rotations, other times using polymeric guidewires to easily glide though the plaque.

Dissection and re-entry: knuckle, R-CART

In 60% of the cases when direct recanalization is not possible, interventional procedures are required to connect proximal and distal regions.

When vessel architecture is unknown, polymer-coated guidewires with knuckle wiring are required to shorten the occlusion with subintimal advancement. Sometimes the antegrade access is required when the proximal entry site or vessel architecture are unknown. Similarly, in cases of severe calcifications, these polymer-coated guidewires with or without knuckle wiring are advanced inside the occluded segment through the subintimal space by excluding calcium and advancing towards the proximal region. If one of the guidewires is in dissection and cannot be redirected, a DLM (Sasuke, ASAHI) can be used through the retrograde access to canalize a different region of the occluded segment.

When the guidewires cannot be connected, the R-CART (reverse controlled antegrade and retrograde subintimal tracking) is necessary.[42] First, it is advisable to use this technique with IVUS through the antegrade access to see the position of the antegrade guidewire and the size of the balloon that will be used for antegrade dilatation. The antegrade segment is dilated with a balloon and the retrograde guidewire is oriented towards it; when it is near, the balloon is deflated to enter the dilated space through the balloon to connect both lumens. Using an extension of the guide catheter like the Trapliner balloon (Teleflex) may help. When both spaces are connected through interplaque or subintimal passage, a 300 cm-guidewire is externalized to end the procedure. After finishing the intervention, possible damage to the donor main vessel (dissection) and collaterals (tear) should be verified.

COMPLICATIONS

The rate of complications is a little higher compared to the general interventional procedure:[42] Q-wave myocardial infarction, 2.5% vs 0.02%; urgent revascularization surgery, 0.1% vs 0.03%; stroke, 0.01% vs 0.04%; death, 0.2%-0.9% vs 0.14%; and perforation, 2%-4.8% vs 0.38%.

The most common extracardiac complications are vascular complications (2%) and contrast-induced nephropathy (3.8%). Radiation-induced lesions may appear weeks or months after catheterization and are often misdiagnosed and misreported in studies.[43]

Coronary cardiac complications are perforations of main, distal or collateral vessels that may lead to cardiac tamponade, donor vessel acute occlusion, dissection, aerial embolization, and device entrapment.

STENTS AND DUAL ANTIPLATELET THERAPY

CTOs are lesions with higher risk of restenosis and thrombosis: they are longer, more calcified, more tortuous, and require longer stents and even overlapping stents. Since the arrival of drug-eluting stents, restenosis, revascularizations, and thrombosis reduced significantly compared to the use of bare metal stents.[44]

The CIBELES study[45] showed that the late loss of everolimus-eluting stents at 9 months was 0.13 ± 0.69 mm promoting better results for this kind of patients. Lee et al.[46] analyzed a consecutive series of 539 CTOs including everolimus-eluting stents (n = 313) and zotarolimus-eluting stents (n = 226), and obtained a composite event rate (death, infarction or target vessel revascularization) of 12.2% at the 3.3-year mean follow-up.

Antiplatelet therapy should not differ from the pattern established by the underlying coronary disease. If the risk of bleeding is low, a 1-year course of dual antiplatelet therapy plus acetylsalicylic acid and clopidrogel should be prescribed.

LINGERING CONTROVERSIES

There is great variability among patients undergoing interventional procedures on their CTOs: with angina, asymptomatic, ventricular dysfunction or positive ischemia detection tests. It is still under discussion how to define objectively in a definitive clinical trial what patients would benefit in terms of event-free survival. Future challenges include to define symptomatology, ischemia, viability for every patient, and to standardize a highly successful interventional technique easily reproducible regardless of the operator. Another important aspect is to determine how the results of the angioplasty actually impact the preservation of microcirculation.

INNOVATIVE TECHNIQUES

Innovation in this field is based on 2 strategies: devices and 3D anatomic reconstruction techniques. The angioplasty guidewire is a key element here. Success will come from a technology using multiple coils and hydrophilic coatings to facilitate tactile sensation, and oriented directivity. There are new devices available that apply energy to the angioplasty guidewires using radiofrequency, with very promising results.

The same way as when driving we turn the steering wheel left and right when a curve is ahead, we could open a coronary artery with specific devices by moving precisely in 3 dimensions inside the vessel architecture to enter and exit the distal lumen quickly and safely. This could be done with software tools added to the angiography and coronary CT scan.

CONCLUSIONS

The evidence available favors performing interventional procedures on CTOs because they clinically improve angina, ventricular function when there is viability, and increase event-free survival. The rate of success of experienced operators is close to 90% with few complications, which benefits all patients. Performing interventional procedures on coronary arteries makes the interventional cardiologist be more prepared to face daily routine interventions and benefits all patients undergoing PCIs.

CONFLICTS OF INTEREST

None reported.

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Debate: Chronic total coronary occlusions. The interventional cardiologist perspective

A debate: Oclusión coronaria total crónica. Perspectiva del intervencionista

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Question: Do we have enough evidence to be able to say that the coronary recanalization of a chronic total coronary occlusion (CTO) improves the prognosis of patients?

Answer: I would say so. I believe it is hard to have well-designed, randomized clinical trials with large populations of patients and long follow-up periods on this issue comparing the 3 possible strategies of treatment (drugs, surgery, and percutaneous coronary interventions) which, by the way, are the prerequisites to show some mortality net benefit in this group of patients. Also, the results from the procedures performed in the different groups are not comparable whatsoever.

On the other hand, if we look at the registries already published and presented in congresses over the last few years (3-4 years), we will see that only those with long follow-up periods are positive. Usually, the revascularization of a CTO has no implications in the rate of infarction at follow-up, yet the overall and cardiac mortality rate of non-revascularized patients compared to revascularized patients (both percutaneously and using surgery) trebles compared to the population of patients with CTO who are on medical treatment.

The only 2 randomized clinical trials ever published that compare the clinical evolution of patients with a CTO based on the treatment received (medical vs interventional) are the EuroCTO[1] and the DECISION-CTO trials.[2] Unfortunately, both were interrupted before reaching the population for which they were designed due to their low patient inclusion rate. Their results are contradictory, unfavorable in the DECISION-CTO and favorable in the EuroCTO trial, but their designs are very different. In the DECISION-CTO trial, patients with multivessel disease received treatment in non-occluded vessels at the interventional cardiologist's criterion; as a matter of fact, 50% of the patients in both groups received treatment with angioplasty of vessels without chronic occlusions. On the other hand, in the EuroCTO trial the non-occluded vessels of patients with multivessel disease were systematically revascularized and then randomized to receive medical treatment or undergo angioplasty for their CTO. Also, in the DECISION-CTO clinical trial there is a high rate of crossing between the different modalities of treatment: 3 days after randomization, 19.6% of patients form the medical treatment arm crossed to the revascularization arm vs 7.3% at 12 months in the EuroCTO trial. In the DECISION-CTO trial, at the 4-year follow-up, no differences were seen between the 2 arms in the following events: death, infarction, stroke, and revascularization (22.3% vs 22.4%; $P = .86$) or in the quality of life test results. Conversely, in the EuroCTO clinical trial the scores measuring the quality of life improved significantly in the invasive treatment arm, and the 12-month adverse events were similar in both arms.

Q.: In what subgroups of patients or situations should we expect to see greater prognostic benefits?

A.: We should focus on higher risk populations that are probably under-represented here.

Diabetics with CTO have a higher incidence of multivessel disease, more calcified blood vessels, and more risk factors compared to non-diabetic patients. Insulin-dependent diabetic patients with renal failure are the subpopulation with the most somber prognosis of all. In all the clinical trials conducted so far, the success rate of the angioplasty in the management of CTO is lower than that of non-diabetic patients. Also, to this day, from the prognostic point of view, surgery is superior to angioplasty, meaning that we should probably be very cautious when indicating an angioplasty for a CTO in these patients.

The subgroup of elderly patients (≥ 75 years) is a particularly frail population with worse left ventricular ejection fraction (LVEF), worse renal function, and a higher incidence of multivessel disease and left main coronary artery disease compared to patients < 75 years. The oldest patients are revascularized less frequently and with a lower success rate, but procedural complications are similar to the ones we find in younger patients. When selecting our patients, we should take into consideration that the

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age, creatinine, and ejection fraction (ACEF) score, high SYNTAX scores, and damage to the left main coronary artery are prognostic factors that we should take into consideration in this population of patients regardless of short-term mortality. We should not forget that, at the 4-year follow-up, the mortality rate of patients ≥ 75 years with CTO doubles that of patients < 75 years with CTO and that, in non-revascularized elderly patients, mortality doubles compared to revascularized patients. So maybe we should take a different approach towards this often-under-represented population.

Even though women with CTO have a higher incidence of risk factors compared to men with CTO and even though they amount to 15% of the studies population, the rates of success and complications between sexes are similar.

Another especially sensitive group is that of patients with CTO and a low LVEF. The angioplasty of the CTO is not accompanied by higher rates of complications or lower rates of success, and the improved prognosis is obvious because even though it is indicated it has proven to improve the LVEF.

Q.: And regarding symptom and functional improvement?

A.: The answer is affirmative in both cases. The studies conducted so far using magnetic resonance imaging allow us to say that the revascularization of a CTO in patients with preserved LVEF is accompanied by significant reductions in the amount of ischemic segments and the corresponding improvement of segmental contractility. There is a positive remodeling of the left ventricle with reduced end-diastolic volume. Also, if the necrotic mass is compared at baseline and at 6 months, we will see that it does not grow any bigger, which shows how safe the procedure of revascularization really is.

If we focus on the most fragile patients of all with the highest possible benefits such as patients with CTO and a LVEF < 40%, the results are more noticeable. Our group published the results of the 6-month follow-up of a group of 29 patients in whom we also found less ischemic segments, better contractility, and a 6 percentage-point improved LVEF (31.3% ± 7.4% vs 37.7 ± 8; $P < .001$) with significant functional repercussion, reduced brain natriuretic peptide levels (323 ± 657 pg/mL [95% confidence interval (95%CI), 60.4-238.2] vs 123 ± 151 pg/dL [95%CI, 40.6 ± 154.5]; $P = .004$), improved heart failure functional classification (New York Heart Association baseline functional class I and II: 72% vs 100%; $P = .004$), and improved angina pectoris (34.4% in baseline situation vs 3.1% at follow-up; $P = .002$).[3]

The greatest contribution of the EuroCTO trial after the 12-month follow-up is showing that there is a significant improvement in the scores used to measure quality of life (Seattle Angina Questionnaire) with a lower frequency of angina (5.23; 95%CI, 1.75-8.71; $P = .003$), better quality of life (6.62; 95%CI, 1.78-11.46; $P = .007$), fewer limitations to do physical activity (81.1; 95%CI, 77.6-100 with angioplasty vs 75.9; 95%CI, 71.3-80.5 with medical treatment; $P = .02$), and a larger number of patients completely asymptomatic in the group treated with angioplasty compared to the group that received medical treatment (71.6% vs 5.8%; $P = .008$).

Q.: What clinical indications does the percutaneous revascularization of a CTO have?

A.: If we follow the recommendations established by the European Society of Cardiology,[4] the revascularization of CTO has a grade IIa indication with a B-level of evidence as long as patients have medical treatment-resistant angina or a well-documented wide ischemic region. As far as I know, these recommendations are not consistent with the routine daily practice.

The requirements to revascularize a CTO should be the same as for the revascularization of significant stenosis, that is, confirmed ischemia, current feasibility, and symptoms. However, regarding the symptoms, at least in my own experience, most patients with CTO also have anginal equivalents, and often complain that they get tired easily and unjustifiably for their age or LVEF; and when they have progressive angina pectoris, most of the times it is due to a developing stenosis in the donor vessel of collateral circulation.

We know that if the underlying myocardium is viable, a CTO behaves functionally like a 99% stenosis. So, I believe that the revascularization of CTO should have the same indications as the revascularization of any other lesion, as long as the procedure is performed with guarantees and by experienced interventional cardiologists.

Q.: What practical recommendations can you share with us to approach the interventional management of CTO with higher levels of success?

A.: The field of CTO is really something special because it requires not only particular skills but also a special attitude. In my personal opinion, all interventional cardiologists who want to deal with CTO should have 2 basic characteristics: patience and perseverance.

Perseverance is key because, even if we are pretty good interventional cardiologists for all other types of lesions, the management of CTO requires a very specific and prolonged learning curve, estimated at around 50 annual cases for a minimum of 3 years to be able to reach an acceptable rate of success. Therefore, it is advisable that not all interventional cardiologists of the same center specialize in the management of CTO because nobody would reach the level of expertise required. A reasonable idea would be to estimate the number of interventional cardiologists based on the number of actual patients who would be treated based on the volume of cases handled by each center.

One can never stress enough something so simple as preparing the cases properly. It is essential to have deep knowledge of the coronary anatomy, that is, carry out a careful frame-by-frame review of the diagnostic coronary angiography to be able to characterize the plaque and the collaterals. Also, it is imperative to think of the material and the possible techniques that will be used. Added to the coronary anatomy, we also need good in-depth information on the patient, in particular his renal function, risk of bleeding, therapeutic adherence, capacity of collaboration, osteoarticular situation, and frailty.

We also consider the possibility of asking for help from other colleagues more experienced than us both at the beginning of the activity, and in second attempts in patients in whom we have already failed.

Another important issue is the material we plan to use because this is a field in continuous evolution. Although it is not possible to know every piece of equipment currently available, once we have made our choice, we need to know its characteristics, how it has been built, what it is designed to do, and how it should be used. Ongoing training is also important, so periodically attending specialized congresses are a good resource if we want to keep up to date.

It is essential to guarantee the patient's safety; we should not forget that success means achieving TIMI (Thrombolysis in Myocardial Infarction) grade III flow without significant residual stenosis, loss of branches (a prognostic factor already confirmed long ago) and without any associated complications. The implementation of simple resources within our routine cath lab practice may help; here are a few examples: stop the procedure if losing collateral circulation and resume it if we think we can introduce some changes in the technique that we still have not used or have used incorrectly; ask the heart team to signal us whenever we have passed 3.7 times the volume of contrast administered in relation to the patient's creatinine clearance levels to avoid contrast-induced nephropathy; and avoid high doses of radiation by asking the heart team to signal whenever we have reached the 3 Gy mark, and consider stopping the procedure whenever we come close to the 5 Gy mark if we have not made very significant advances, basically if we have not crossed the lesion with the guidewire.

CONFLICTS OF INTEREST

V. Martin-Yuste declared no conflicts of interest whatsoever regarding the writing of this manuscript.

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Debate: Chronic total coronary occlusions. The clinician perspective

A debate: Oclusión coronaria total crónica. Perspectiva del clínico

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Question: Is there enough evidence to be able to say that the coronary recanalization of a chronic total coronary occlusion (CTO) improves the prognosis of patients?

Answer: No, there is not. However, many cardiologists believe so based on observational studies that report that patients with CTO who are successfully treated have better prognosis compared to those who undergo failed procedures.[1] In many of these registries, the baseline characteristics, risk factors, ventricular function, and coronary anatomy are substantially different between patients treated successfully and those treated with failed procedures.[2,3] When the outcomes are adjusted by these confounding variables, success in treatment does not condition the prognosis anymore.[4]

One less biased way to know the effect this has on the prognosis of patients undergoing percutaneous treatment of their CTO is to compare them to those who receive medical treatment. In this sense, several registries have been published with different results. For instance, in a study of patients with CTO treated percutaneously versus patients treated medically (using propensity-score matching), Ladwiniec et al.,[5] showed a lower rate for the composite endpoint of death or myocardial infarction at 5 years, but not death as the single event that was favorable to those patients treated percutaneously. However, Yang et al.,[6] with a similar matching of patients, did not show any benefits derived from treating the CTO. This shows that dozens of registries on CTO still cannot replace the need for randomized clinical trials.[7,8]

Very few studies randomizing patients to having their CTO treated or not have been published so far, and not all of them have had the assessment of cardiovascular events as their primary endpoint. The EXPLORE trial included 304 patients with a CTO as the non-culprit artery in individuals with ST-segment elevation myocardial infarction treated with primary angioplasty.[9] At 4 months no differences were seen in the ejection fraction, the left ventricular end-diastolic volume (the primary endpoint) or cardiovascular events analyzed through cardiovascular magnetic resonance. By the way, the result of this study had somehow already been anticipated in a Spanish registry.[10] The REVASC clinical trial randomized 205 patients with stable chronic coronary artery disease to treat or not to treat a CTO.[11] At 6 months, no differences were seen in the global or segmental left ventricular function (the primary endpoint) or cardiovascular events analyzed through cardiovascular magnetic resonance between the 2 groups. The EuroCTO trial ranzomized 396 patients (2:1) to treat or not to treat a CTO.[12] At the 12-month follow-up, no differences were seen in the rate of cardiovascular or cerebrovascular events reported in the arm where the CTO was treated. It should be mentioned that this study anticipated including 1200 patients but had to be interrupted prematurely due to its low inclusion rate. The IMPACTOR-CTO clinical trial randomized 96 patients with a CTO in their right coronary artery to receive percutaneous treatment or not.[13] This study conducted in a single Russian center showed a reduction of ischemia and improved 6-minute walk test results without any changes in cardiovascular events.

Finally, the DECISION-CTO clinical trial has been the most important study published so far with 834 randomized patients.[14] During a mean 4-year follow-up, the incidence of the composite endpoint of death, myocardial infarction or stroke was similar in both arms.

Therefore, to this day no randomized clinical trial or meta-analysis of all randomized clinical trials[15] published so far has been able to prove that treating a CTO changes the prognosis of patients.

Q.: In what subgroups of patients or situations should we expect to see greater prognostic benefits?

A.: There is something clear: the CTO is a common lesion in patients with ischemic heart disease[16] and its presence is associated with poor prognosis.[17] Therefore, the issue is to be able to identify those patients whose prognosis may change with a percutaneous coronary intervention. The revascularization of a CTO that causes significant ischemia (> 10% quantified using imaging

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modalities) may improve long-term prognosis as a clinical trial is trying to prove: the ISCHEMIA-CTO (Nordic and Spanish Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy in Chronic Total Coronary Occlusions with Myocardial Ischemia; NCT03563417). But before the ISCHEMIA-CTO findings become available, we will probably have the results of the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches, NCT01471522) clinical trial first. This study has been trying to prove something similar in patients who do not necessarily have a CTO. If the ISCHEMIA trial is positive, the hypothesis of revascularizing a CTO based on the presence of significant myocardial ischemia will be much more attractive.

Q.: And what about symptom and functional improvement?

A.: There are at least 2 studies that indicate that symptomatic patients can improve once their CTO has been treated. The FACTOR is a non-randomized clinical trial that showed improved quality of life test results in symptomatic patients.[18] This is a small study of 125 non-randomized patients in whom the quality of life test is analyzed 1 month after the procedure. Also, it compares patients successfully treated versus patients with failed procedures. The benefit derived from successful treatment was greater in symptomatic patients and significant with respect to physical activity and quality of life according to the Seattle Angina Questionnaire. However, the most significant evidence of symptom improvement after treating a CTO comes from the EuroCTO clinical trial that showed modest symptomatic benefits in the quality of life test results after percutaneous treatment.[12] However, the premature interruption of the study and its low inclusion rate make the results questionable.

Regarding functional improvement, there is also evidence that the treatment of a CTO modestly reduces the ischemic region in patients with at least mild to moderate ischemia[19] and barely improves ventricular function,[20] although we still do not know how these aspects may impact the patient's clinical signs.

Q.: What clinical indications does the percutaneous revascularization of a CTO have?

A.: Today, the main indication for treating a CTO should be to improve symptoms in patients who remain symptomatic despite the optimal medical treatment.[19] In order to achieve this, the occluded artery needs to be recanalized effectively, which totally depends on its angiographic characteristics and the experience of the interventional cardiologist in charge.

The current clinical guidelines of the European Society of Cardiology contemplate 1 indication only for the management of a CTO: patients with angina refractory to treatment and a significant ischemic region as seen on the imaging modalities.[21] This is a class IIa indication with a B-level of evidence. As long as we don't have any other evidence, we encourage all Spanish interventional cardiologists experienced in the management of CTO, who are actually many and with very good results,[22] to include patients in the current ISCHEMIA-CTO randomized clinical trial. This clinical trial is essential and will shed light on many of the issues we have discussed here.

CONFLICTS OF INTEREST

None declared.

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Clinical case

The difficulty of interventional cardiology in routine everyday practice. Paying the price of a sigh

La dificultad de la cardiología intervencionista en el trabajo diario: el precio de un suspiro

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CASE PRESENTATION

We hereby present the case of a 73-year-old male with a past medical history of high blood pressure, diabetes mellitus type 2, dyslipidemia, and former smoker as cardiovascular risk factors. The patient showed chronic ischemic heart disease that started as unstable angina with coronary artery disease of the right and circumflex coronary arteries, undergoing complete percutaneous revascularization in 2008 with everolimus-coated stents.

Ten years later the patient suffered from a non-ST segment elevation acute coronary syndrome of inferior location with low blood pressure and need for vasoactive amines, which is why he was transferred to the cath. lab for an early invasive strategy.

The diagnostic coronary angiography performed using the right radial access showed the presence of a plaque complicated with a thrombus in the ostium of the right coronary artery with Thrombolysis in Myocardial Infarction grade flow 3 (figure 1).

A 6-Fr JR guiding catheter and a Sion guidewire (Asahi) were selected for the procedure. Predilatation was attempted with a 3.5 × 10 mm noncompliant balloon (figure 2) and a 3.5 × 18 mm Orsiro sirolimus-eluted stent was implanted covering the ostium (figure 3).

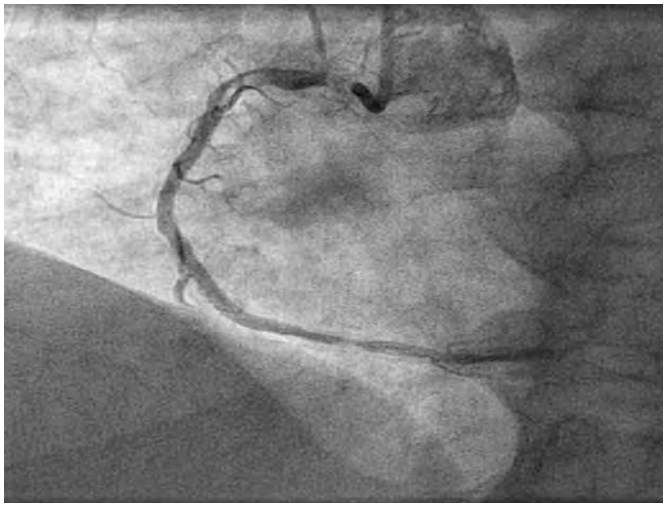

Figure 1. Acute complicated lesion in the ostium of the right coronary artery.

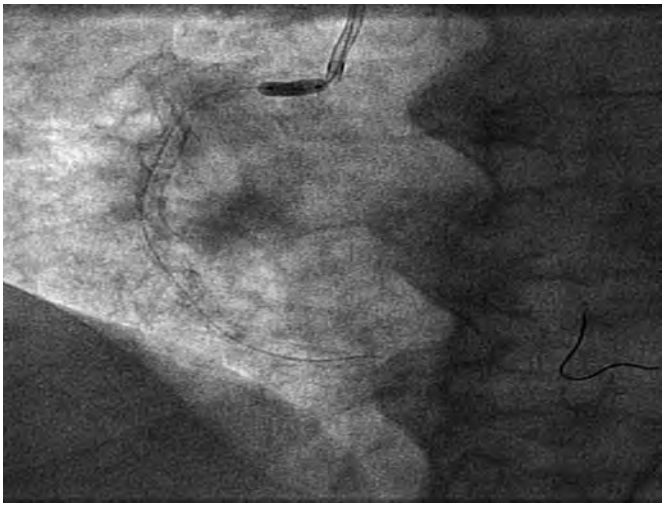

Figure 2. Predilatation with one 3.5 × 18 mm noncompliant balloon inflated at 14 atm, with adequate expansion.

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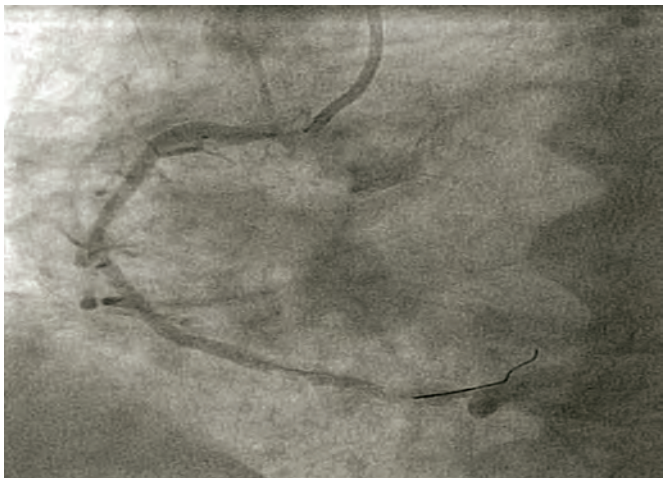

Figure 3. Angiography prior to the implantation of the stent adjusted to the ostium of the right coronary artery.

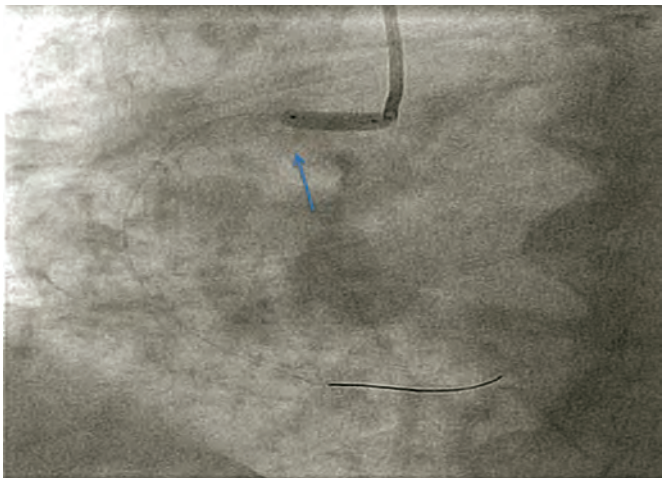

Figure 4. Stent displaced towards the aorta is observed. The arrow shows the mark of calcium in the sinus of Valsalva.

When the stent was deployed and inflated at 6 atm, with the patient in a state of agitation given his hemodynamic situation, he took a deep breath that caused the displacement of the stent towards the aorta (figure 4), that was deployed completely outside the ostium of the right coronary artery.

Therefore, we found ourselves with one under-expanded, displaced or loose stent inside the aorta that made maneuverability difficult with an uncovered thrombus in a complex ostial lesion and in the clinical context of an acute coronary syndrome.

The difficulty of interventional cardiology in routine everyday practice. Paying the price of a sigh. How would I approach it?

La dificultad de la cardiología intervencionista en el trabajo diario: el precio de un suspiro. ¿Cómo lo haría?

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HOW WOULD I APPROACH IT?

We are facing a challenging situation here both from the clinical–a patient with an acute coronary syndrome with hemodynamic impairment– and technical point of view –the procedure became complicated due to the accidental displacement of the stent from the coronary ostium towards the aorta–.

This is not something rare or due to any technical mistakes, we simply encountered a complication that can occur when treating ostial lesions in 15% of the cases. Even so the best thing to do here is to think about how it could have been prevented.

The management of ostial lesions is effective and safe but there are difficulties too. What we have here are plaques with more fibrosis and calcification that can lead to the infra-expansion and further restenosis or thrombosis of the stent.

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Also, it makes arterial catheterization more difficult, there is this possibility of blood pressure drops when inserting the catheter, issues with the positioning and release of the stent and, as it was the case here, even inadequate results.

In order to have some guarantees in the management of these lesions we need to choose a guiding catheter capable of providing good support, prepare the lesions with predilatation or use rotational atherectomy devices, and ultimately be very precise when positioning the stent. In this sense, it is advisable to implant it in the aorta with a 1 mm protrusion to make sure that the entire plaque has been covered.

This last step became complicated, yet different maneuvers have been described in the medical literature to avoid stent displacement. The first thing to do is to identify which is the ideal position here by using different views; then, we are supposed to keep firm and constant pressure over the stent during implantation. Leaving a second guidewire as a marker of the aorta can be helpful here. Also, the same intracoronary guidewire can be used to immobilize the stent in the position we want through ventricular pacing through the angioplasty guidewire.[1]

The use of guiding catheter extension devices has been suggested here to improve the positioning of the stent during implantation.

With this idea in mind, we can try to stabilize it by using the buddy balloon anchor stent technique.

Szabo described one technique that used a second guidewire in the aorta to anchor the stent to the ostium by passing its proximal edge through the last cell of the stent. It is a relatively complex technique, success rate is between 78% and 90%, and there are risks involved (stent displacement, guidewire crossing, damage to the stent, etc.)

Several devices have been designed with this idea in mind such as the FLASH Ostial System, (Cardinal Health, California, United States) that uses one distal balloon angioplasty plus another proximal anchoring balloon for proximal stent edge apposition to the aorta or the Cappella system, (Cappella Medical Devices, Ireland), that includes a self-expandable stent to provide optimal ostial coverage, although in the case of hard fibrocalcific plaques it does not have enough radial power. The Ostial PRO system (Merit Medical Systems) helps in the ostial positioning of the stent by placing nitinol legs against the aortic wall to avoid implantations that may be too distal. However, none of these systems is used routinely for the management of ostial lesions and although these techniques can be used occasionally, the planning and careful performance of the procedure by an experienced interventional cardiologist should are still the treatment of choice as it was the case with our patient.

The fact of the matter is that, despite of everything, we found ourselves with an under-expanded stent that was displaced towards the aorta and implanted outside the coronary ostium. This excessive protrusion can originate thrombi, anticipate a future risk of embolization, and most assuredly complicate access to the coronary in new procedures.

Several options can help us to solve this problem:

- Stent removal:

By having a guidewire through the under-expanded stent and protruding into the aorta, the first maneuver here would be to advance the balloon through the stent in order to dilate the coronary artery proximal segment to guarantee its patency. Then the partially inflated balloon is smoothly removed up to the distal edge of the under-expanded stent, the stent is displaced towards the aorta and, if removed, it is advanced towards the guiding catheter. If the stent is partially implanted in the vessel wall, this maneuver won't probably by successful. Another option here would be to use the loop snare technique to capture the proximal edge of the stent that is protruding into the aorta. Some of the cases published[2,3] describe stent "explants" performed using this technique in ostial lesions with stents displaced towards the aorta. However, there is a risk of endothelial damage, dissection, and perforation with this maneuver. Also, after capturing the stent with the loop snare, the movement of traction to attempt the stent retrieval would probably lead to losing the intracoronary guidewire with the corresponding risk of vessel occlusion.

- Stent "modification":

In order to avoid the risks involved in this retrieval maneuver, we could also solve this complication by inserting a second intracoronary guidewire through the same guiding catheter or, if an alternative vascular access is possible, by using another guiding catheter to allow optimal coaxiality such as the Amplatz Right guidewire. We would have to orient the catheter to pass the new intracoronary guidewire through one cell of the stent segment that protrudes into the aorta and very close to the coronary ostium. Here we would need to advance a 1.5 or 2 mm balloon to open the struts in the stent and then proceed to dilate using gradually larger balloons until we would be able to open our way and deploy a new stent to cover the diseased area of the proximal coronary artery and the under-expanded distal segment of the first stent. Finally, we would have to over-dilate the proximal edge at a high pressure by using a long enough noncompliant balloon to guarantee the crushing of the stent that is protruding into the aorta and its apposition to the aortic wall. The very few cases published on this regard describing this maneuver for the management of stents with excessive aortic protrusion have shown favorable outcomes.

Although a good prior strategy and preparation of the lesion are essential to prevent complications from happening, unexpected sudden situations can trigger all sorts of complications. The interventional cardiologist's experience, expertise, and caution are crucial to solve these complications.

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The difficulty of interventional cardiology in routine everyday practice. Paying the price of a sigh. Case resolution

La dificultad de la cardiología intervencionista en el trabajo diario: el precio de un suspiro. Resolución

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CASE RESOLUTION

Given the partial opening of the stent, it was decided to proceed with an increased pressure and assess the stability of the stent.

The stent seemed to have been deployed totally outside the right coronary artery, which is why we tried to capture it using a semi-compliant balloon in order to try to drag it towards the radial artery for implantation purposes, but such a maneuver failed (figure 1). This is how we confirmed that the stent was anchored to the ostium by just a few millimeters. Initially the intravascular ultrasound was not used here to assess the location of the stent to avoid any possible moves and manipulations of the implanted stent.

In order to protect the stent from the deformation by the tip of guiding catheter, the Guideliner guiding catheter extension device was used (Vascular Solutions, Inc., Minneapolis, Minnesota, United States). One semi-compliant balloon of 2.5 mm in diameter was advanced towards the proximal segment of the right coronary artery where it was inflated. It was then that the Guideliner device was advanced and the inflated balloon was slightly pulled (anchoring) by placing the tip of the guiding catheter extension device into the proximal segment inside the displaced stent (figure 2).

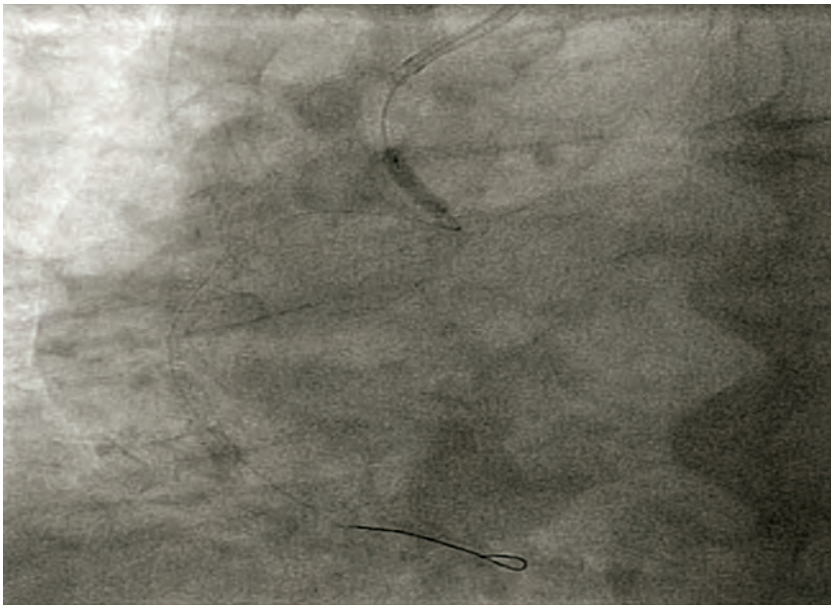

Figure 1. Attempt to drag the stent out of the coronary artery with a semi-compliant balloon.

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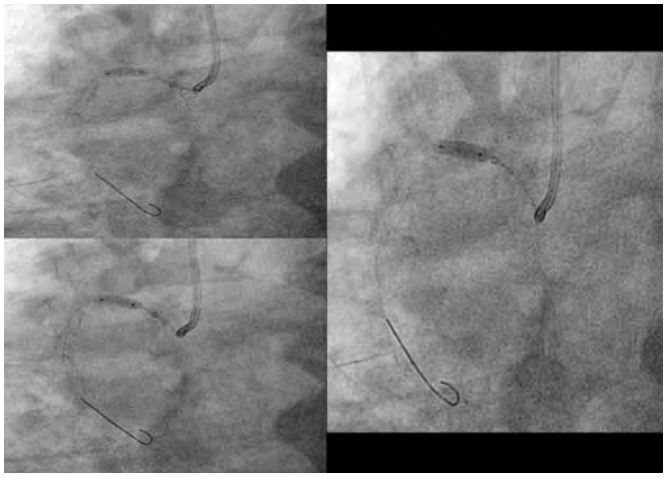

Figure 2. Advancement of the guiding catheter extension device towards the proximal segment of the right coronary artery.

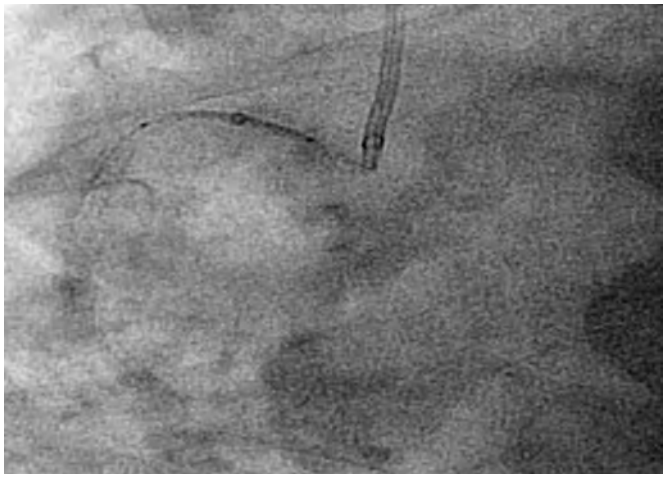

Figure 3. Implantation of zotarolimus-coated stent in the proximal segment of right coronary artery.

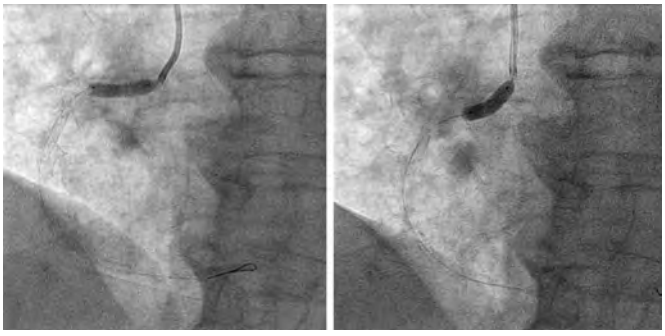

Figure 4. Post-dilatation with balloon of the previous implanted stents especially of the portion protruding into the aorta in order to achieve the greatest possible longitudinal shortening.

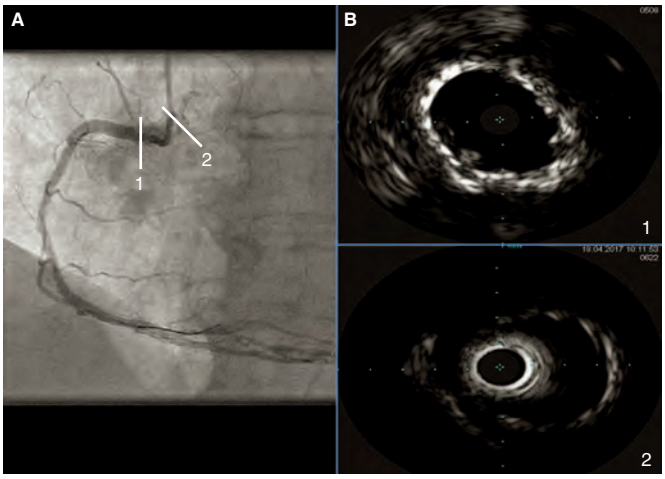

Figure 5. A: final angiographic result. **B1:** intracoronary ultrasound image showing the double layer of stents at ostium level with good stent apposition and expansion. **B2:** intracoronary ultrasound image showing the stent implanted in the first place, protruding into the aorta, and showing wide overexpansion.

Afterwards we proceeded with the eventless advancement of a new zotarolimus-coated stent (Medtronic Resolute Onyx, 4 × 22 mm) towards the proximal segment by navigating inside the guiding catheter extension device (figure 3). This second stent was implanted and anchored to the previous one and adjusted to the ostium. It was dilated with high pressure with the delivery balloon including the visible segment protruding into the aorta in order to achieve the longitudinal shortening of the stent by overexpansion (figure 4).

The angiographic results were good (figure 5A) and the intravascular ultrasound examination conducted showed the double layer of stents at ostium level with good stent apposition and expansion (figure 5B1) and the stent deployed protruding into the aorta showed wide overexpansion (figure 5B2).

We learned that the monorail extension of the guiding catheter helped us maneuver the intracoronary devices and protect the devices already implanted, which in the case of ostial lesions can prevent the deformity and the possible longitudinal shortening of the stent induced by guiding catheters.

The most radio-opaque stents can be a good option for the management of ostial lesions because of their better angiographic visualization. In this sense, chrome-cobalt alloys and, especially, chrome-platinum alloys have higher density and radiopacity. However, the chrome-platinum platform was not selected here due to its association with longitudinal deformity, especially in ostial lesions, where repeated proximal traumas are possible with the guiding catheter.

Finally, in order to avoid stent displacements with respiration we could have asked the patient to hold his breath for a few seconds, just long enough to be able to deploy the stent. However, in the presence of agitation preventing the patient's collaboration, as it was the case here, it is advisable to use powerful sedation or analgesia, or both, to avoid complications such as stent displacement during stent deployment or issues derived from the loss of the angioplasty guidewire.

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Clinical trial review

COMPLETE revascularization after STEMI? Sure, go ahead

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ABSTRACT

Primary angioplasty is now clearly established as the best reperfusion strategy for patients with ST-segment elevation myocardial infarction (STEMI), but the best strategy for significant stenosis at non-culprit vessels has not been adequately studied. Several randomized trials have been previously performed, but all of them with soft primary endpoints and consequently a low number of patients. The COMPLETE trial, for the first time, provides us with solid scientific evidence about what we should do in patients with STEMI and multi-vessel disease. This study included more than 4000 patients and has shown that complete revascularization reduces significantly the risk of cardiovascular death or myocardial infarction.

Keywords: STEMI. Percutaneous coronary revascularization. COMPLETE trial.

¿Revascularización completa en el infarto de miocardio con elevación del ST? Sí, no lo dude

RESUMEN

La angioplastia primaria está reconocida como la mejor estrategia de reperfusión en el infarto de miocardio con elevación del segmento ST. No obstante, la mejor estrategia para el tratamiento de las lesiones coronarias significativas en arterias no relacionadas con el infarto no se había estudiado convenientemente. Hasta la fecha se habían realizado varios estudios aleatorizados pero con objetivos de beneficio clínico de gravedad menor o «blandos» y pocos pacientes. Por primera vez, el estudio COMPLETE proporciona evidencia científica sólida sobre la estrategia terapéutica en pacientes con infarto de miocardio con elevación del segmento ST y enfermedad multivaso. Este estudio, que incluyó a más de 4.000 pacientes, ha demostrado que la revascularización completa reduce significativamente el riesgo combinado de mortalidad o infarto de miocardio.

Palabras clave: IAMCEST. Revascularización coronaria percutánea. Estudio COMPLETE.

Abbreviations

STEMI: ST-segment elevation myocardial infarction.

The solid results of the recently published COMPLETE trial[1] clearly show that the revascularization of nonculprit lesions after successful primary percutaneous coronary intervention (PCI) for the management of ST-segment elevation myocardial infarction (STEMI) improves long-term outcomes. This is evident today, will probably be accepted as a general strategy, and is one of the last steps in a long journey (figure 1). It all started a long time ago when a gradually better and more aggressive management of acute myocardial infarction improved short and long-term prognosis, and reduced mortality rates to unimaginable levels only a few years ago. Once upon a time, and based on anatomopathological findings, there was this wrong assumption that coronary artery occlusions during acute myocardial infarction were the consequence of myocardial necrosis and not the other way around. Only in the 1980s it became clear that opening the culprit, occluded coronary artery improved the outcomes. Immediate revascularization procedures played a significant role together with better medical therapies, reorganizing the existing strategies, and much better secondary prevention measures immediately after an acute event.[2-4]

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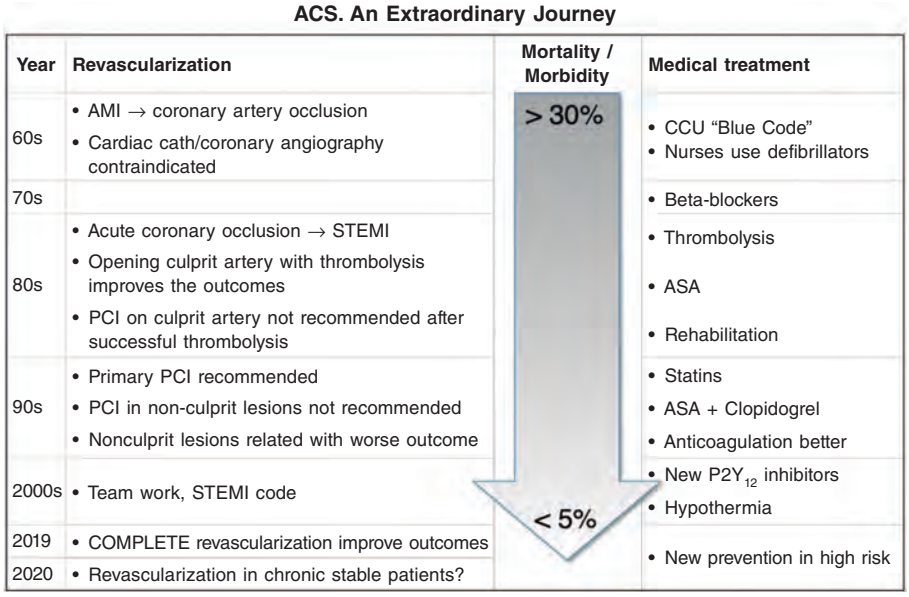

Figure 1. Evolution of revascularization, medical therapies, and outcomes in the management of STEMI. ACS, acute coronary syndrome; AMI, acute myocardial infarction; ASA, acetylsalicylic acid; CCU, coronary care unit; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

To this day, all advances made on revascularization were associated with the culprit vessel (the immediate, successful and sustainable recanalization of the culprit vessel), yet the efforts made with diseased non-culprit vessels have yielded unclear results.

The COMPLETE trial compared a strategy of culprit lesion only versus complete revascularization in patients with acute STEMI with other significant coronary artery stenosis identified at the time of the primary PCI. The study included 4041 patients with a median follow-up of 3 years. Significant reductions in the first coprimary endpoint of cardiovascular death or myocardial infarction and second coprimary endpoint of cardiovascular death, myocardial infarction or ischemia-driven revascularization were seen in the complete revascularization arm compared to the group where only on the culprit artery was revascularized. The benefit favoring complete revascularization was observed early after inclusion in the trial and became more evident through the 3-year follow-up (figure 2). These observations were consistent through the different subgroups. There was a small, nonsignificant increase in major bleeding and contrast-induced acute kidney injury. The benefit was mainly driven by significant reductions in myocardial infarction and ischemia-driven revascularization.

Previous studies with soft primary endpoints failed to show that complete revascularization could be beneficial in terms of death or myocardial infarction, but the number of patients included in these trials was very small,[5-10] ranging from 69 patients in the HELP-AMI trial[6] to 885 patients in the COMPARE-ACUTE.[8] These trials combined represent just a small fraction of the number of patients included in the COMPLETE trial.

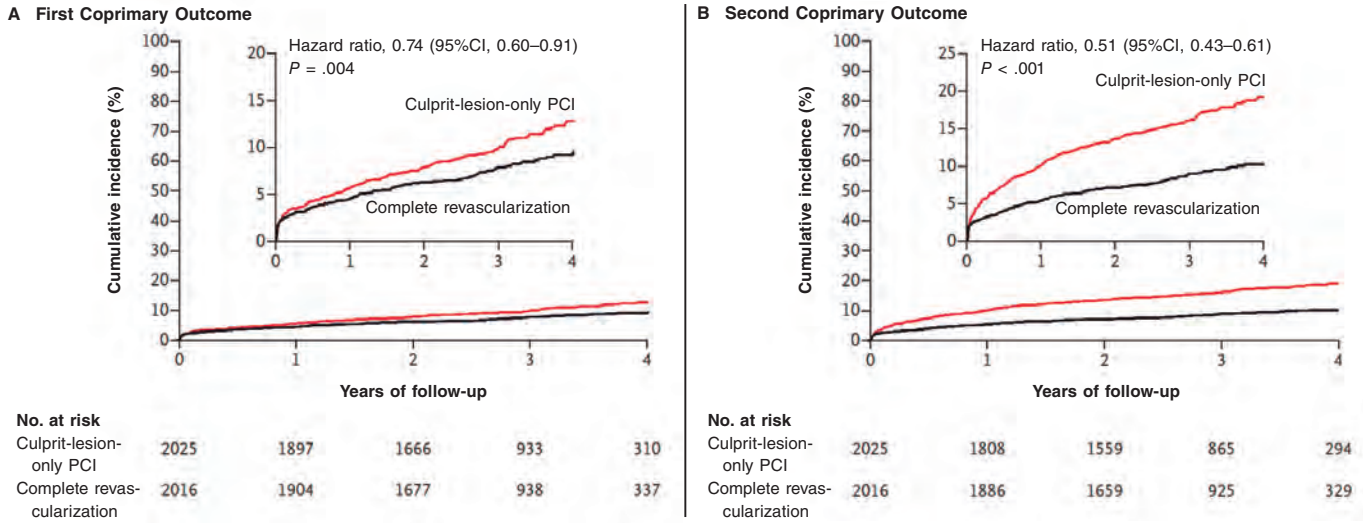

Figure 2. COMPLETE trial main results. Kaplan-Meier estimates for the first coprimary outcome (cardiovascular mortality or new myocardial infarction) and second coprimary outcome (cardiovascular mortality, new myocardial infarction, or ischemia-driven revascularization). CI, confidence interval; PCI, percutaneous coronary intervention. Reproduced from Mehta et al.[1] with permission.

Table 1. Eligibility of patients in the COMPLETE trial. Major inclusion and exclusion criteria

Inclusion criteria
STEMI
Successful PCI on the culprit lesion
At least 1 non-culprit lesion
Non-culprit lesion diameter ≥ 2.5 mm
Non-culprit lesion stenosis > 70% or
50%–60% stenosis and FFR ≤ 0.8
Immediate revascularization within 72 h following the index PCI
Exclusion criteria
Planned surgical revascularization
Prior bypass surgery

FFR, fractional flow reserve; PCI, percutaneous coronary revascularization; STEMI, ST-segment elevation myocardial infarction.

As most trials, the COMPLETE also raises some practical questions. First, is the benefit clinically significant? The COMPLETE trial showed robust results but failed to show reductions of cardiovascular mortality, heart failure and all-cause mortality. It is well accepted that multivessel disease is a clear risk factor for mortality after STEMI;[11] however, the inclusion and specially exclusion criteria of the COMPLETE trial selected a group of low risk patients. Cardiovascular mortality was only 1% per year and it is almost impossible to show mortality reductions in this population. But there was a significant reduction in the rate of myocardial infarction (2.8% vs 1.9% per year), unstable angina (2.2% vs 1.2% per year), and ischemia-driven revascularization (2.8% vs 0.5% per year) without an excess of major complications. This will make most interventional and clinical cardiologists take this strategy seriously. Although the recommendations established by the guidelines on secondary prevention were followed in the trial, secondary prevention is evolving very fast,[12] complementing revascularization strategies, but also decreasing the relative role of each component.

Second, is routine complete revascularization for all? Actually it is in all the cases that meet the COMPLETE inclusion and exclusion criteria (table 1), but not in patients with small vessel disease, non-significant epicardial coronary artery stenosis, prior bypass surgery, and others. We should not forget that the COMPLETE trial excluded patients with cardiogenic shock, and routine complete revascularization has proven harmful in these patients.[13] The question of whether all patients that meet the COMPLETE criteria should undergo complete revascularization is more difficult to answer. Identifying patients at higher risk, based on clinical characteristics, and additional information on coronary anatomy and in particular on plaque stability is indicative of the target population that may benefit the most. This information may be obtained from the trial database.

Third, a key question related to the timing of complete revascularization. The COMPLETE trial recommended a staged rather than a single revascularization procedure. Other trials have assessed complete revascularizations in a single procedure in patients with STEMI and multivessel disease with good safety and efficacy data.[7,10] Complete revascularizations in a single procedure reduced cardiovascular events compared to staged-revascularizations in patients with NSTEMI.[14] Currently, the BioVasc trial (NCT03621501) is comparing complete revascularizations in single procedures to staged procedures in patients with STEMI and NSTEMI. According to the COMPLETE trial, complete revascularization should be performed during index hospitalizations, but it did not show data on single-stage revascularizations.

Finally, could revascularization improve the outcomes of stable coronary disease? Actually this is out of the scope of the COMPLETE trial, and so far the evidence available today is very weak, with only marginal benefits for revascularization, if any.[15] The ongoing ISCHEMIA trial[16] is comparing the benefit of revascularization plus medical therapy versus medical therapy alone in over 5000 patients and its results will be published very soon. Obviously, the results will be crucial to improve the invasive strategy for the management of coronary heart disease. Would complete revascularization be beneficial in patients with non-ST segment elevation acute coronary syndromes? Probably, but we do not know it yet and there are no studies exploring this hypothesis.

Meanwhile, please go ahead and check if STEMI patients with prior successful primary PCIs qualify as eligible candidates for COMPLETE revascularization within 72 hours (before hospital discharge).

CONFLICTS OF INTEREST

J. López-Sendón reported having received grants from McMaster University (Hamilton, Ontario, Canada) while conducting this study. J. López-Sendón and R. Moreno are coauthors of the article reviewed on this paper. R. Moreno is Associate Editor of *REC: Interventional Cardiology*; the journal's editorial procedure to ensure impartial handling of the manuscript has been followed.

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Eccentric mitral regurgitation through the LAmbre closure device

Insuficiencia mitral a través del dispositivo LAmbre

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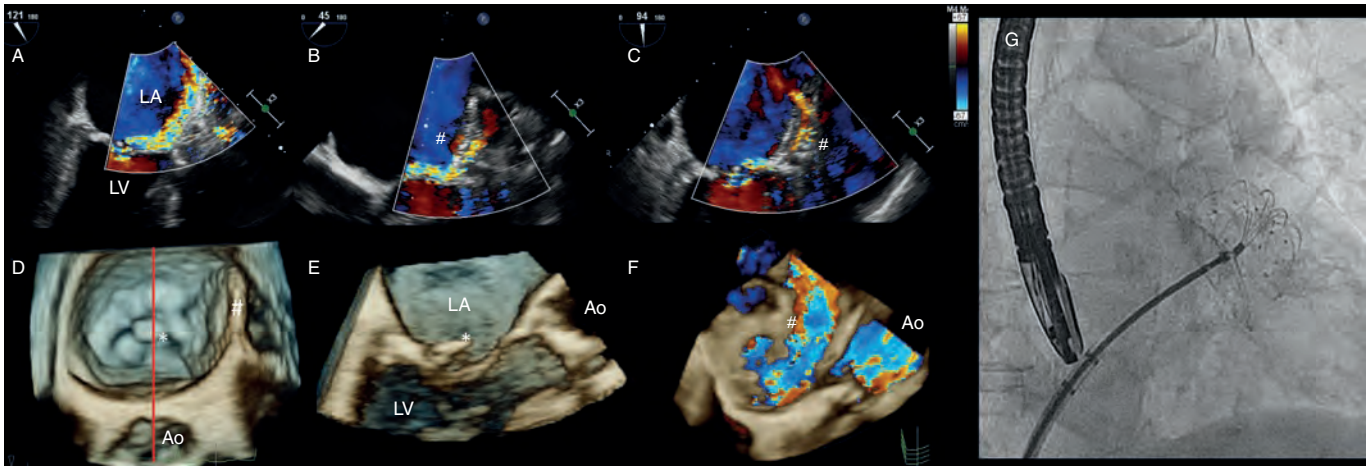

Figure 1.

An 83-year-old female with severe asymptomatic mitral regurgitation (MR) was admitted for an elective percutaneous left atrial appendage occlusion (LAAO) due to severe gastrointestinal bleeding under anticoagulant treatment. The transesophageal echocardiography (TEE) conducted before the procedure confirmed the presence of severe MR due to a flail P2 segment with a jet lesion on the sliding atrial wall adjacent to the appendage. An LAAO procedure was performed and the LAmbre system (Lifetech Scientific) was successfully deployed. A first assessment confirmed the presence of MR jet over the external lobe of the device (figure 1A; LA, left atrium; LV, left ventricle), but detailed scanning detected one MR jet pathway below the LAAO device (figure 1B,C). The 3D-TEE of the mitral valve P2 scallop (*) is shown on figure 1D-F (Ao, aortic root; LAAO device (#); the 3D-volume is cropped according to red line to create figure E). The pre-LAmbre device fluoroscopy image is shown on figure G. The steps of this procedure are available at video 1 of the supplementary data. Device change or relocation were not considered. We thought that a LAmbre device was the best option for a cone-shaped appendage since the external disc is far enough from the mitral valve and the internal lobe was at the deepest position possible, totally occluding the appendage. A matter of discussion was whether a shorter disc and lobe would have pulled inside the disc with better results. Double antiplatelet therapy was maintained, and no embolic events or thrombi were seen in the follow-up TEE.

As far as we know, this is the first time that one MR jet running through a percutaneously occluded atrial appendage has ever been reported.

CONFLICTS OF INTEREST

I. Cruz-Gonzalez is a proctor for St. Jude Medical and Boston Scientific.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M19000022.

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Multiple devices inside a large stent

Múltiples dispositivos dentro de un stent grande

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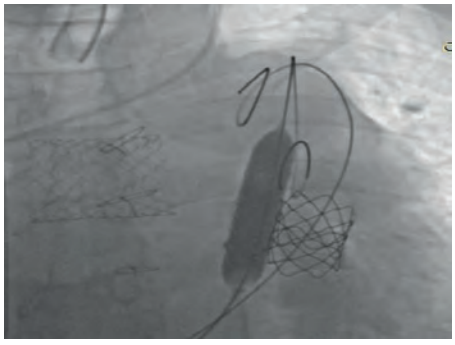

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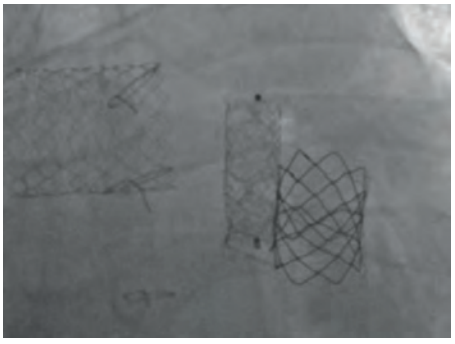

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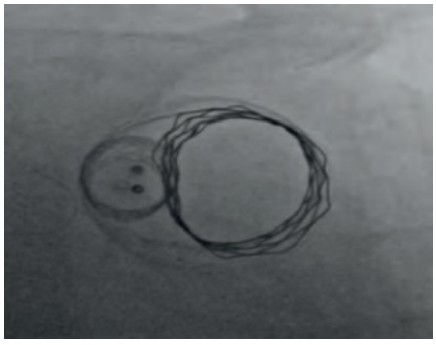

Figure 3.

A 51 year-old-male, with a diagnosis of severe pulmonary stenosis treated with surgical commissurotomy at the age of 4, was admitted due to severe right heart failure.

The echocardiography showed severe pulmonary regurgitation, severe right ventricular dilatation with moderate systolic dysfunction, severe tricuspid regurgitation with mild pulmonary hypertension. The magnetic resonance angiography showed pulmonary trunk dilatation. Surgery was ruled out due to high risk (morbid obesity, chronic dialysis).

A staged percutaneous procedure was planned, including pre-stenting with one XXL AndraStent premounted on a 30 mm balloon. After placing the stent embolized to the right pulmonary artery. Recovery was unsuccessful and a second stent had to be deployed (premounted on a 35 mm balloon). The pulmonary annulus size was 31 mm, so the direct implantation of a conventional valve (SAPIEN XT or Melody) was not recommended.

Several weeks later, a 22 mm Melody valve and a 37 mm long covered BeGraft stent premounted on a 12 mm balloon were simultaneously placed in parallel inside the stent and sequentially inflated (figure 1). Then a 16 mm AVP-2 device was placed inside the stent to occlude the lumen (figure 2 and figure 3). The final result was good, with mild pulmonary regurgitation (video 1 of the supplementary data). Follow-up at 16 months shows normal valve function and mild pulmonary regurgitation.

This hybrid technique with a covered stent and a Melody valve can be a safe alternative therapeutic option for patients with very large native right ventricle outflow tracts. These techniques should be reserved for patients with high surgical comorbidity.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M19000031.

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Perception and experience of spontaneous coronary artery dissection in Spain. Results of a national survey

Percepción y experiencia sobre la disección coronaria espontánea en España: resultados de una encuesta nacional

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To the Editor,

Spontaneous coronary artery dissection (SCAD) is a low incidence disease that can cause acute coronary syndromes.[1,2] Although substantial advances have been made in the knowledge of the physiology, diagnosis, clinical management, and prognosis of SCAD, the degree to which such knowledge has entered the medical community is still uncertain. For this reason, it was decided to conduct a descriptive research on the knowledge and attitude of the Spanish interventional cardiologists towards SCAD.

The authors developed a 24-question survey including the clinical presentation, diagnosis, and acute and postcritical management of SCAD.[3] The initiative was approved and supported by the Working Group on Hemodynamics and Interventional Cardiology of the Spanish Society of Cardiology. The survey was closed in December 2018 with 161 answers from 72 centers (26 respondents did not complete the variable "center").

Figure 1 shows the answers given to the question "diagnosis". Two thirds of the respondents associated the SCAD with the profile of a young woman without any risk factors or pregnancy/puerperium-related. Regarding the angiographic manifestation, the most common pattern recognized by the respondents was not an angiographic dissection, but the loss of diffuse caliber in the blood vessel (type 2). Also, most respondents reported a low use of intracoronary imaging for the diagnosis of SCAD. More detailed answers to other questions can be found on the supplementary data.

On suspicion that a stenosis can be a SCAD in the mid anterior descending artery with preserved flow in a patient with acute coronary syndrome, 40% of the respondents said they would use intracoronary images to clarify the diagnosis, while 58.7% responded that they would choose a purely conservative approach and complete the procedure; most of these respondents (72.4%) would perform a follow-up coronary angiography.

Another question in the survey revealed the lack of consensus on the time frame recommended to perform the follow-up coronary angiography. On the indications for performing a coronary computed tomography angiography, 39.8% of respondents said they use it for follow-up purposes of SCADs with high-risk anatomies without revascularization (proximal/multivessel), while 39.1% said they use it for routine follow-up. A minority of respondents (18.6%) indicated the coronary computed tomography angiography in patients diagnosed with SCAD with recurring pain and no confirmed ischemia.

During the acute management at the cath lab, most respondents (54.7%) claimed that less than 20% of the patients with SCADs are treated using percutaneous angioplasties at their centers. For patients with SCAD who require interventional management, 67.7% of respondents said they choose drug-eluting stents; 14.3%, bioresorbable stents; 3.1%, conventional stents, and 14.9% said they always try to avoid implanting a stent (angioplasty without stent). To the question on the experience with cutting balloons, only 8.1% claimed to have used them in the past, while 45% thought this technique was interesting. Coronary revascularization surgery had been indicated as a bailout surgery for percutaneous angioplasty (19.3%) more or less for the left main coronary artery/multivessel (34.7%). However, 46% of respondents admitted they had never indicated surgery.

Figure 2 shows the answers given to the question of postcritical care in patients with SCAD in the mid left anterior descending artery undergoing conservative therapy. It should be mentioned that most respondents recommended prolonged monitoring (> 3 days).

In the medical practice, there is a great variety of antiaggregant drugs and other therapies to be prescribed; still, beta-blockers are indicated by most respondents (82.6%) in patients with preserved ventricular function.

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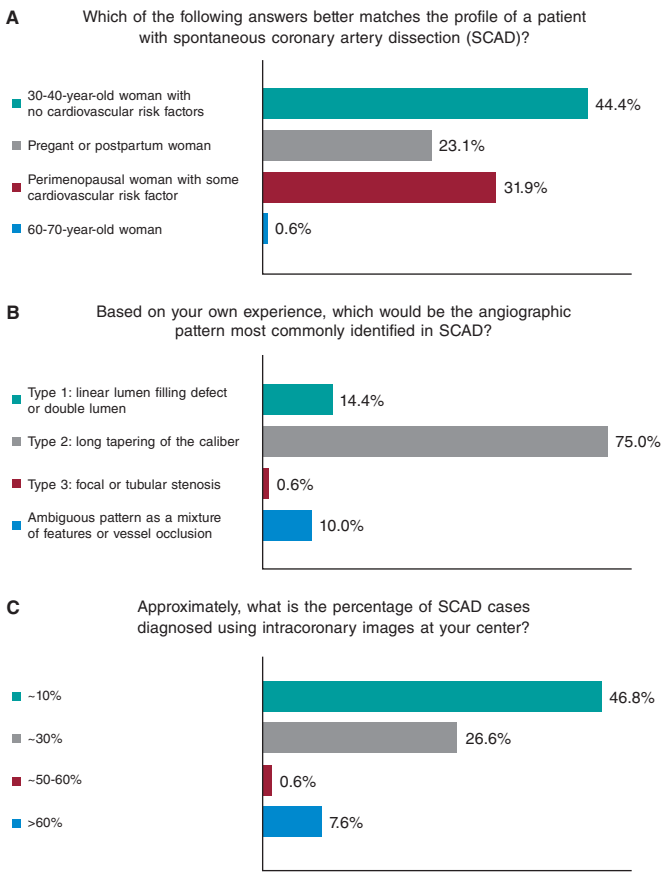

Figura 1. Questions on presentation and diagnosis.

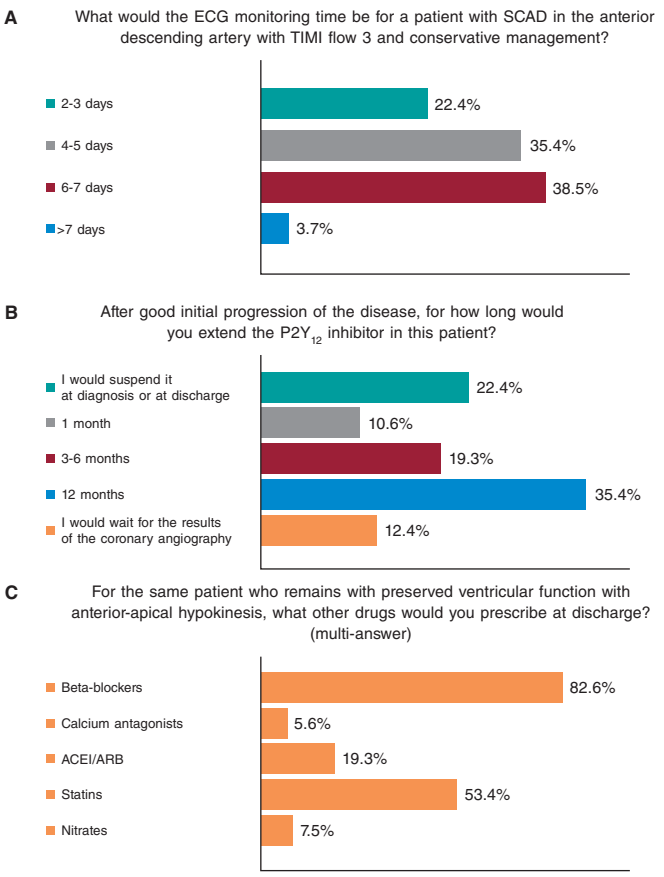

Figura 2. Questions on the postcritical care of patients with spontaneous coronary artery dissections treated conservatively. ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ECG, electrocardiogram; SCAD, spontaneous coronary artery dissection; TIMI, Thrombolysis in Myocardial Infarction.

The systematic practice of screening extra-coronary arteriopathy is performed by 44.8% of respondents. On this regard, the most widely used imaging modality is the computed tomography scan (76.4%) followed by magnetic resonance imaging (27.6%) and invasive catheterization (18.1%).

The results from this survey show that there is a significant variety in the perception and management of SCAD by the interventional cardiologists of our country.

Contrary to the classical profile of a fertile young woman, contemporary epidemiological data on SCAD reveal the prototypical profile of a 50-year-old woman during perimenopause and with a few risk factors.[2]

On the other hand, becoming familiar with the angiographic manifestation of this disease has facilitated diagnosis and reduced the use of intracoronary images, a technique with associated risks.[4]

When it comes to the time frame for performing the control coronary angiography, we have seen that most SCADs improve or resolve within a month; however, waiting a little longer turned out to be safe and can improve the diagnostic performance of this second coronary angiography.[2]

The percentage of conservative management reported in this survey is below the percentage reported in other series published, which may be a positive piece of information if we consider the preference of conservative treatment for this pathology.[1] Choosing prolonged monitoring in these patients makes total sense and is consistent with the fact that recurring events happen during the first week of convalescence.[5] Finally, the predominant use of beta-blockers is also logical considering their potential advantages and effects. Also because these are the only drugs with some degree of evidence of prophylaxis against SCAD recurrences.[1]

Despite the recent advances made on what we know about this disease and the clinical management of SCAD, there are some key issues in the clinical management of these patients that still need to be solved. The present survey showed a moderate degree of acceptance of the evidence and recommendations available today,[1,2] but also lack of consensus on other issues. If we want to move forward, a huge collective effort for the study of this disease is required through collaborations and prospective registries.

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SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M19000059.

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Percutaneous valve-in-ring procedure for the management of failed tricuspid annuloplasty

Prótesis valvular percutánea para tratar la anuloplastia tricuspídea fallida

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To the Editor,

Over the last few years we have become aware of the adverse impact of tricuspid regurgitation on morbidity (worse quality of life, hospital admissions...) and mortality with the corresponding increase in the number of interventions performed on the tricuspid valve both surgically and percutaneously.[1,2] From the surgical point of view, the most widely used technique for the management of tricuspid valve disease is repair with an annuloplasty to reduce the size of the ring and facilitate leaflet coaptation, usually with incomplete rings, in an attempt to spare the septal conduction system. Short-term results are satisfactory in most cases but according to the series published so far, up to 25% of the patients show moderate or severe regurgitation at 5 years. Overall, we are talking about patients of great complexity, multiple comorbidities, and several prior cardiac surgeries with the corresponding surgical risk, which is why the development of percutaneous coronary intervention techniques may be a great ally.

Currently the treatment of tricuspid valve dysfunction through valve-in-valve procedures is the percutaneous treatment of the tricuspid valve for which we have more and most successful experience. The percutaneous implantation of valves in dysfunctional rings are usually procedures with a series of difficulties due to the great heterogeneity of size, shape or rigidity of the rings. In many cases there are incomplete rings, which complicates the correct adaptability of the valve and often triggers the appearance of paravalvular regurgitation. Therefore, the correct planning of the case is required. For that purpose, imaging modalities are essential to obtain adequate results. However, these are frequently "compassionate use" procedures with a reported experience of just a few isolated cases or small series.[3-5]

We present the initial experience of 2 different centers with 2 cases of tricuspid percutaneous implantation with 2 of the most widely used bioprosthetic valves currently available for the treatment of tricuspid valve disease both aortic and pulmonary: the Edwards Sapiens XT valve (Edwards Lifesciences, Irvine, California, United States) and the Melody valve (Medtronic, Minneapolis, United States).

The first case is a 19-year-old female carrier of a heart transplant of 10-year duration with tricuspid annuloplasty with a dysfunctional, incomplete Medtronic 25 ring, and clinical signs of congestive heart failure refractory to medical treatment, and advanced renal failure. She was considered a very high-risk patient for reintervention, which is why percutaneous treatment was decided. In this case, the ring was measured using a 3D transesophageal

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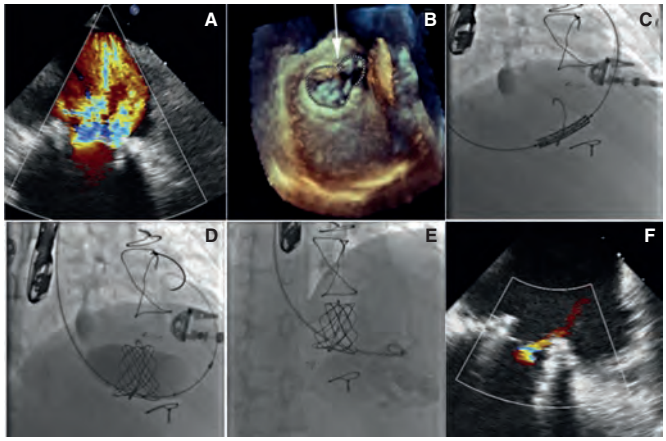

Figure 1. A: transesophageal echocardiogram (TEE) showing severe tricuspid regurgitation. **B:** measurement of the ring using 3D TEE. **C:** tricuspid valve-in-ring implantation using the Melody valve. **D:** post-dilation of the valve using a 24 mm-balloon. **E** and **F:** right ventriculography and TEE with correct valve apposition and without significant regurgitation.

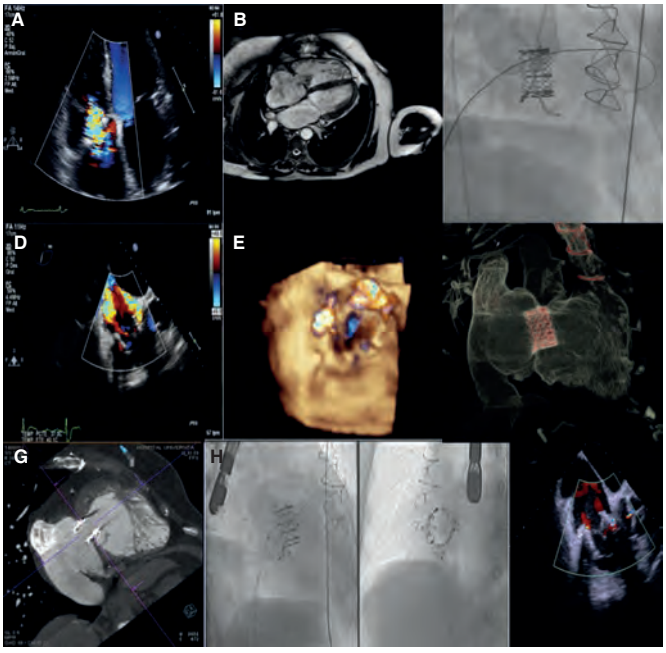

Figure 2. A: transthoracic echocardiogram showing severe tricuspid regurgitation. **B:** CT scan prior to valve implantation. **C:** implantation of the Edwards bioprosthetic valve using the Safari guidewire. **D** and **E:** severe residual tricuspid regurgitation due to 2 perivalvular leak. **F** and **G:** CT scan prior to the closure of paravalvular leaks. **H:** closure of posterior inferior leak. **I:** closure of septal leak. **J:** final outcome without significant tricuspid regurgitation.

echocardiogram to minimize the use of contrast while the use of a planning CT scan was discarded (figure 1A,B). Due to the size of the ring, it was decided to implant a Melody bioprosthetic valve using the 22 mm Ensemble balloon delivery system that was dilated using a 24 mm-balloon and remained in good ring apposition without significant residual periprosthetic regurgitation (figure 1C-F).

The second case is a 53-year-old woman with multiple comorbidities (pulmonary emphysema, peripheral vasculopathy), congenital heart disease operated 25 years ago (closure of interventricular communication [IVC], ductus, and correction of partially anomalous pulmonary venous drainage), reintervention the following year due to IVC patch dehiscence, new heart surgery a year ago due to IVC patch endocarditis and tricuspid valve abscess with IVC closure and tricuspid annuloplasty using the Carpentier-Edwards Physio 32 incomplete ring and resection of tricuspid septal tissue. In the immediate postoperative period, severe tricuspid regurgitation was found but reintervention was disregarded due to its high surgical risk (figure 2A).

A percutaneous valve-in-ring implantation was proposed as an alternative procedure and, in a second procedure, the closure of all paravalvular defects that would have likely occurred after the implantation since we are dealing with an incomplete ring (posterior region) added to the resection of the native valve septal tissue in the previous surgery (figure 2B). The diameter of the ring was measured using a CT scan to decide the size and type of bioprosthetic valve.

In a first procedure, the Edwards XT 29 bioprosthetic valve was implanted via femoral access with overpacing through the Safari guidewire with good ring apposition but 2 residual paravalvular leaks, 1 septal and 1 posterior (figure 2C-E). In a second procedure, and after performing a detailed planning, cardiac CT scan (figure 2F,G) and a rotational angiography, the percutaneous closure of all paravalvular defects was attempted using 2 Amplatzer Vascular Plug III devices with good final outcomes and residual mild tricuspid regurgitation (figure 2H-J).

In both patients, functional class improved and there were no hospital readmissions due to decompensation. With these cases we aim to illustrate that the percutaneous implantation of bioprosthetic valves not designed for this purpose is feasible for the management of dysfunctional tricuspid rings in patients non-eligible for surgical reintervention. In these cases, it is important to carry out detailed prior studies using multimodal imaging (3D echocardiogram, multislice CT scan, rotational angiography...) based on the availability and experience of each particular center, because tricuspid rings are usually asymmetric and often incomplete devices upon which the correct apposition of the valve can be difficult and with significant chances of perivalvular regurgitation that can be usually solved percutaneously.

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