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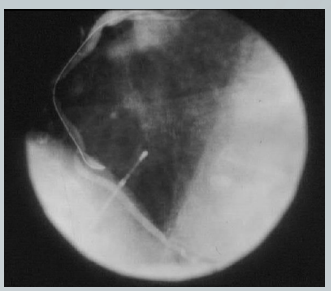

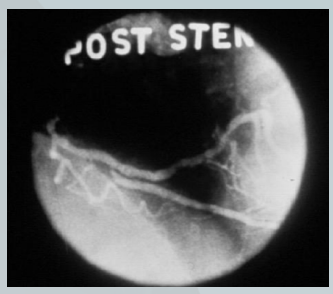

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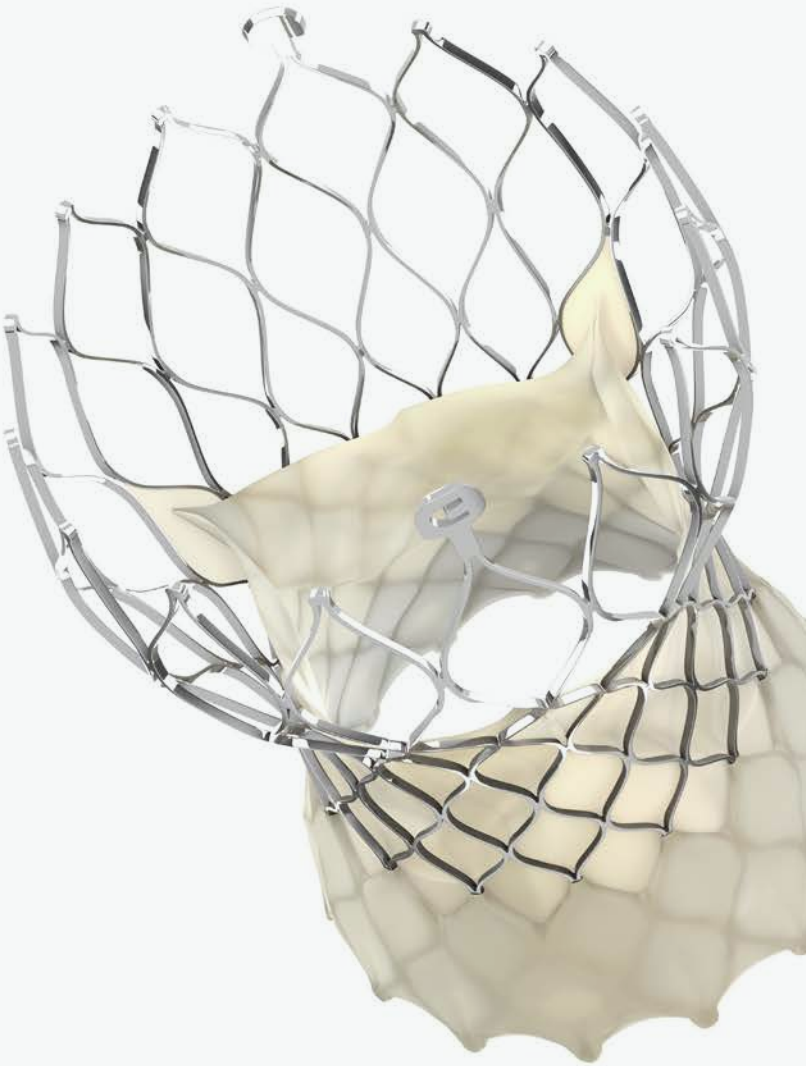

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Summary

Sumario

Analytical summary

Sumario analítico

EDITORIALS / EDITORIALES

EDITORIAL

Rodríguez AE

This year, 12 years are commemorated since I assumed as Editor-in-chief of the Argentine Journal of Interventional Cardioangiology (RACI). For years, we have seen its growth, which can be quantified. However, the acknowledgement received from our colleagues as well as the new generations of specialists' growing interest in publishing are much more important.

THE CORONARY STENT: THE ROCKET ENGINE THAT LAUNCHED CONTEMPORARY CARDIAC AND VASCULAR INTERVENTION

Roubin GS

If Andreas Gruentzig's balloon catheter was the launchpad for coronary and vascular intervention, then the metallic stent was the rocket engine that thrust interventional cardiac and vascular therapies into orbit. Once confidence about the fate of metallic stents in the coronary arteries was established, the entire field flourished1. Rigorous evidence based outcomes were established by scientific work, unparalleled in medicine up to that time. There was an overwhelming commitment to rigorous,randomized, prospective clinical studies, an enlightened advance that continues to this day. Progress in establishing clear, superior clinical outcomes for patients with wide ranging vascular conditions lead to massive clinical adoption and enthusiastic and aggressive investments by commercial entities and entrepreneurs.

CONSENSUS AND RECOMMENDATIONS / CONSENSOS Y RECOMENDACIONES

RECOMMENDATIONS FOR ADEQUATE CORONARY REVASCULARIZATION

Coordinadores: Fernández Murga A, Torresani EM

La revascularización coronaria se inició en el siglo pasado con procedimientos quirúrgicos que fueron evolucionando desde la cirugía de revascularización indirecta (Vineberg, etc.) a la directa (endarterectomía, bypass, etc.). Una vez establecida como técnica, se la comparó con el tratamiento médico de entonces buscando de a poco su lugar en el arsenal terapéutico. En la misma época fue irrumpiendo lentamente la angioplastia(3) como una novedosa opción. Felizmente todo esto ha ido evolucionando con mejoras tanto desde los métodos diagnóstico como terapéuticos (médico, quirúrgico y endovascular) que aún hoy no dejan de sorprendernos. La disponibilidad de semejante arsenal y la complejidad y diversidad de pacientes tratados hace a veces difícil una adecuada elección. El objetivo de este documento es esclarecer las pautas actuales recomendadas para una adecuada revascularización coronaria. Para ello hemos convocado a un grupo de expertos nacionales que desarrollaron los distintos aspectos del tema.

ORIGINAL ARTICLE / ARTÍCULO ORIGINAL

A RANDOMIZED PILOT STUDY OF THE AMICATH® II MICROCATHETER USE FOR THE INTRALESIONAL INFUSION OF DRUGS IN PATIENTS WITH STEMI TO IMPROVE MICROCIRCULATION AND VENTRICULAR FUNCTION. AMIWAY STUDY

Santaera O et al.

In this pilot study it was possible to observe that the Amicath® II catheter was able to cross the lesion in all the patients that was attempted, being able to observe the vessel of the involved territory and infuse the study drugs without complications. LVEF improvement was observed in the medium term in patients where microcirculation was treated ultra-selective in patients with a high thrombotic burden.

CASE REPORTS / CASOS CLÍNICOS

PERCUTANEOUS CLOSURE OF CORONARY-PULMONARY FISTULA WITH MICROVASCULAR PLUG IN AN ADULT PATIENT: CASE REPORT

Nóbile N et al.

Coronary fistulas are rare anomalies that can be asymptomatic or cause serious complications such as myocardial ischemia or heart failure. In the presence of complications, their closure is indicated, either by surgical or percutaneous approach. We present the case of an adult patient with a coronary-to-pulmonary artery fistula, complicated by myocardial ischemia and ventricular arrhythmia, in which percutaneous closure with a Micro Vascular Plug (Medtronic®) was chosen. This is the first report on the use of the device in this clinical scenario in an adult patient in our setting.

LETTER FROM THE PRESIDENT / CARTA DEL PRESIDENTE

Letter from the President of CACI

Cisneros M

Dear colleagues, not only another year finishes, but also another management finalizes, in a country context where uncertainty controls the scenario and we are immersed in a very difficult situation regarding health. Professionals were forced to generate alerts, to get involved so that both patients and government become aware of the critical condition in which we find ourselves.

Editorial

Editorial

Revista Argentina de Cardioangiología Intervencionista 2023;14(4):155. https://doi.org/10.30567/RACI/202304/0155-0155

This year, 12 years are commemorated since I assumed as Editor-in-chief of the *Argentine Journal of Interventional Cardioangiology (RACI).*

For years, we have seen its growth, which can be quantified. However, the acknowledgement received from our colleagues as well as the new generations of specialists' growing interest in publishing are much more important.

Today *RACI* has its own identity; it has kept a quarterly publication of at least 9 articles in each issue among which we can find originals, clinical cases, reviews, consensus and editorials.

Specialists from the most different regions of the world have published reviews, editorials and even original articles in it for years. Among them, we can mention almost all of the best known representatives of our specialty such as the United States of America, Canada, Europe, India, China and of our region, Latin America.

In these 12 years including this issue, 46 specialists from abroad have contributed in *RACI*, which means almost an article by issue.

In the same year of incorporation, we obtained the ISSN number and we started achieving indexations in well-known and different search engines and databases, such as Google Scholar, Latindex, WorldCat, REDIB, J-Gate etc., and so far we have succeeded in being indexed in 11 of them.

Furthermore, all the articles have their own DOI number since the article has been accepted and it is in press.

We are also working with the Editorial in achieving soon a completely automated system for sending articles, via web, within the journal website, which is a very important requirement to be able to index the journal in the biggest search engines and databases, such as PubMed, Embase and Scopus.

Since the year 2020, we started the edition of all the issues in English, which has enlarged the offer to our readers.

This year, by my own decision, and due to new editorial challenges about me, I have decided to leave the Managing position of *RACI Journal*. I believe it is time for new generations of the specialty to continue with this job. There are many young specialists who are very interested in the scientific activity. It is time they took over the task.

From another place, I will continue supporting in what the new authorities may desire.

For all these years, we have shared with the different authorities of CACI, full of new generations of interventional cardiologists, and I have seen their interest regarding the sustained growth of *RACI journal*.

I think it can be no other way: CACI scientific growth must be surely accompanied by a scientific body with its own scientific production, which makes scientific societies survive over the years.

I thank all the different boards of directors for the support they have had for these 12 years, as well as the editorial board that has accompanied me in this adventure.

An affectionate greeting to everybody including firstly to readers, authors, editorial board and to my secretary, Anabel Chesini.

Dr Alfredo E. Rodríguez MD, PhD, FACC, FSCAI, IAGS
Editor-in-chief Argentine Journal of Interventional Cardioangiology (RACI)
Period 2012-2024

The coronary stent: the rocket engine that launched contemporary cardiac and vascular intervention

El stent coronario: el motor cohete que lanzó las intervenciones cardíacas y vasculares contemporáneas

Revista Argentina de Cardioangiología Intervencionista 2023;14(4):156-159. https://doi.org/10.30567/RACI/202304/0156-0159

INTRODUCTION

If Andreas Gruentzig's balloon catheter was the launchpad for coronary and vascular intervention, then the metallic stent was the rocket engine that thrust interventional cardiac and vascular therapies into orbit. Once confidence about the fate of metallic stents in the coronary arteries was established, the entire field flourished[1]. Rigorous evidence based outcomes were established by scientific work, unparalleled in medicine up to that time. There was an overwhelming commitment to rigorous,randomized, prospective clinical studies, an enlightened advance that continues to this day. Progress in establishing clear, superior clinical outcomes for patients with wide ranging vascular conditions lead to massive clinical adoption and enthusiastic and aggressive investments by commercial entities and entrepreneurs.

Today's large and impressive array of percutaneous interventional technologies and procedures largely depend on placing stent based devices in the cardiovascular system. Start with the undeniable and hugely important treatment of STEMI in patients with coronary disease. Move forward to the management of unstable coronary syndromes and unremitting angina in patients with stable disease. Then on to stroke prevention in stenting the carotid artery. And to the stent clot retriever for treating intracranial embolic stroke and the stent flow dividers for intracranial aneurysms. Or "covered stenting" the opening of the clot filled left atrial appendage to prevent stroke in patients with atrial fibrillation.

The entire amazing field of structural cardiac intervention, notable percutaneous valve replacement is largely based on balloon expandable and self-expanding stents. Then comes the clinically invaluable covered stents for aortic and arterial aneurysm, dissection and rupture. And the peripheral stents that are now used to maintain side branch and especially renal and mesenteric artery patency.Last but certainly not least, is the array of stent technologies that, despite exciting alternative revascularization technologies, ultimately underpin safe and reliable revascularization of the the lower extremities in treating severe claudication and critical limb ischemia.

The metallic stent was the engine that informed the future that was to become interventional cardiac and vascular work. No one individual was responsible for this turn of events. Many extraordinary individuals, over a generation of innovation, clinical experience and scientific validation were responsible.

ORIGINS OF THE STENT

Investigation into intra-vascular prostheses dates to work in the late 19th century and notably vascular radiologists and surgeons in the mid 20th century[2]. Robert Ersek patented an expandable mesh stent device in the 1950's to assist in aorto-iliac graft surgery and Charles Dotter, the grandfather of all percutaneous vascular intervention, placed coil stents in animal arteries in the 1960's. Dotter was the first to use the term stent to describe the metallic intra- arterial prosthesis. Dotter borrowed the term from the dental surgical literature after Charles Stent developed a technique using Gum Arabic to hold tissue "in place" – Stents' Compound. There were multiple innovative surgeons, angiologists and radiologists in the 1970's that proposed stenting techniques of various types in order to expand tubular structures in the body. But the one individual to actually advance his ideas to clinical practice was Cesare Gianturco. A retired radiologist from Champaign Illinois, Gianturco developed a self-expanding, Z shaped stainless steel stent device that could be collapsed into a delivery catheter and deployed by a push-pull release technique. The device was manufactured by Cook Inc. (Bloomington IN) and used in patients with encroaching malignant tissue obstructing the vena cava. In retirement, Cesare Gianturco worked part time at the MD Anderson Cancer Center in Houston TX. His self-expanding Z design was to become, in time, the fundamental design of all the forthcoming stent graft technology for large arterial work. But Gianturco is recognized for much more. Along with Dotter**,** Eberhardt Zeitler and other pioneering radiologists of that time, Gianturco was fascinated by Andreas Gruentzig' inflatable balloon technology. In 1979 at MD Anderson Hospital Gianturco wrapped a clever interwoven coil on a "Gruentzig balloon" and successfully deployed the device in the iliac artery of a dog.

As the 1980's progressed others around the world were working on arterial stenting. Hans Wallsten, an engineer was working in Switzerland on a clever woven nitinol device he named the Wallstent. This was to become the first metallic device used clinically in the coronary arteries. In the Soviet Union, Iosif Rabkin an interventional radiologist placed a "Dotter like" coil in a patient's iliac artery and also reportedly did a similar procedure in a carotid artery.

THE UNMET CLINICAL NEED

Clinical device development requires more than clever ideas and one off 'heroic' procedures. As Andreas Gruentzig demonstrated to the world and taught, the process requires dedicated, rigorous and scientific validation – first in bench top and in vivo animal studies – and then rigorous prospective clinical studies. Most importantly, there needs to be a well-defined, unmet clinical need. And then detailed engineering, product development and regulatory support.

As Gruentzigs' balloon angioplasty gained acceptance around the world, the development of coronary stenting was driven by an obvious, unmet clinical need. By the mid 1980's thousands of anatomically suitable patients were benefiting from acceptable balloon outcomes. But Andreas Gruentzig and the cardiology community were acutely aware of the shortcomings of PTCA. The overwhelming problem was the risk of abrupt closure of the artery either during the procedure or in the hours or days after balloon dilatation. Abrupt closure resulted in significant myocardial infarction and death[3]. Even if emergency CABG was available it resulted in suboptimal outcomes. The need for back up CABG severely restricted the practice of PTCA. And the risk of abrupt closure was significantly higher in severe diffuse, calcified and tortuous lesions and in treating multi-lesion and multivessel disease and this severely limited the application of PTCA. Balloon dilatation alone in this anatomy and even "ideal" lesions invariably resulted in plaque and intimal tearing and dissection. This was often flow limiting and was rapidly associated with thrombus accumulation and occlusion.

It is also worth noting that antiplatelet regimens were as yet poorly developed and limited to aspirin, dipyridamole and dextran infusions.

In the early 1980's much thought and innovation was being directed towards plaque modification to overcome the shortcomings of simple balloon dilation. The disrupted plaque and in eccentric disease, temporary stretching of the normal vessel wall. Gruentzig's lab at Emory University was focused on developing a laser catheter and Andreas openly discussed the use of heated balloons. Others, were investigating atherectomy with a variety of approaches including John Simpson's directional cutting device. None of these approaches were to prevail in solving the problem of abrupt closure and restenosis after balloon angioplasty of coronary stenosis.

ENTER THE CORONARY STENT

Legions of stent designs, innovative concepts and commercial coronary stent products would evolve. But the genesis of all the clinical progress that was to come, arose from 3 groups around the world who were working on the challenge of a safe and effective stent device for the coronary arteries. The obstacles and unknowns were many and those of us developing the first coronary stent devices were, as is often the case with device development, completely naive to the challenges ahead.

In early 1985, Cesare Gianturco visited with Andrea Gruentzig and myself at Emory University. In his hand he had a tiny plastic tube with a braided guide wire "pusher" inside and compressed in one end, a small self-expanding Z stent. The rudimentary device that he presented us with was a miniaturized version of the large Z stents that Cook Inc (Bloomington IN) had made for his use in IVC stenting. When he pushed on the wire, the stent "sprung out" of the "catheter" on to Andreas' desk. He handed me the device and said "Gary go and see what happens when you put these into the dog coronary artery". Easier said than done – as I was to discover. Andreas Gruentzig was to die tragically in an airplane accident some months later and was never to participate in the stent development. The self-expanding Z was a failure in about every way imaginable but it did focus our attention on what would be required for a safe and effective coronary stent. Cesare Gianturco was to return some weeks after Andreas' passing to offer commiserations and in response to my feedback about the shortcomings of the self-expanding stent approach, we set about improving a balloon expandable design he had conceived and reduced to practice over a half decade earlier!

Now 40 years on it is almost impossible to understand how challenging was the task! To begin, guide catheters, guide wires and PTCA balloons were still "primitive".

Safety and efficacy involved designing a stent device that could be safely tracked through a guide catheter to the lesion and not be dislodged from the balloon in the process. It had to be deployed precisely in the correct place and be reliably expanded to a predetermined diameter. The stent needed to hold the tissue apart and not migrate, or fracture or perforate or thrombose. Choice of material and biocompatibility was a huge unknown.

For the cardiology and scientific community and FDA regulators and potential industry supporters – the fate of a tubular metal device in the constantly moving, twisting coronary arteries was the primary question. With the assistance of Keith Robinson PhD, I set up the animal Lab at Emory University and acquired the funding to place stents in multiple animal models, short term and long term, normal and atherosclerotic, coronary and iliac. We studied the angiographic outcomes, the histologic and scanning EM responses and the integrity of the devices. We published in multiple peer reviewed journals and sent our primary specimens for independent review by the National Institutes of Health[4,5]. My colleague Julio Palmaz thanked me for this work as he wrote "I regard your work as objective, honest and smart. This is very important for all of us in this subject". One "lightbulb moment" occurred during work in the severely atherosclerotic rabbit iliac arteries. Balloon dilatation had completely disrupted the plaque and compromised the lumen. Stent placement completely transformed the angiographic appearance! [6]

Progressing to clinical evaluation was the next hurdle. Surgical aortic valve implants had created liability problems and Cook Inc were reluctant to commit. I submitted an investigator sponsored IDE (Investigational Device Exemp-

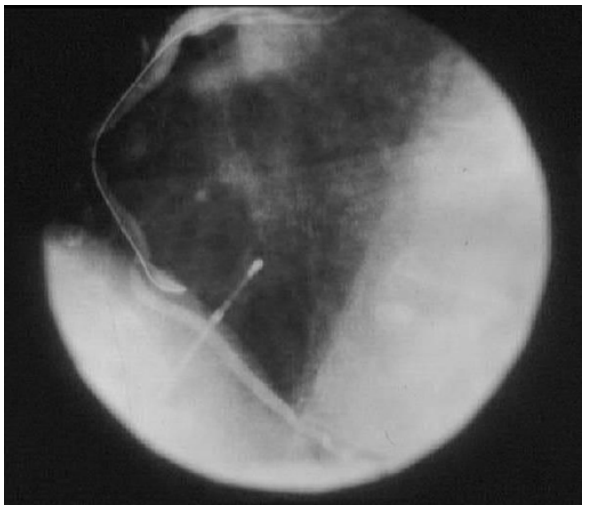

Figure 1. *Abrupt closure of the right coronary artery after elective PTCA. The patient experienced severe chest pain and ST-segment elevation in the lateral leads of the ECG. 1987, Emory University Hospital.*

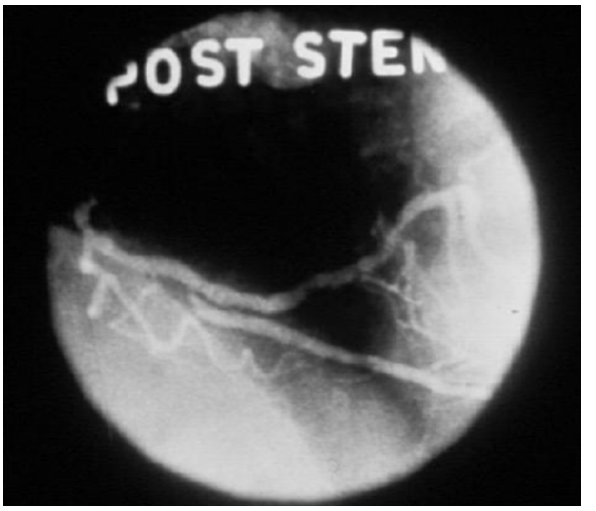

Figure 2. *A 3 mm by 20 mm Gianturco-Roubin stent is advanced to the PTCA site with restoration of TIMI3 flow, complete resolution of chest pain and ECG changes.*

tion). No one in the world at that time had implanted a balloon expandable coronary stent. Today it would be called an investigator sponsored EFS (Early Feasibility Study). The protocol was specifically designed to test the hypothesis that a coronary stent could solve the problem of abrupt closure after balloon angioplasty and turn Andreas' method of revascularization into a reliable and safe procedure. The first balloon expandable coronary stent in man was implanted in September 1987 **(Figures 1 and 2).** It opened the artery and reversed the evolving myocardial infarction. The rest is history.

Multiple multicenter studies followed[7,8]. The FDA were to finally approve the Gianturco-Roubin Stent in 1994, 1 year before the approval of the Palmaz-Schatz stent[1].

The availability of the coronary stent facilitated the rapid expansion of coronary intervention. Operators were finally able to approach more complex lesions and multivessel disease and do so with much greater safety.

Rodriguez et al. in Argentina[9,10] were the first to study if the luminal improvement brought about by the stent would improve restenosis rates. They showed it did but incompletely. Time was to prove that optimal results required the stent to deliver antimitotic drugs. This ultimately revolutionized percutaneous coronary intervention.

It is noteworthy that before drug eluting stents, a huge effort was devoted to testing systemic agents to reduce restenosis rates. The stent was to provide the ultimate solution. Just as Andrea Gruentzig taught us that we did not need to open the chest to treat a 10 mm coronary stenosis – the stent facilitated focused drug delivery for restenosis, avoiding systemic side effects. This concept was an early element of stent development even before FDA approval[11].

In Switzerland, Hans Wallsten was able to miniaturize his self-expanding, nitinol mesh sleeve and design a delivery catheter and retractable sleeve that could potentially track through a coronary guide. He wanted to take this device to a cardiologist Jean Marco in Toulouse France but Jean Marco was not available that day and his colleague Jaques Puel is credited as being the first to implant a self -expanding metallic device in the coronaries. After this initial implant, Ulrich Sigwart in Lausanne took on "the charge" and without much thought to study objectives and prospectively defined endpoints, placed a series of Wallstents after PTCA electively and emergently in a variety of clinical settings. The results were mixed with episodes of stent thrombosis, MI and adverse outcomes. Sigwarts's work was the first to be published in the New England Journal of Medicine[12], but it was a note of caution for those of us coming close behind - albeit with different, balloon expandable stents with less metal and less moving components. Self-expanding stents were never to become effective devices for the coronary arteries. Ulrich Sigwart, to his credit, went on to develop one of the best designed laser cut, balloon expandable, tubular stents to make it into clinical practice.

In San Antonio, TX, Julio Palmaz an innovative radiologist was busy miniaturizing the balloon expandable stent he had conceived for peripheral vessels. The tubular mesh design was inherently too stiff and unyielding for easy placement in the coronaries. Palmaz was ultimately to team up with Richard Schatz to modify his design for a coronary application.The idea was to simply cut the device and link the 2 halves with a single connector.

The Palmaz Schatz stent IDE was an "all comers approach" with elective placement in the majority of appropriate lesions and additional use for threatened (severe dissection) or actual abrupt closure patients. The results of this study were difficult to interpret and the FDA panel decided against PMA approval until I year after the approval of the Gianturco-Roubin stent[1]. Randomized trial data was to ultimately launch the Palmaz-Schatz[12].

The demand by the interventional cardiology community for a device to make PTCA safe was tremendous. Over 100 thousand GR stents were distributed in the first 18 months of availability. Early in the investigation phase of coronary stenting, we were able to show the value of stenting for the treatment of ST elevation myocardial infarction[10,14]. But the Palmaz-Schatz stent was a better design in terms of plaque coverage and was to prevail in the market place. It would soon become apparent that the multiple laser cut tubular designs that were to follow, were more ideal for the local drug delivery that would largely solve the second challenge of late restenosis[15].

CONCLUSION

There is much more to the story of coronary stent development. The low profile, trackable devices we use today were but a dream during the early work required to validate coronary stenting. Forty years ago we struggled with the bulky devices using 8F and 9F guiding catheters and 0.16" and even 0.18" guide wires to get the stents down the coronaries. Optimal dual antiplatelet therapy (DAPT) was unknown and we struggled with both stent thrombosis and hemorrhagic complications as we first "under shot" then "over shot" therapeutic efforts. Antonio Colombo in Milan was to direct us to an optimal "DAPT" regimen. Other colleagues including Patrick Serruys in Rotterdam, Marty Leon in the USA and Jean Marco in France made invaluable contributions. Richard Stack at Duke contributed to many stent designs and notably the bioabsorbable platforms that are not yet perfected but will ultimately find their place.
But finally, let us all acknowledge that the coronary stent to this day functions on the basic brilliance of Andreas Gruentzig's balloon device.

Gary S. Roubin MD PhD FSCAI FACC.

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Recommendations for adequate coronary revascularization

Recomendaciones para una adecuada revascularización coronaria

Authors: The names of the authors appear in the respective sections. Coordinators: Arturo Fernández Murga, Ernesto M. Torresani. Reviewers: Aníbal Agustín Damonte, Alejandro Palacios, Antonio Alberto Pocoví, Juan Manuel Telayna

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INTRODUCTION

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Coronary revascularization began during the last century with surgical procedures which evolved from indirect revascularization surgery Vineberg, etc.) to direct one (endarterectomy, bypass, etc.)[1]. Once established as a technique, it was compared with the medical treatment of that time[2], looking little by little for its place in the therapeutic arsenal. At the same time, angioplasty[3] was slowly emerging as a novel option. Fortunately, all this has been evolving with improvements in both diagnostic and therapeutic methods (medical, surgical and endovascular) that still surprise us. The availability of such arsenal and the complexity and diversity of the treated patients sometimes makes it difficult a proper choice. This document objective is to clarify the current guidelines recommended for an adequate coronary revascularization. That is why, we have convened a group of national experts who developed the different aspects of the issue.

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1) DIAGNOSTIC TOOLS

A) Non-invasive

a) Search for ischemia. Role of functional testing. *Dr. Leonardo De Benedetti (Clinical Cardiologist, Specialist in Nuclear Medicine), Dr. María Silvia Bidonde (Clinical Cardiologist, Specialist in Echocardiography), Dr. Adrián Hrabar (Clinical Cardiologist).*

Graded Ergometric Test. Ergometry (**ECG**). It remains the initial diagnostic test recommended in patients undergoing stable ischemic cardiopathy with intermediate probability who can exercise and have an interpretable resting electrocardiogram[1]. Detrano et al [2] reported 68% sensibility and 77% specificity for the detection of coronary artery disease in a meta-analysis which included more than 24,000 patients and 22 years of investigation. The ST-segment depression along with exercise duration and capacity are considered strong predictors of future cardiac events[3]. The Duke Treadmill Score (DTS) is a widely accepted tool which gives prognostic additional information combining exercise duration, ST segment changes and angina[4]. However, DTS is less useful when test result falls in the intermediate risk category which leads physicians to order additional images to increase sensitivity.

Myocardial perfusion studies with radioisotopes: Myocardial perfusion studies in SPECT with radioisotopes and their different protocols (physical or pharmacological stress) are distinctly functional studies which assess both relative perfusion and cell functional integrity. They are useful in the angina symptoms evaluation and patient selection for eventual revascularization, they allow cardiovascular risk stratification into high (>3% death and/ or annual AMI or low (<1% death and/or AMI annual) when assessing the severity and extent of myocardial ischemia quantified by scales such as the summed stress score (SSS: % myocardial damage), summed rest score (SRS: 0% scar and/or hibernating tissue) and summed difference score (SDS: % ischemic myocardium) with a high prognostic value of ischemic events (non-fatal AMI, death due to AMI, death or need for revascularization)[5]. Triggering addition allows the evaluation of functional parameters such as global and regional parietal motility, the parietal systolic thickening, the ventricular volumes (VES, VFD), the left ventricular (LV) ejection fraction (EF) at rest and post-exertion and the pulmonary radiotracer uptake (PRU), right ventricular uptake (RVU) and left ventricular transient dilation (LTD) in stress having independent value in diagnosis, prognosis and risk stratification with 83% sensibility for the detection of single vessel disease in comparison with 93% for patients with 2-vessel disease and 95% with 3-vessel disease[6]. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging, obtained after stress with exercise or vasodilators, report 87% and 89% sensibility, 73% and 75% specificity and 91% and 90 normality rate, respectively. The patients who benefit most[7] from the utilization of perfusion studies in triggered SPECT are those who have intermediate probability of coronary heart disease, with poor exercise capacity and/ or who do not have an interpretable electrocardiogram at rest (BCRI, pre excitation, pacemaker, ventricular hypertrophy, etc). A combined analysis of 19 studies with the participation of 39,173 patients informed an event rate of 0,6% per year for patients with normal explorations. Patients with abnormal pharmacological stress studies have more annual rate of cardiac events (1.78%) than those with normal exercise exploration; in a combined analysis of 69,655 patients, those with moderate or severe abnormal explorations had an annual cardiac death rate or AMI of 5.9% per year (average follow-up of 2,3 years)[7]. The major prognostic indicators of high risk[5,6] are: a) Severe left ventricular dysfunction (EF and LV <35%) associated or not with myocardial ischemia, b) High treadmill score (score <11), c), Post-stress severe left ventricular dysfunction (EF and LV drop >5% post-stress), d) Extensive perfusion defects (>20% of LV myocardium or proximal LAD territory), e) Multiple profusion defects of moderate extension (multiple vessel disease, f) Extensive fixed defects (> 10% scar) associated with ischemia, g) Ventricular volumes rise (EDV, ESV) at rest or stress, h) Left ventricular dilatation and lung uptake after stress where revascularization has shown prognostic improvements and guidelines endorse the use of stress images due to the strong evidence that revascularizations guided by ischemia improve symptoms and survival free from events in comparison with a guided strategy by coronary stenosis alone. Meanwhile, results without significant ischemia or presence of extensive myocardial infarction (>10% scar) identify patients unlikely to benefit from revascularization [8]. Another SPECT application has been in emergency units or in patients with acute thoracic pain in the first hours of pain, with inconclusive ECG, normal biochemical markers with high sensibility and specifici-

ty close to 100%, in AMI diagnosis in low or moderate risk patients with a negative predictive value of 99% [9]. The latest generation of SPECT CZT equipment allows the functional study, assessment of myocardial flow and coronary reserve adding the microcirculation assessment which also has prognostic and therapeutic implications in the management of patients undergoing angina pectoris and coronary arteries without obstructive lesions. In the future, hybrid equipment SPECT/CT will enable, apart from the perfusion assessment with function data provided by SPECT, the anatomy assessment (culprit vessel) characteristics of coronary plaque and calcium score provided by angiotomography which would increase the diagnostic specificity (from 63% to 95%) and the method´s positive predictive value (from 31% to 77%) [10].

Stress Echocardiogram: It is a functional test designed to identify ischemia presence and characterize it by assessing its extension, anatomical distribution and functional repercussion in the left ventricle. Its main purpose is the diagnosis, prognosis and appropriate risk stratification of cardiovascular events (11,12). Myocardial ischemia diagnosis is performed through identifying motility disorders or regional parietal thickening (al rest or stress induced) or EF drop and post-exertion, being the systolic thickening alteration the most specific sign. It is also possible the assessment of other auxiliary parameters such as the myocardial deformation (strain rate) and the coronary flow reserve (11,12). The stress echocardiogram can be done with exercise (vertical or supine cycle ergometer and treadmill) or with vasodilator drugs like dipyridamole (reduces subendocardial flow supply) or positive inotropics like dobutamine associated with atropine which will determine an increase in myocardial oxygen demand through the increase in heart rate, blood pressure and parietal motility, being this drug combination the most used. Echo stress with physical as well as pharmacological urgency has similar diagnostic accuracy (11,12). On the one side, echo stress with exercise is recommended in most cases because it preserves the normal electromechanical response and provides prognostic information on functional status with lower cost and lower incidence of complications regarding pharmacological urgency (12,13). On the other side, pharmacological stress is reserved for patients unable to perform an adequate level of exercise (intermittent lower limbs claudication or low functional capacity) and/ or not interpretable electrocardiogram (LBBB, pacemaker rhythm), it can also be used for the myocardial viability recognition through the analysis of contractile reserve using low-dose of dobutamine. The biphasic response is a characteristic of viable myocardium, and predicts, with high specificity, ventricular function recovery after revascularization [5,11,13]. This is an effective study for stratifying patients according to the risk of later cardiovascular events, being the most useful test when there is an intermediate probability of coronary artery disease. It presents sensibility and specificity for the diagnosis of obstructive coronary disease of 80-85% and 80-88% respectively with an excellent negative predictive value in patients with a negative test (without inducible parietal motility alterations) and a very good prognosis with an annualized events rate (death or myocardial infarct) of 0.5%[5,12,13]. The fundamental objective in noninvasive assessment of stress studies is to identify patients at high risk for adverse events, with wide range of abnormalities of parietal motility posterior to stress (3 from 16 segments), as well as transient ischemic dilation of the left ventricle and presence of severe mitral regurgitation since this patients´ group are at high risk of death or myocardial infarction of 3% per year, allowing an appropriate indication of early revascularization, and, in this way, improving the prognosis (11,12). The stress echocardiography has some limitations due to poor echocardiographic window, operator subjectivity, suboptimal endocardial visualization, impossibility of reaching the planned heart rate. However, its high availability, low cost, non-invasive character and absence of radiation prove it to be, in general, an excellent technique election in experienced centers (11).

Role of non-invasive functional testing in ischemia detection: The performance of non-invasive functional tests depends on the clinical probability of suffering from coronary heart disease, acquiring its results greater likelihood in patients with intermediate pretest probability (**Table1**)[14]. The sensibility and specificity of graduated ergometric test are far from optimal, making the probability of short-term and medium-term prognosis of an ischemic event to be low. Associated to imaging like in stress echo or with the myocardial perfusion studies with SPECT, diagnostic and prognostic accuracy increases. Choosing the test type depends on the availability, expertise and performance of the test regarding the characteristics of each case (**Table 2**) [5,14,15]. The non-invasive tests are commonly used in 2 different scenarios, Acute Coronary Syndrome (ACS) and Chronic Coronary Syndrome (CCS). In ACS, patients at low risk are treated or having diagnostic doubts about chest pain areas for diagnosis and re-stratification of ischemic risk [16]. In CCS, functional non-invasive tests are useful for diagnosis and risk stratification making the difference between low risk population with negative results (AMI annual risk and cardiovascular mortality < 1%) and that one with positive results, high risk, with ischemic amount > 10% in, and/or development of 3 or more new dyskinesia segments with ecostress with an event rate of > 4% [17,18]. In 2011, the unicentric registry results (Cedars-Sinai) were known after more than 7-year-follow up including 10,627 patients, showed that those with ischemic amount of < 10% evolved better from me-

Table 1. Pre-test probability of obstructive coronary artery disease in 15,815 symptomatic patients according to age, sex and nature of symptoms in a combined analysis of contemporary data. [1]

	Typical		Atypical		Non-anginal		Dyspnoea	
Age	Man	Woman	Man	Woman	Man	Woman	Man	Women
30-39	3%	5%	4%	3%	1%	1%	0%	3%
40-49	22%	10%	10%	6%	3%	2%	12%	3%
50-59	32%	13%	17%	6%	11%	3%	20%	9%
60-69	44%	16%	26%	11%	22%	6%	27%	14%

Table 2. Diagnostic testing performance to detect anatomically significant coronary artery disease (>50% stenosis).

Test	Sensitivity (%, 95% IC)	Specificity (%, 95% IC)	+ LR	- LR
Ergometry	58 (46-69)	62 (54-69)	1.53 (1.21-1.94)	0.68 (0.49-0.93)
Stress echo	85 (80-89)	82 (72-89)	4.67 (2.95-7.41)	0.18 (0.13-0.25)
SPECT	87 (83-90)	70 (63-76)	2.88 (2.33-3.56)	0.19 (0.15-0.24)

+LR Positive likelihood ratio. **-LR** Negative likelihood ratio. **SPECT** Myocardial perfusion test (exercise with or without dipyridamole or adenosine). **Stress echo** (with exercise).

dical treatment, and those with > 15% of induced ischemia with non-invasive stress tests, evolved better from invasive strategy regarding mortality [6].

Due to available evidence, non-invasive functional tests are essential tools for diagnosis and risk stratification of patients undergoing coronary disease, and they are a useful guide in decision making with regard to the therapeutic strategy to follow, dubious and controversial, impressing that those with high ischemic amount and/or those non-responsive to medical treatment applying current guidelines, would benefit from an invasive strategy, emphasizing that the decision must be individualized for each patient, carefully evaluating risk-benefit balance.

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b) Feasibility assessment. *Dr. Mirta Diez (Clinical Cardiologist).*

Coronary heart disease (CHD) is the major etiology of heart failure (HF) in developed countries. Definition of ischemic-necrotic cardiomyopathy requires the presence of severe left ventricular dysfunction (LVD) and significant CHD. LVD not always is an irreversible process related to previous AMI, it is also observed when there is viable dysfunctional myocardium, but with capacity for contractibility recuperation with revascularization. Viable myocardium physiopathology involves metabolic, neuro-humoral and inflammatory changes leading to adverse myocardial remodeling and to contractile dysfunction due to significant deterioration of myocardial blood flow and/or reduction of coronary flow reserve. Strictly, within feasibility concept, we recognize the hibernating and stunned myocardium. The first is a process of reduced of coronary flow at rest which only enables to perform basic functions and conduct to myocyte structural alterations and to chronic contractile dysfunction: in the second the coronary flow reserve is altered and changes are mainly metabolic [1].

Next, imaging methods used for feasibility assessment are described.

Doppler echocardiogram: It is indicated in all patients undergoing ischemic-necrotic cardiomyopathy. It allows evaluating ventricular function, cardiac cavities diameters, mitral regurgitation and pulmonary pressure estimation. Facts associated with feasibility absence are: LV severe dilation and end-systolic volumes higher than 79 ml/m^2. Parietal thickness to end-diastolic higher than 6 mm is associated with function recovery with 94% sensibility (Sen) and 48% specificity (Spec); when the contractile reserve is lower rarely is present[2]. Through stress echocardiogram with dobutamine IV, biphasic response can be seen with contractility increase with low doses, and deterioration with high doses considering highly suggestive of viable myocardium with 82% sensibility and specificity [3,4], having some limitations such as inter-observer variability, and occasionally the absence of appropriate window; 3D echo may be a more favorable option in these cases.

Myocardial perfusion SPECT: It is based on the measurement of myocardial uptake of radiotracers including thallium 201 and technetium-99m. It is widely available and provides information on perfusion at rest, stress-induced ischemia and eschar. It has (83-87%) high sensibility, but (53-68%) low specificity.

Nuclear magnetic resonance: It provides us information on structure and cardiac function, size, volume and parietal motility. With the addition of gadolinium, it informs about the viability presence and quantifies the myocardial eschar with 83% sensibility and 88% specificity. When es-

char transmurality exceeds 50%, the possibility to recuperate function is less than 10%. In these cases, the use of dobutamine improves detection of contractile reserve. The method´s limitations are its low availability, the higher cost and time required to acquire imaging,

Positron emission tomography (PET): It is a technique which identifies myocardium with intact metabolic function; it uses two radiotracers, ammonia ($N\text{-}NH_3$) and fluorodeoxyglucose (FDG) which evaluate glucose perfusion and metabolism. The mismatch between reduced perfusion and hypocontractility, but with preserved metabolism reflects hibernated myocardium with 92% sensibility and 63% specificity to predict contractile function recuperation after revascularization [7]. We can mention disadvantages such us the necessity of a cyclotron to generate tracers and the complex protocols in patients with metabolic disorders.

Conclusions: Studies which intended to evaluate the viability and ischemia role to decide revascularization showed dissimilar results, and its limitation are: variability in the imaging technique used and lack of adherence to revascularization recommendations depending on the presence or absence of viability [8,9]. Multimodality imaging assessment allows improving precision and we must always prioritize the individualized decision to each patient´s characteristics and to discuss them in a Heart Team.

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c) Coronary CT Angiography. *Dr. Pablo Pollono (Interventional Cardioangiologist - Imaging Specialist).*

Jumping from axial tomography to helical tomography with multiple detectors has opened a new world for this method, allowing the correct visualization of mobile structures like the heart. This has been achieved from: a) optimization of spatial resolution, favored by a large number of detector rows which increases the coverage area, new generation of small detectors and new acquisition protocols, and b) temporal resolution improvement from gantry rotation allowing partial acquisitions more effective. These improvements enable to perform a correct visualization of all cardiac structures and the appropriate programming of invasive therapeutic procedures [1].

Patient preparation: The patient should fast; all precautions must be taken for the use of intravenous contrast substances. Low and stable cardiac frequency is the best friend of cardiac tomography, being necessary in some cases, oral or intravenous beta-blockers premedication before the procedure even with the new tomographs. To explain the patient how to breathe and contain breathing reduces the respiratory motion artifacts, details that allow us to perform quality acquisitions.

Image acquisition: Images can be acquired in prospective or retrospective format. In the retrospective format, radiation is used during all cardiac cycle, and even if any phase of cardiac cycle could be used for coronary reconstruction, a diastolic phase is usually used. On the one hand, this type of reconstruction also allows evaluating left and right ventricular functions, ventricular volumes measurement, parietal motility abnormalities, thinning area or ventricular aneurysms. On the other hand, prospective acquisition has the advantage to reduce radiation quantity drastically and the disadvantage of just permitting the reconstruction of only one phase of cardiac cycle in diastole, not allowing ventricular function assessment [2].

Coronary calcium score: Even if the presence of calcium in the coronary arteries increases with age, deposits can be find in all age groups, being an atherosclerotic burden signal and also having higher probability of "soft" plaques. The more coronary calcium we have, the higher possibility of significant obstruction and the higher risk of cardiovascular events. In CT, we use Agatston score based in the analysis of imaging without contrast having established an arbitrary value of 130 Hounsfield Units (HU) in order to separate true calcifications of high pixels density; thus a scale was set which evaluates the calcium score from 0 to > 400 Agatston Units establishing in this way the probability of plaque presence (from null to very high) and with this the cardiovascular risk. Usually, the major calcium quantity is observed in proximal and medium segments of coronary arteries. In symptomatic patients, it has high sensibility (>90%) but low specificity (≤50%) for detecting severe obstructions compared with conventional Cine-coronary angiography. Additionally, in asymptomatic patients or with atypical chest pain and intermediate CV clinical risk, calcium score would permit to identify who do not undergo coronary disease making it possible a better stratification [3].

Non-invasive coronariography: It is positioned by the current indications as the study of choice upon admission of low or intermediate risk patients who consult about a probable coronary syndrome for evaluation of coronary artery disease [4]. The greatest strength of the method is to discard coronary disease due to its high negative predictive value. With the non-invasive coronariography using tomography we can perform multiplanar reconstructions allowing us to visualize coronaries in axial, sagittal, coronal, longitudinal slices, as well as to rotate them 360 degrees and generate similar views IVUS, being able to carry out a proper assessment of the plaque, presence or not of calcification, degree of obstruction and its lengh. We can also evaluate indirect signs of vulnerable plaque, such as: low-attenuation lipid core (< 30 HU), b) positive remodeling, c) punctiform calcifications (< 3mm that occupy < 90 degrees of vascular wall, d) significant obstruction, and e) napkin ring sign, characterized for a plaque with central core of low attenuation with outer edge of greater attenuation which would represent a thin-cap fibroatheroma [5,6]. In total occlusions, tomography allows us the characterization of proximal cap, if it is concave or convex, calcification degree and extent, occlusion length and distal beds evident through collateral circulation not often visible in angiography. Patients with prior revascularization surgery require a different programming in image acquisition, so a wider FOV (field of view) must be used from clavicles to whole cardiac silhouette. Besides bridges characterization (breast, radial and venous), we can evaluate its permeability, describe its course, lesions, diameters and lengths [7]. In patients with stents, we should previously know its location, material, diameter, etc., bearing in mind that metal generates artifacts which make it difficult an adequate assessment of vessel lumen and thereby the obstruction degree (if there are any) specially if they are ≤ 2.5 mm. A slightly different situation arises in the stents evaluation of ≥ 3.0 mm, however, artifacts are present depending on the strut thickness and/or the overlapping cases or the bifurcations where the visualization of the stent lumen and the origin of the secondary branch is difficult. Consequently, state-of- the-art tomographs count on tools that allow reducing motion artifacts, of calcium and metal [8]. The study may not be of utility if a proper preparation is not performed: cardiac frequency, in the presence of arrhythmias (auricular fibrillation, frequent extrasystoles, bigeminy, etc.), in extensive calcification cases, small caliber stents and/or respiratory artifacts in aged patients, hearing-impaired or with severe pulmonary diseases. Finally, acquisition artifacts for electrocardiographic trigger errors exist, which can be improved with raw data analysis in the post-processing.

The future of cardiac tomography: Even if, tomography is mainly an anatomic study, lately we find the possibility to merge images with radioisotope functional studies to be able to evaluate exactly which of myocardial territory corresponds to each vessel [9]. Undoubtedly, the major breakthrough is the possibility to perform a functional evaluation with data from the cardiac tomography acquisition thanks to the use of complex algorithms that allow analyzing the coronary fractional flow reserve (FFR-CT) in non-invasive form, and in this way improve diagnostic strategy in comparison with invasive angiography [10].

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B) INVASIVES

a) Cineangiocironariography. *Dr. Oscar Carlevaro (Interventional Cardioangiologist).*

Coronariography (CCG) is a luminogram (negative visualization of arterial lumen) which provides anatomical data, severity and extension of coronary heart disease. In spite of its limitations remains the reference pattern providing prognostic information as well. Complication risk is very low, with a lower mortality of 0.2%, and a higher complications incidence less than 0.5%.

Indications: 1) Acute coronary syndromes (infarct, instable angina, etc.) where clinical suspicion is confirmed or discard and sometimes it is complemented with endovascular therapeutic, 2) in patients undergoing known or suspected coronary heart disease, asymptomatic or symptomatic stables per angina with previous functional studies positive for ischemia, 3) patients with arrhythmias whose trigger may be ischemia, 4) as part of preoperative evaluation in valvulopathies, 5) as evaluation in cardiomyopathies, or 6) as patient assessment prior to non-cardiac surgery. It is important to evaluate if the patient has relative or absolute contraindications in the

moment of the procedure, such as: febrile or infectious states, severe renal insufficiency with risk of decompensation and dialysis, etc., or irreversible severe compromise of general state implying futility. There are appropriate criteria for the use of CCG as diagnostic method [1] and it depends on: a) presence/absence of angina symptoms or cardiac insufficiency, b) stress test trough gamma camera or positive stress echo for ischemia, c) risk level reported by these studies and d) pre-test probability of the disease. Generally, it is suitable to perform in patients with acute coronary syndromes or in severely symptomatic patients or with progression of angina, and unsuitable in those asymptomatic or with pre-test low probability in spite of positive findings in functional studies.

Vascular access: It can be divided between upper limbs (radial, cubital, brachial and axial), and the common femoral in lower limbs. Being possible priority should be given to radial access since it has lower incidence of serious vascular complications (pseudoaneurysm, hematoma and retroperitoneal hematoma) [2]. Radial access has other advantages: it is more comfortable for the patient, and permits precocious walking. Its disadvantages are: the presence of vasospasm, limited caliber, marked tortuosity in some patients, and a slight learning curve. It also must be avoided in patients under dialysis and considered its eventual use as a conduit in coronary surgery because a thrombosis incidence of approximately 5% is observed after being used as access. Femoral access must be used when the diameter of radial artery does not accept thick diameter materials (7 french or higher). If possible, puncture must be performed in the anterior face of common femoral artery below the emergence of inferior epigastric artery and, if available, under ultrasound guidance. It must be considered also the heparin reversal with protamine, especially in obese patients.

Complications: Among CCG more frequent complications, those related to the access which changes depending on localization can be mentioned. In radial or cubital routes, hematoma is rare as well as hand ischemia. Radial route has an incidence of thrombosis of about 5% so the habitual dose of heparin is doubled, and on rare occasions an arteriovenous fistula can be observed. In femoral route, thrombosis is rare as well as distal embolism. Local hematoma is usually common and retroperitoneal is exceptional, can be serious; pseudoaneurysm could also occur at the puncture site. Arteriovenous fistula can be rarely observed. The rate of complications can be reduced by ultrasound-guided access and the use of radioscopic anatomical repairs during puncture. When the approach is through puncture, humeral route has high incidence of hematoma and pseudoaneurysm, but it hasn't in the cases of artery dissection. With regard to the complications related to coronary access, the trunk or right coronary dissection can be observed, particularly if vessels are thin or the catheter produces vasospasm and neither catheter bcoaxiality nor invasive pressions are controlled. The dissection of ascending aorta and air embolism or distal thromboembolisms due to inadequate handle of catheters and tubing as well[3]. Another important aspect is the possibility of idiosyncratic reactions similar to iodine allergies or anesthetic drugs, consequently low osmorality contrast and prepare the allergic patient with medication being an essential study. Other possible complications are the arrhythmias (ventricular fibrillation, bradycardia, AV block), and myocardial contractibility depression. If ventriculography is performed may occur cavity perforation and the consequent cardiac taponade due to hemopericardium. The usage of atraumatic catheters such as pig-tail avoids this complication.

Stable and unstable plaques, morphological characteristics: CCG allows establishing what type of lesions are acute and complex or chronic, always is important to correlate with the patient's clinical state. The acute or complex plaques may correspond to acute thrombosis, and can be observed abrupt vessel occlusion, without collaterals, with contrast retention in the thrombus or permeable vessels with eccentric, ulcerated plaques or with filling defects due to thrombosis presence and/or dissection. It is habitual, in the case of chronic lesions, the presence of multi-vessel disease, concentric, sub-occlusive lesions or also total occlusions with supplementary collaterals which point out a slow progression of obstruction and severely calcified plaques. Currently, angiography is complemented in the diagnostic process with IVUS, OCT and physiological measurements (FFR).

Culprit vessel identification: It is important in the case of acute coronary syndromes to be able to treat the patient properly, particularly, in multi-vessel disease and without location of faces or segments through echocardiogram or ECG. The culprit vessel can be suspected in case of thrombotic lesions or with antegrade flow deterioration or in those patients with angiographic characteristics of complex plaques. In multi-vessel disease, usually vessels with greater territory, length and with ostial and proximal lesions are responsible for the clinical picture. Angled lesions or in bifurcation are also predictors [4].

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b) Invasive physiologic assessment of coronary lesions. *Dr. Pablo Kantor (Interventional Cardioangiologist).*

The need to intervene a lesion in stable coronary syndromes or another non-culprit lesions of acute coronary syndromes is based in the amount of myocardial ischemia generated by these lesions. Historically, in cath-labs, the decision to intervene a lesion was guided by anatomic criteria (obstruction percentage) adding the clinical picture

and the non-invasive complementary studies. This strategy motivated that approximately 20% of lesions treated by their anatomical obstruction degree belonged to lesions which do not generate myocardial ischemia, and on the contrary, about 30% of the lesions whose percentage of obstruction did not indicate its treatment if they were functionally significant [1]. This discrepancy takes clinical relevance when considering that the treatment through angioplasty of those lesions which generate ischemia are associated with benefits regarding the conservative treatment while the revascularization of lesions which do not generate ischemia not only does not bring clinical benefits, but also add potential short and long term complications of an unnecessary procedure [2,3]. Invasive functional assessment of coronary lesions using hyperemia index (FFR) or with its equivalents free from hyperemia (iFR, DFR, etc.) allows identifying those coronary lesions which generate myocardial ischemia and those which do not generate, in order to guide the revascularization treatment based on a physiologic and not merely anatomic criterion. FFR or fractional flow reserve, index obtained measuring average distal pressure to the lesion to be evaluated regarding the average pressure at the aorta level in maximum hyperemia (maximum vasodilatation of coronary microcirculation). Generally, to achieve this maximum coronary hyperemia, adenosine is used, administered in intracoronary bolus, but also through continuous intravenous drip or using other less studied drugs such as: sodium nitroprusiatum, papaverin or dobutamine. This index values under 0.8 determine functional or physiological severity of the lesion. Considering only a determined segment of diastolic component of pressure curve, obtaining an equivalent index to FFR, without requirement of hyperemia is possible, avoiding in this way, the unfrequent secondary effects of dilatators drugs and transforming the procedure into a faster and safer one. There are different indexes free from hyperemia among which can be mentioned: iFR (instantaneous wave-free ratio), DFR (diastolic hyperemia-free ratio), dPR (diastolic pressure ratio), RFR (resting full cycle ratio) all of them validated in laboratory and clinical studies [4]. For the functional assessment of coronary lesions, a guide of coronary pressure of 0.014" is used and handled similarly to the guide cords used in most angioplasties, serving these pressure guides in turn to perform angioplasty in the case of obtaining a positive value.

Special scenarios

Multi-vessel Disease: The categorization of coronary lesions from the functional point of view takes special relevancy in the group of stable patients undergoing multi-vessel disease where identifying exactly the lesion(s) generating ischemia from those that do not is difficult. Through functional lesion assessment in multi-vessel disease better clinical distance results are achieved with a significant reduction in the number of treated lesions, avoiding stenting in anatomically significant lesions that are not physiologically ones. It is important to remark that in this group of patients possibly candidates to coronary bypass surgery due to the presentation of 3-vessel disease, about half of this population would no longer be sufferers of three coronary vessels from the functional point of view with the potential change in revascularization strategy [5,6].

Left Main Coronary Artery Lesion: Often the presence of an anatomical lesion at the left main coronary artery level, in its origin or in its bifurcation is difficult to stratify, and exists an enormous inter-observer variability of interpreting. This point is of crucial importance considering that the overvaluation of the left main coronary artery lesion will derive in a revascularization treatment, either in a surgical form or stent implant, procedures which would increase unnecessarily the rate of serious adverse events. On the contrary, the underestimation of a significant left main coronary artery lesion will put the patient at a high risk situation typical of the nature of coronary disease in this location. The use of FFR to assess functionally left main coronary artery lesions is a tool of great utility in those lesions with an index showing absence of functional severity set a favorable evolution without the need of revascularization [7].

Bifurcation lesions: In the treatment of bifurcation lesions, 1-stent provisional stenting as initial strategy offers, in most cases, benefits regarding 2-stent approach. When this strategy of 1-stent is selected, a group of patients ends up with a second stenting in the secondary branch due to angiographic presence of anatomically residual significant lesion. However, when the presence of ischemia in the secondary branch is physiologically examined, a significantly smaller number requires a second stenting, transforming the procedure in a simpler and less risky one [8].

Acute coronary syndromes: In acute coronary syndromes, the culprit lesion of the event would have indication of revascularization in its acute stage due to pathophysiology of rupture or plaque accident, independently of the ischemia this lesion could generate. However, usually this group of patients presents apart from culprit lesion other lesions not responsible for the acute event. Functional valorization of these other lesions allows guiding the revascularization treatment towards one functionally complete, reducing in this way residual ischemia in segments other than that of the acute event and improving the clinical evolution distant from the isolated treatment of culprit lesion [9,10].

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c) Endovascular morphological assessment (Intracoronary ultrasound). *Dr. Leandro Lasave (Interventional Cardioangiologist).*

Principles: The intracoronary ultrasound commonly known as IVUS (Intravascular Ultrasound) provides a three-dimensional-dimensional detailed image of the vessel lumen and the three artery layers. Morphology and composition of the plaque is identified by amplitude and frequency of reflected ultrasound signal that corresponds with normal tissue, fibrosis, calcium and necrotic core. The axial resolution is of 100 to 200 µm and the lateral resolution is of 250 µm with the frequencies of 20 to40 MHz [1]. There are two systems of IVUS, a) mechanic system, with one piece rotational transducer, being OptiCross catheter of 40 MHz (Boston Scientific, Santa Clara, California) the most commercialized, and b) digital system with a solid state piezoelectric transducer of 64 elements, Eagle Eye catheter of 20 MHz (Philips, San Diego, California). Philips has also included two new catheters (Revolution and Refinity ST), of one rotational piece of 45 MHz. The only advantage of piezoelectric transducer is its coaxial design avoiding artifacts through not uniform rotational distortion (NURD), the disadvantage is the existence of an information loss zone around the catheter of 1-2mm^2 (Ringdown). Both systems enable a manual and automatic pullback, transversal as well as longitudinal vessel assessment and the possibility of co-registration with angiography. Through offline analysis, vessel (diameter/area) and plaque measurements (%, volume) and length of the lesion can be carried out.

Plaque assessment: It permits to determine the plaque characteristics, calcification degree, intima-media thickness, vessel remodeling, and artery real dimension. Thus, the appropriate diameter and length of the stent to be used and the stent anchoring site in healthy area can be selected, as well as establishing the necessity of pretreatment of a lesion, plaque preparation, use of devices, calcium rupture, etc. The most important limitation in the assessment with IVUS is the need to guarantee the image in an axial position to the vessel in order to perform measurements correctly.

Assessment of intermediate angiographic lesions: The greatest limitation of the angiography is performing a two-dimensional evaluation of a three-dimensional structure so many situations (ostial lesion, eccentric lesion, curve, branch emergency, angulation, diffuse lesions, contrast dispersion) may affect the angiographic analysis of a lesion severity. Consequently, IVUS providing detailed information on artery lumen and walls, gives diagnostic accuracy and precision superior to angiography. A cut point has been treated to establish to determine the clinical significance of a lesion. The Minimal Luminal Area (MLA), the minimum diameter, the plaque burden and the length of the lesion were used as parameters to be evaluated; of all of them MLA and plaque burden are the most relevant. In the evaluation of intermediate lesions, the difference between left main coronary artery lesions (LMCA) and those that are not LMCA lesions must be make. For lesions that are not LMCA, the cut point goes from 2.0 mm^2 up to 4,0 mm^2, with low diagnostic security (accuracy) regarding functional evaluation, so in intermediate lesion FFR is recommended or analogous (iFR/ RFR) [2]. If IVUS must be used, it has been proved that a ALM >4mm^2 has a high sensibility to detect a non ischemic lesion, so it could be safely used to differ an intervention. However, an ALM <4.0 mm^2 does not safely predict an hemodynamically significant lesion, so it should not be used to indicate intervention [3,4]. For LMCA lesions, a good correlation has been observed between ICUS and coronary physiology. A ALM >6 mm^2 allows to identify with a very high sensibility, a non-hemodynamically significant lesion and so gives security to differ the intervention. This situation clinically evaluated in LITRO study [5] showed a low rate of cardiovascular events at 2-year follow-up in patients with ALM > 6 mm^2 non-intervened. Though, due to the low specificity, its use is not recommended to intervene on a lesion [6]. In another study, it was probed that an ALM of < 4,5 mm^2 has 82% specificity to identify lesions with FFR < 0.8, so that in absence of other diagnostic tool, it could be taken as useful cut point for LMCA intervention [7]. For lesions between 4.5 mm^2 and 6.0 mm^2 a functional diagnostic method should be used.

Percutaneous coronary intervention guidance and optimization: Intravascular image allows the accurate assessment of plaque characteristics and determines the need of its pretreatment as well as the use of devices for calcium rupture or progressive dilatation. It is also possible to perform the measurement from the external classical membrane inferring the vessel real diameter and allowing the correct selection of stent size. Similarly, it is possible to evaluate proximal and distal references to avoid stent anchoring in plaque area. Once the stent has been placed, post implant evaluation permits to assess expansion, apposition and stent morphology, need of post dilatation, dissection presence, and stent borders evaluation [8,9]. The IVUS fundamental utility is to guide and optimize a coronary angioplasty. The more complex the intervention, the greater the IVUS benefit [10]. In ADAPDES [11] study which included 8583 patients "all-commers", a very pronounced benefit of the use of IVUS was proved as guide in interventions of patients undergoing acute coronary syndrome and complex lesions. It is almost mandatory for interventions on unprotected LMCA, mainly concerning bifurcation and two-stent use [12]. Various studies proved that the use of IVUS reduces cardiovascular events. AIR-CTO study [13] showed a lower

rate of in-stent restenosis (ISR) in chronic total occlusion interventions guided with IVUS. Likewise, IVUS-XPL study [14] showed a lower rate of recurrent revascularization in > 28mm lesions, and ULTIMATE study [10] which randomized 1500 patients showed a lower rate of clinical events and in-stent thrombosis in patients guided with IVUS. In one of the greatest studies including 1670 patients undergoing LMCA lesion treated with drug-eluting stents, the propensity score proved that IVUS guided interventions were associated with lower rate of cardiovascular events over 3 years [15]. Several meta-analysis observed results in the same direction even in mortality differences in favor of IVUS-guided procedures [16]. Percutaneous intervention of IVUS-guided ISR allows identifying the restenosis mechanism, sub-expansion presence, intimal hyperplasia, stent fracture, neoatherosclerosis, and in this way be able to evaluate the best form of treatment [17], and it has been probed that IVUS-guided ISR intervention reduces cardiovascular events in the short and medium term [18]. Latest European Guidelines (2018) [2] recommend class II-a, level of evidence B, the use of IVUS as angioplasty guide and class II-a, level of evidence C, the use of IVUS to evaluate ISR. Moreover, these guidelines mention that IVUS could be used to evaluate unprotected intermediate LMCA lesions (II-a, level of evidence B). ACC/AHA/SCAI (2021) [19] recommend class II-a, level of evidence B-R, the use of IVUS as coronary angioplasty guides, particularly, on LMCA interventions and complex interventions in order to reduce ischemic events. Additionally, they recommend class II-a, level of evidence C-LD the use of IVUS as interventions guide in ISR or previous stent failure. These guidelines also qualify as reasonable IVUS use to evaluate intermediate lesions in unprotected LMCA (II-a, level of evidence B-NR).

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d) Endovascular morphological assessment (OCT). *Dr. Diego Guzzanti (interventional Cardioangiologist).*

Optical Coherence Tomography (OCT) is a method of endovascular assessment through images sharing certain similarities with IVUS, but instead of ultrasound it uses a broadband light source. It performs high-resolution tomographic imaging (10-15mm) exceeding 10 times the resolution of a conventional coronary angioplasty, and 8 times the intravascular ultrasound. It is a useful tool for studying microstructures and biological materials through the field measurement of delay and the magnitude of reflected light by the investigated tissue, near-infrared spectrum. Dispersion is a physical process in which some forms of radiation (i.e. light) deviate from their straight original trajectory and disperse in all directions through one or more irregular surfaces placed in the path they go through. The dispersion generated by tissues has different forms depending of the tissue. The signal captured by OCT is influenced by the tissue optical properties (absorption and dispersion), as well as optical components of image formation system (**Figure 1**).

Applications: Its high in vivo resolution allows performing an exact assessment of the mechanical interaction between the stent and the vascular wall, included the struts apposition. Besides, it permits to diagnose peri-intervention dissections, thrombus presence and characteristics, re-endothelialization of stents or its reste-

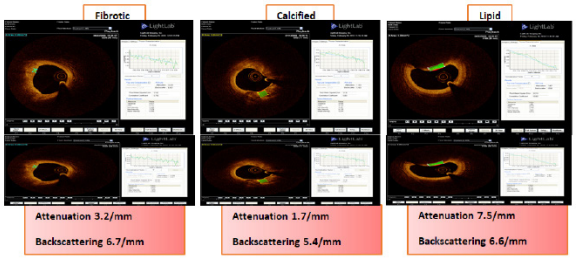

Figure 1.

nosis and finally, eventual late onset of neoatherosclerosis. Another fact to consider is that OCT-guided percutaneous coronary interventions vas associated independently with lower risk of death and infarct [1]. In recent publications, the change of strategy pre-and-post procedure more than 80% and 30% respectively was showed. The principal change on decision making was at the expense of lesion morphology [2]. It is a useful method to prevent stent thrombosis episodes demonstrating incomplete healing, mechanical stent failure or incomplete cover of lipid-rich lesions or with necrotic core, all characteristics related to late thrombosis of these devices [3], allowing also the assessment of stenosis severity. With OCT are evaluated the coronary artery general morphology, dimensions and plaque, being the most precise method, but sharing with ultrasound the adequate evaluation of stent expansion and apposition. Its role is highlighted in the assessment of the stent expansion based on the external classical membrane conveying non-inferiority to ultrasound and superior to angiography; in protocols to guide the stent choice, in those guided by IVUS and OCT (the expansion obtained with IVUS guidance was not superior to that of angiography alone, although this should not discourage the use of IVUS which has enormous evidence) [4]. Among other applications of this method, it is worth mentioning the non-obstructive coronary disease (INOCA), clinical picture with hazardous clinical prognosis winning interest mainly with reference to its correct diagnosis. Micro-vascular disease and vascular spasm are the protagonists in possible etiopathogenesis of these presentations not being able to show in conventional angiography. The determination of the microvascular resistance index and the coronary vasoreactivity testing are the diagnostic pillars of these entities without having a clear idea on the morphological relation of coronary arteries [5]. Shimokawa et al could study patients undergoing INOCA (acute myocardial infarct with lesions less than 50%, vasoreactivity testing, and determination of lactate concentration in order to diagnose epicardial/microvascular spasm) performing OCT of anterior descending artery to analyze the adventitial vasa vasorum density and intra-plaque neovascularization. In turn, the microvascular resistance index was also determined. The focal coronary vasospasm presents through OCT a phenotype of vulnerable atherosclerotic plaque, with a worse prognosis of adverse clinical events regarding diffuse vasospasm or the subgroup of patients with INOCA without coronary vasospasm. The identification of a correlation between coronary anatomy assessed through OCT and the functional anomalies in patients undergoing INOCA is of vital importance the addition of both diagnostic tools in this subgroup of patients. Another of recent applications of these images was the assessment of vasculopathy in cardiac transplant patients allowing the detection of plaque compositions associated with vasculopathy, the early detection and differentiation of non-visible vessel wall disease in angiography. The fibrotic plaque in layers was the most prevalent component, and extension increased with angiographic severity of vasculopathy, it may be associated with the stepwise progression of this presentation caused by the organization of mural thrombi [6,7,8]. Systematic evaluation of these patients with OCT and corresponding measurement alert the transplant team to implement the corresponding treatment t

Conclusions: The use of OCT in coronary procedures allows atherosclerotic plaque evaluation, measurements performance and stenting guidance. It is a tool that conducts us to a pathophysiological analysis far from the anatomical from virtual histology not evaluable with angiography. Its range of observation gives valuable information generating long-term impact on coronariopathies and its treatments, providing quantitative and qualitative information. Currently, it should be a usual adjuvant in the cath lab; however, we still do not count on an algorithm that contemplates it in all TCA cases, due to insufficient data from randomized trials associated with lack of reimbursement for intravascular imaging studies which contributes to the limited use of the method.

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2) CLINICAL SCENARIOS

A) Stable patients

a) Chronic stable angina. *Dr. Gerardo Zapata (Clinical Cardiologist), Dr. Stella Macín (Clinical Cardiologist)*

Myocardial revascularization objective is to enhance survival and/or alleviate symptoms. In the scenario of chronic stable coronary disease, currently called Chronic Coronary Syndromes[1], an initial invasive strategy, determined by coronariography and myocardial revascularization with angioplasty or coronary artery bypass surgery, has not been able to demonstrate clear superiority compared with an optimal medical treatment in terms of death or infarct[2,3]. The analysis of various studies which summarize the information are of particular interest since they have included special populations, they present designs and different primary endpoints and were carried out over several years in which the technical characteristics, revascularization devices, and advances in pharmacological therapy have presented different modifications requiring particular considerations.

COURAGE trial (Optimal Medical Therapy with or without PCI for Stable Coronary Disease). It evaluated the benefits of an optimal medical therapy with or without coronary angioplasty in stable coronary disease. It included 2,287 patients in functional class I-III (Canadian Cardiovascular Society) or IV stabilized with stenosis ≥ to 70% in a main artery, at least in a vessel capable of TCA and ischemia evidence spontaneously or induced by studies. It is important to highlight that the patients refractory to treatment, with recent infarct, cardiac insufficiency, FEy < 30%, and high risk ergometry were excluded from the trial. The primary endpoint was a compound of death due to any cause and non fatal infarct in a mean follow up period of 4, 6 years. It were registered 211 events in TCA group compared with 202 in the without ATC group (19% vs. 18.5%; HR 1.05; IC 95% 0.87 to 1.27, p=0.62). In secondary endpoints, differences were not observed. The study concludes that TCA in addition with medical treatment does not reduce major cardiovascular events, being its use and utility secure to lessen symptoms[4]. In perfusion sub-study COURAGE 621 patients with cardiac SPECT were analyzed, showing in TCA group associated with medical treatment a reduction of ≥ 5% of the ischemic amount in a 33% against a19% in the group of medical treatment alone. In patients with ischemia resolution, in almost 80%, it was observed angina-free evolution. It was also observed positive interaction between SPECT induced ischemia and the anatomic burden of coronary disease[5].

FAME 2 trial (Fractional Flow Reserve-Guide PCI versus Medical Therapy in Stable Coronary Disease). With the hypothesis that the benefit of percutaneous revascularization could be related with ischemic amount, this study was designed evaluating in 1220 patients the stenosis severity in a major coronary artery through fractional flow reserve (FFR) to guide TCA taking as cut-off point a value of 0.80 or less. The primary endpoint made of death, myocardial infarct or urgent revascularization was determined during a follow-up period of 214 days. In 447 patients FFR-guided TCA was performed plus complete medical treatment, in 441 medication only and 332 with significant angiographic stenosis, but with FFR greater than 0.80 were included in the registry with complete medical treatment. Results showed that events in TCA group were significantly lower (4.3% vs. 12.7%; HR 0.32; IC 95% 0.19 to 0.53, p<0,001) at the expense of a significant decrease of urgent revascularization, and not of death or myocardial infarction[6]. The extended follow-up at 3 years, also presented benefit in FFR-guided TCA group (10.1% vs. 22% - p <0.001) for primary endpoint.

ISCHEMIA trial (Initial Invasive or Conservative Strategy for Stable Coronary Disease). Multicenter randomized and controlled trial designed to evaluate in 5,179 stable patients with moderate to severe ischemia in stress images, if an initial strategy with cardiac catheterization and revascularization (TCA or MRS) plus an optimal medical treatment could reduce an endpoint combined with cardiovascular death, non fatal infarct or hospitalization for unstable angina, cardiac insufficiency or cardiac arrest recovered, compared with medical treatment alone. Results at 3,2 years average follow-up showed 318 events in the invasive strategy group compared with 352 in the conservative strategy group (HR 0.93; IC 95% 0.8 to 1.08 - p=0.34). After 5 years, the accumulate frequency was 16.4% and 18.2% respectively (difference of -1.8 points, IC 95% -4.7 to 1). These results must be interpreted analyzing some limitations or considerations of the study. The power of the trial was calculated with a sample size of 8.000 patients, so, it was affected when reducing the sample to 5.000, with event rates lower than expected with a follow-up period of immediate duration, being necessary to increase the primary events as a result of slow recruitment. The results cannot be applied to patients undergoing acute coronary syndromes, severe obstruction of left main coronary artery, low EFy of left ventricle, and symptomatic patients in spite of complete medical treatment. Myocardial infarction was evaluated according to the third universal definition with troponins of high sensitivity. Peri-procedural myocardial infarctions (4a and 5) were greater at the beginning of the study in the branch of invasive intervention, while spontaneous infarctions (1, 2, 4b and 4c) were greater in the conservative group from the second half of the follow-up period[7]. Several meta-analysis compared invasive with conservative strategy in this population of patients undergoing chronic stable coronary disease not being able to prove myocardial revascularization superiority, considering a marked crossover of patients towards the invasive branch in the follow-up[8,9].

Possible differences between randomized studies and daily practice. In analyzed studies, patients received an optimal medical treatment with efficiency objectives and permanent monitoring assuring a high range of adherence totally different from real world, where an important number of patients do not achieve the established goals. Non-fulfillment of modifications in the lifestyle as well as in the drug therapy is a matter of concern and development of programs with the use of tools in order to increase adherence. Real life data, could establish a strong relation among the ischemic induced rate, EFy of left ventricle and early revascularization with significant reduction of cardiovascular events during the follow-up[10-11].

General Considerations. Therapeutic Algorithm. Stable coronary disease needs a global therapeutic approach in order to modify and control risk factors associated

with disease progression and thrombosis risk. Appropriate intense and sustained lifestyle changes and drug therapy based in evidence must be the initial management. Besides, an important group of patients presents angina with non-obstructive coronary disease, needing only an adequate medical treatment to prevent infarction or death. Patients undergoing left main coronary artery disease or severe and extensive coronary disease, low ejection fraction of left ventricle, angina pectoris refractory to complete initial treatment, and a subgroup with high risk ischemic studies with hemodynamic alterations or arrhythmias, should received a surgical or percutaneous myocardial revascularization (**Figure** 2).

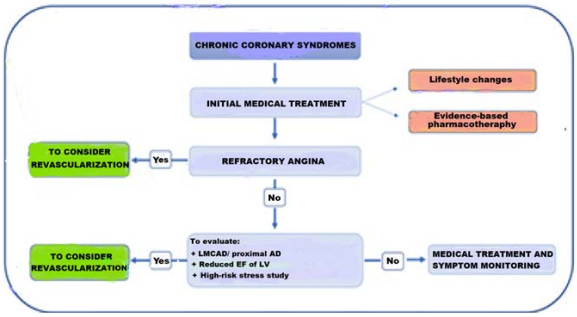

Figure 2. *Therapeutic algorithm in CCS.*

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b) Cardiac insufficiency. Lessons learned from different trials. *Dr. Alberto Fernández (Clinical Cardiologist).*

The main cause of chronic cardiac cause, in the western world, is coronary disease, considering from years that the myocardial revascularization through surgery (MRS) or Angioplasty (CTA) could reduce morbi-mortality from decreasing ischemic events, or turning back myocardial hibernation process with the consequent recovery of ventricular function. During many years, this theory could not be supported because in most studies patients with severe deterioration of ventricular function were excluded. Just in 2010, with the publication of STICH trial, first information was obtained being discouraging data, since after 56 months follow-up in a population with EFy of ≤35%, revascularization do not prove positive results regarding medical treatment, with the addition of ischemia objectivation or feasibility do not identified a population which will benefit from surgical intervention compared with medical treatment [1]. When the 10-year follow up of the same study finished, STICHES instead showed an advantage in the primary endpoint in the surgery group (58.9% vs. 66.1%; HR 0.84; IC95%; 0.73-0.97; p≈0,002), considering MRS late benefit, once overcoming early risk, inherent in surgical procedure. NNT was of 14 MRS to save a life in 10 years, so maybe this is applicable to a young population where an early diagnosis of coronary disease translates into significant clinical and epidemiologically results. It is important to consider that this study benefit was fundamentally due to a reduction in fatal late infarctions and to a lesser extent of sudden death, with only marginal reduction in death through IC [2]. The following step, and since in practice CTA usually is the most used revascularization method in this population, it was necessary to evaluate both methods with each other. The direct comparison of both procedures arises from studies of different characteristics that evaluated specific sub-groups (diabetic patients) such as the FREEDOM trial [3] or those that are based on registry data, such as APPROACH (Alberta provincial program for outcome assessment in coronary heart disease) [4], while showing better benefits with MRS did not allowed this question to be clearly defined. A recent meta-analysis on 21 studies with 16,961 patients, comparing medical treatment vs. CTA vs. MRS in patients with IC and FEVI <40%, showed a significant death reduction with MRS (HR 0.66; IC95%: 0.61-0.72; p<0.01 on medical treatment, this independently of feasibility testing [5]. Bangalore et al., from the analysis of a registry of New York city, compared MRS vs. CTA (with DES stent), in patients with FEVI <35%, and in 2 to 9-year follow-up proved similar survival with both methods, with greater repetition of revascularization in CTA group though with smaller number of CVA [6]. In this course of action and considering the current pharmacological therapy breakthrough, the idea of comparing CTA with medical treatment in this population comes out. So in 2022, REVIVED-BCIS2 (Revascularization in Ischemic Ventricular Dysfunction) trial was published, and 700 patients were recruited with FEY ≤ 35%, obstructive coronary disease liable for CTA with evidences of myocardial feasibility [7], failing to demonstrate superiority regarding optimal medical treatment, after 41-month follow-up for the combined endpoint of death and hospitalization due to cardiac insufficiency (37.2 vs. 38.0%; HR 0.99; IC95%: 0.78-1.29 p≈0.96). In the same way, the assessment of

quality of life through different questionnaires (KCCQ and EQ-5D-5L), at the end of the follow up, it did not show a favorable impact, and an interesting fact and physiologically disturbing is that there was not differences in terms of improvement of EFy at 6 and 12 months. Numerous questions remain open such as the presence or not of angina (only 33% of the patients presented it), the proportion of revascularized vessels (anatomical revascularization index of 71%), the myocardium at risk percentage according BCIS (British Cardiovascular Intervention Society) jeopardy score, 9.3 prior to procedure vs. 2.7 after it which could condition neutral results in terms of reverse remodeling and symptomatology. Finally, a recently published study based on an analysis "in silico" through a complex selection from an English hospitals database comparing patients treated with surgery vs, CTA, both plus medical treatment, and adjusted by different risk and confusing factors showed a clear advantage in favor of MRS in the endpoint reduction combined with all causes of mortality and cardiovascular hospitalization to 5-year follow-up [8]; its authors suggested the possibility of randomized studies in order to evaluate this hypothesis. Undoubtedly, in an optimal moment for patients undergoing ICFSD in terms of morbid-mortality and life quality, based on a very important development of the medical treatment with the appearance and consolidation of the quadruple therapy (IECA/ARA II/ARNI; B-blockers, aldosterone antagonists and iSGLT2) [9], to which we should add pharmacological and non-pharmacological methods evolution of primary and secondary prevention in ischemic cardiopathy, which has resulted in a reengineering regarding the indication of revascularization procedures which should be applied in very specific subgroups such as symptomatic patients due to angina with recent CI presentation, young patients or with life expectation ones which justify the mention treatments. To conclude, we should mention the lack of imaging methods standardization allowing us to define clearly myocardial feasibility percentage to be able to identify patients with higher benefit potential with guided invasive therapy **(Table 3).**

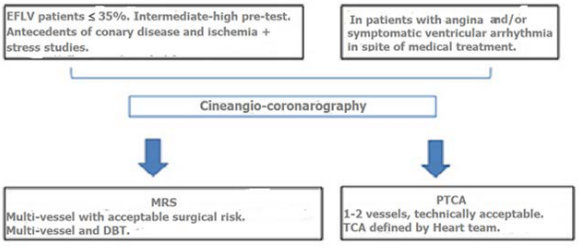

Table 3. *Algorithm for study indication and invasive treatment in chronic HF.*

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B) Unstable patients

a) Acute coronary syndrome without ST segment elevation. Clinical aspects. *Dr. Juan Muntaner (Clinical Cardiologist), Dr. Rodrigo Zoni (Clinical Cardiologist).*

Acute coronary syndrome (ACS) involves a heterogeneous group of entities with different clinical, electrocardiographic (ECG) and biochemical (biological markers) presentations which establish its classical classification forms in ACS with ST persistent elevation (STEMI) and ACS without ST persistent elevation (NSTEMI). The last one presents two variants, the first with positive biological markers, defining acute myocardial infarction without ST elevation (NSTEMI), and the other with negative biological markers defining Unstable Angina symptoms[(1)].

Diagnostic algorithm

1. Clinical. In-depth evaluation, interview and clinical examination (I B).
2. ECG within 10 minutes of first medical contact (PMC) (I B).
3. Biological markers. Preferentially, high-sensitivity troponin.
4. Risk stratification.
   i) Ischemic: Score GRACE 2.0 (IIa-B) is suggested.
   ii) Hemorrhagic: CRUSADE - ARC-HBR (IIb-B) is suggested.

Risk stratification in NSTEMI allows guiding the therapy to follow in these patients as early as possible. It will guide health personnel to decide whether the therapeutic approach must be invasive or conservative, and in the first case the right time to be performed. Invasive treatment reduces morbi-mortality, however, its benefit is not always so clear[(3)]. This will depend on several markers of very high, high, intermediate or low risk, which will also guide the moment to perform invasive coronary angiography (CCG)[(1)]. In patients with very high risk, like those undergoing cardiogenic shock, cardiac insufficiency due to NSTEMI, recurrent precordial or refractory pain, arrhythmias that put life at risk or different changes in ECG (de Winter's pattern[(4)], Aslanger's pattern[(5)]) an immediate invasive strategy must be carry out (within 2 hours of PCM)[(1,3)]. In patients with high risk are included

those with a GRACE punctuation >140, age ≥75 years and/or with cardiac markers elevation in whom is recommended the early invasive strategy (within 24 hours of PCM)[3]. In elderly patients, fragility does not seem to be a conditioning factor to opt for a conservative strategy[6]. In the intermediate-risk group are those who do not meet any of the conditions before mentioned, but present other risk markers such as diabetes mellitus, renal insufficiency, cancer or previous coronary revascularization, in whom a deferred invasive strategy (within 72 hours of PCM)[1,3,7,8] is suggested. The low risk group is formed by those who do not fulfil the criteria before mentioned. An ischemia-guided strategy is suggested for them, in which after the first 72 hours of PCM and stabilized the symptoms, some study of cardiac images (functional or anatomical according to availability or experience at the centre) could be performed that will guide the next step towards an invasive or conservative strategy[1,2]. It is important to bear in mind that in spite of the risk stratification and the suggested strategies, some characteristics or presentations of NSTEMI patients could exist, in whom an early or immediate invasive strategy evaluation is suggested and perhaps morbi-mortality decreases[9]. Pretreatment with dual antiplatelet therapy (DAPT): The evidence of not performing routine pretreatment is limited to 2 trials, AC-COAST[10], with burden of prasugrel 30 mg at the moment of NSTEMI diagnosis (it happened 4.2 hours before CCG) and ISAR REACT-5[11] where CCG was performed with a medium <60 min. after randomization. These trials do not provide evidence that support a period beyond 4 hours from PCM to CCG without pretreatment with DAPT. It is not recommended the routine administration of an inhibitor of P2YI2 (iP-2YI2) receptor in patients with NSTEMI in whom the coronary anatomy in an early invasive management < 4 hours is unknown. Pretreatment with iP2YI2 in patients with NSTEMI between 4 and 24 hours in whom coronary anatomy is unknown should be established evaluating ischemic/hemorrhagic risk, and that due to several logistic or clinical reasons could not undergo an early invasive approach. It is strongly recommended the administration of a routine pretreatment with iP2YI2 in patients with NSTEMI in whom the coronary anatomy is unknown in an invasive management beyond 24 hours. A pretreatment with ticagrelor over clopidogrel in NSTEMI patients in whom the coronary anatomy is unknown in a management beyond 24 hours. Pretreatment with prasugrel is not recommended in patients with coronary anatomy unknown independently of the strategy to use.[12] **(Table 4)**.

Table 4.

Class of recommendation	Level of evidence	Recommendation
I	A	In patients at high-risk of recurrence/isquemia and feasibles of revascularization, an invasive strategy is recommended.
I	C	In patients at very high-risk, an immediate invasive strategy (within 2 hs of FCM) is recommended.
IIa	B	In patients at high-risk, an early invasive strategy (within 24 hs of FCM) is recommended.
IIa	B	In patients at intermediate-risk, a deferred invasive strategy (within 72 hs of FCM) is recommended.
IIa	C	In patients at low-risk, an ischemia guided strategy is suggested.
IIa	C	Even if in NSTE-ACS patients a strategy according to the patient risk is sugested, it is also suggested to analyze the individual risk of each case beyond de risk estratification to opt for an immediate or early invasive strategy, thus morbi-mortality may be reduced.
III	B	Cardiogenic shock in patients who will be revascularizated with coronary angioplasty, the routine non-culprit multivessel angioplasty is not recommended.

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b) Acute coronary syndrome with ST segment elevation. Clinical aspects. *Dr. Daniel Mauro (Interventional Cardioangiologist).*

There is a general consensus that coronary heart disease is the leading cause of death globally, with a worrying increase in frequency. In spite of a general tendency to mortality reduction due to coronary heart disease has been observed in Europe in the last 3 decades[1], it is estimated that it reaches 20% of all deaths in that continent but with marked variations among countries. During the past 20 years, primary Coronary Angioplasty (CTA),

that is to say, the intervention performed in the context of an Acute Coronary Syndrome with ST segment elevation (STEMI) without prior fibrinolytic treatment has shown a better and faster restoration of coronary flow, higher permeability rate with less reocclusion of the responsible vessel and better residual left ventricular function after acute infarction. These are consistent results mainly in patients with an evolution period between 6-12 hours treated in experienced centers with adequate case volume as it arises from numerous randomized clinical trials (ECA) in which primary CTA was compared against hospital fibrinolytic treatment.[2] Looking a little closer, STEMI incidence seems to be progressively smaller in Europe as well as in the United States, but affecting younger people and with clear prevalence of male sex each time, while patients affected from Acute Coronary Syndrome without ST segment elevation are in progressive increase with higher incidence in older people[3,4]. On the one hand, factors which increase STEMI mortality are well known and are those of each patient, such as: DBT condition, severe kidney insufficiency, multi-vessel disease, prior infarction, ventricular function and old age. On the other hand, factors related to reperfusion strategy, emergency system and the access or not to primary TCA are identified. Therefore, numerous publications show a STEMI mortality reduction during hospitalization, and proportionally in a long term towards better and more efficient reperfusion therapies, such as primary PCI. In addition, more powerful antithrombotic therapies, progressively greater awareness on the part of population towards primary prevention and early consultation, and of course, secondary prevention[5,6].

Scenario in Argentina: With the limitations imposed from a registry, it is very important to highlight the data on our country revealed from Argentine Registry (ARGEN-AMI-ST). This inter-society joint work included a total of 2,464 patients by the end of 2019 distributed in 78 public and private centers of 19 provinces and the Autonomous City of Buenos Aires. Almost two thirds of the centers count on capacity to perform TCA, and almost half of the patients was transferred to another level of complexity for the final attention. 88% of all patients (n = 2,178) received reperfusion therapy with 21% use of fibrinolytics, and in 89% of the cases, TCA was performed within the first 24 hours of AMI with 8% of cases of rescue TCA and only 3% with pharmaco-invasive strategy. Coinciding with international literature, demographic data proved an average age of 60 ± 12 years with 80% of male sex and 13% of patients already underwent antecedents of coronary heart disease. The cases which do not received any reperfusion therapy (11%) mainly because they were "out of the therapeutic window" due to initial consultation delay.

Time to reperfusion: Regulations based on international guidelines indicate that it is mandatory to perform all the efforts to reduce waiting time, especially during the first 2 hours after the onset of the symptoms. Ideally, referring the patient to a center with primary TCA performed by experienced operators in a 24/7 scheme, and that this therapy becomes available to as many patients as possible, without delays, emphasizing that this type of patients must be **directly** transferred to the cath-lab, without going neither trough the Emergency Room nor trough Coronary Intensive Care Unit, first (*Class I indication, level of evidence B, for European guidelines for AMI management in STEMI patients from 2017*)[8]. Those patients admitted in centers not having primary TCA must be transferred to a center with TCA and should not receive fibrinolytics if the waiting time between the first medical contact (FMC) and the vessel opening (FMC/Balloon) is less than 2 hours. On the contrary, if the estimated time is over 2 hours (or > to 90 minutes in patients under 75 years of age with STEMI of anterior localization and very recent symptoms) must be **immediately** treated with fibrinolytics and then transferred to a center with TCA so that angiography and TCA are performed within the first 3-24 hours[9,12]. In the ARGEN AMI-ST, more than 2/3 of the individuals were admitted within 6 hours the symptoms start. The door-balloon time for patients that consulted a center with possibility to perform angioplasty was 100 minutes (RIC 25-75: 60-174), compared with 192 minutes (RIC 25-75: 98-395) in those patients who must be transferred to another center for their treatment. Only 35% had a door-balloon time less than 90 minutes[7].

Mortality: In spite of the great improvement of reperfusion therapies and the joint efforts of scientific societies and health politics of numerous countries for the early recognition of this entity, hospital mortality of STEMI remains high even among the most developed countries. Figures from European countries place them between 4 and 12% while the mortality per year is around 10%[13]. Local data from the mentioned registry ARGEN AMI-ST showed hospital mortality of 8.7% with a strong correlation between consultation delay (first medical contact) and mortality. Remarkably, in the multivariate analysis the direct care in a center with hemodynamic availability was not associated as an independent variable with a better survival[7].

Female sex: It is a known fact that in a 30% of the cases, womenusually present atypical symptoms or non-characteristic of STEMI. Added to this is the already mention circumstance in which in population under 60 years, acute infarction prevalence triples and more in men. Although these parameters become equal after 60 or 65 years and even reverse after 75 years with a higher prevalence of women with acute infarction. Undoubtedly, these circumstances conspire against the diagnostic suspicion and derive proportionally in smaller amount and later reperfusion therapies received by women with regard to men as it was stated in the literature many times[14,15]. So, women usually present higher rate of morbi-mortality, among other things, at the expense of a higher rate of hemorrhagic complications. Then it must be emphasized the need to sharpen STEMI diagnostic suspicious in women, do not minimize symptoms that may result "non-typical" and assume that in prognostic terms female sex is an independent variable associated significantly with higher mortality along with age, presence of cardiogenic shock and lack of reperfusion.

Risk assessment: The risk score GRACE (Global Registry of Acute Coronary Events)[16] is recommended by the current guidelines as a tool to count on an early risk assessment on a short-term in all patients undergoing STEMI. This assessment includes a myocardial damage weighing, if reperfusion resulted successful or not, patient´s age, and other risk markers such as heart rate on admission, hypotension, Killip class, localization of acute infarction, kidney damage, prior cardiac insufficiency, and peripheral vascular disease. Prior to patients discharge, a long-term risk evaluation that contemplates left ventricular function, coronary disease extent, residual ischemia and the necessary determinations to establish metabolic risk and not only anatomic or angiographic risk must be performed. Patients who do not receive an adequate reperfusion form a special interest population due to count on higher risk of early complications and death. This initial risk assessment is closely related with the patient´s permanence in CICU area, generally observing a progressive decrease of these times, according to the high rate of primary success of PCI, and of course, the coronary anatomy knowledge. It was observed that early mobilization and early discharge, 2nd or 3rd day, is not associated to higher long-term mortality. These patients may be recognized using PAMI-II criteria which identify as low-risk patients < 70 years with Ejection Fraction (LVEF) > 45%, 1 or 2-vessel disease, successful PCI, and absence of significant arrhythmias[17]. It is important to highlight that early dismissed must go with firm recommendations on risk-factors correction, outpatient consultation within the following 7 days, and the inclusion in a cardiovascular rehabilitation program.

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c) Complete vs. Culprit Vessel Revascularization. *Dr. José* Álvarez *(Interventional Cardioangiologist).*

In patients with Myocardial Acute Infraction with ST elevation (STEMI), the presence of disease in more than a main coronary vessel (MVD) is an indicator of the worst immediate and remote prognosis [1]. After the culprit vessel revascularization, three possible therapeutic scenarios are presented:

- Complete revascularization (CR) guided by the presence of symptoms or ischemia in functional tests.
- Complete revascularization guided by anatomy or invasive functional evaluation performed at the time of primary angioplasty (PA).
- Complete revascularization guided by anatomy or invasive functional evaluation performed in a staged manner.

Until 2013, the outcomes of some observational studies were conflictive and the guidelines recommended not treating lesions in AMI non-culprit vessels [2,3]. However, the most contemporary evidence suggests that CR in patients with AMI and MVD is associated with a more favorable evolution with lower incidence of major cardiovascular events.

Principal randomized trials in patients with STEMI. PRAMI trial performed in five British centers enrolled 465 patients with STEMI and MVD and randomized them to CR performed in the same procedure as PA or culprit vessel-only revascularization; the trial was stopped early due to a significant lower incidence of major cardiovascular events in CR group [4]. In CVLPRIT trial published two years later, the staged CR (27% during the first intervention) showed a lower incidence of combined events (that included re-hospitalization due to cardiac insufficiency) without significant differences regarding cardiovascular death (CVD) or AMI in the follow-up [5]. In DANAMI-3-PRIMULTI a "functio-

TABLE 5. Principal controlled trials in patients undergoing AMI-STEMI and MVD.

	PRAMI	CVLPRIT	PRIMULTI	COMPARE	COMPLETE
Year of publication	2013	2015	2015	2017	2019
Strategy	Imm or Sta	Imm or Sta	Sta	Imm or Sta	Imm or Sta
Assessment of non-culprit vessel	%ste >50%	%ste >70% or >50% in two views	%ste >50% and FFR < 0.80 %S >90%	%ste >50% and FFR <0.80	%ste>70% or %ste50-69% with FFR <0.8
Bivalirudin or GPI IIb/IIIa	79%	83%	97%	56%	n/i
Primary Endpoint	CVD/AMI/ RI HR 0.35 (0.21-0.58)	GM / AMI / IGR/ HF HR 0.45 (0.24-0.84)	GM /AMI/ IGR HR 0.56 (0.38-0.83)	GM/ AMI/ IGR/ CVA HR 0.35 (0.22-0.55)	1.- CVD/ AMI HR 0.74 (0.60-0.91) 2.- CVD/ AMI/ IGR HR 0.51 (0.43-0.61)
CVD/GM or non-fatal AMI	4.7% vs 11.7% p=0.004	4.0% vs 9.6% p=0.06	6.4% vs 8.0% p=0.47	3.7% vs 6.4% p=0.10	7.8% vs 10.5% p=0.004

%ste: percent diameter stenosis. Imm: Immediate. Sta: staged. CVD: cardiovascular death. AMI: non-fatal Acute Myocardial Infarction. RI: Refractory Ischemia. GM: global mortality. IGR: ischemia-guided revascularization. HF: Heart failure. Isc-trig revasc: Ischemia-triggered revascularization. HR: Hazard Ratio (95% CI).

nal" CR strategy was investigated, in which non-culprit lesions of between 50 and 90% were evaluated trough flow reserve measurement (FFR) two days after PA and treated consequently [6]. In COMPARE – ACUTE trial, revascularization of non-culprit vessel was also guided by invasive functional criteria, but with difference to the previous one, FFR was performed immediately after the culprit vessel treatment during PA [7]. Finally, the international trial COMPLETE is the major trial published so far with 4041 randomized patients. The outcomes favored CR strategy with significant differences in the combined event of CVD or AMI. Furthermore, in this trial was explored the difference between an immediate CR strategy (a day average post PA) vs. staged CR (23-day average post PA) and differences were not observed in the endpoints of security or efficacy related to the time it was performed [8].

Certainties and questions. Taken as a whole, current evidence states that in patients with AMI treated with PA, the revascularization of all significant lesions in non-culprit vessels reduces recurrent AMI risk and cardiovascular death, the need of new revascularizations, and the patients proportion with residual angina, without increasing adverse effects such as bleeding, stroke or kidney injury [9]. Some questions persist, especially concerning the right time when significant lesions in non-culprit vessels must be treated, and their evaluation method (angiographic or invasive functional). With exception of the mentioned sub-trial COMPLETE, it does not exist firm evidence that specify the optimal time to complete the revascularization, however, guidelines recommendations suggest a principal indication for staged procedures (within 45 days from principal event) although complete revascularization at the time of PA can be performed according to the operator´s criterion [10]. Regarding invasive functional evaluation, the evidence that supports its use is not conclusive and its superiority with respect to angiographic evaluation has not been proven especially in STEMI where the capacity of vasodilation of the bed could be affected, situation that would conduct to underestimate the severity of some intermediate lesions (**Table 5**).

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C) Particular scenarios

a) Revascularization in patients with prior myocardial revascularization surgery. Dr. Gustavo Lev (Interventional Cardioangiologist).

Coronary artery bypass surgery is a challenge due to the possibility of periprocedural infarction, higher in-hospi-

tal mortality, restenosis and occlusion, adding from the technical point of view, unusual origins, severe tortuosities, friable lesions with distal embolic risk around 15% of cases. The lesion occurred within a year is due more often to intimal hyperplasia while atherosclerotic plaque is the more frequent from three years of evolution.

Venous bridges: Stenosis are located in less than 7% of proximal anastomosis, 40% in the middle segment of the body, 30% in the proximal body and 23% in the distal one. Recent stenosis are related with surgical suture and the related oedema. In this type of lesions in order to reduce disruption risk, pre-dilation should not outweigh a relation 0.8/1 with the reference distal segment and must be count on stent graft due to rupture possibility. Subacute and chronic stenosis are softer, friable, large and are associated with greater thrombus frequency. Plaques with higher risk of embolism are related with acute coronary syndrome, venous bridge antiquity (> 5 years), the ones placed in the body, plaque volume, bypass degeneration degree, ulcers, and the presence of endoluminal filling dfects. It was evaluated to reduce the embolic risk relating overdilation for the impact of the stent diameter with the bypass distal reference and classifying them in three groups: I: < 0.89 mm with CPK elevation > 3 times in 6%, II: 0.9-1mm: 9% and III: > 1mm: 19% (p = 0.003). Direct stent reduced in 50% CPK elevation, with lower AMI incidence nor Q [1], and in a subanalysis of the DIVA trial [1] lower incidence was observed to 2.7 years of thrombosis (1% vs. 5% - p < 0.009) and of AMI (8% vs. 14% - p< 0.02. It is recommended predilation in ostial lesions for better positioning of the guide catheter and in distal ones for higher calcification and fibrosis. Severely calcified or fibrous stenosis may require high pressure balloons, rotational atherectomy, cutting balloon or intravascular lithotripsy (Shockwave IVL®) [2]. LASER might be useful reducing the volume in complex or ostial plaques. High speed rotational atherectomy is only reserved for restenosis cases with very severe calcification. In cases with higher risk of embolism, the use of systems of distal protection and thromboaspiration may result very effective. In VeGAS 2 [3] and X-SIZER trials was evidenced significant lower incidence of periprocedural AMI and bleeding [4]. In the cases of venous bridge occlusion, the best strategy is not to treat it, and if possible treat the native vessel unless its angioplasty is not feasible. In these cases, if it is imperative to treat the venous bridge, it is recommended recanalization with microcatheter or over-the-wire balloon, thrombectomy and/or distal protection systems, but knowing that successful rates and restenosis to 18 months are of 68% [5]. Thrombolitics inside the bridge are not recommended since they have been associated with AMI, hemorrhagic complications and long-term low permeability [6]. ACC/AHA/SCAI guidelines consider them as class III [7]. In cases of stenosis with intermediate lesions, ideally is to establish their severity and eventual demonstration of ischemia; we must mention that in Veleti and Veleti II trials [2] drug-eluting stents vs. medical treatment in intermediate stenosis of 12-year-old venous bridges were randomized, and in 4 year-follow-up there was a reduction of 35% in major cardiovascular events.

If it is necessary angioplasty of **mammary bridge**, it is recommended performing it through brachial access (particularly radial or cubital). 85% of stenosis are found in the distal anastomosis and 14% in the body of the mammary artery which can be secondary to technical problems during the surgery including hematoma or twisting of the artery. There are some reports of isolated cases successfully treated and without complications with drug-eluting stents and controlled by IVUS [9]. Also, we must analyze the presence of possible obstructions in the left subclavian or brachiocephalic/ subclavian trunk in case the right mammary had been used. Even if the angioplasty outcomes in these territories have very low incidence of complications, it was reported that in 21 patients [10] undergoing left subclavian severe stenosis treated with stent, in 33% of the cases, they presented mortality to 30 days of 9.5% and reestenosis of 29% at a year follow-up. Although the mammary body affection is unusual, there are publications of isolated cases with acute coronary syndrome caused by plaque rupture in 8-year evolution bridges and with filling defect in its distal segment being successfully resolved with antithrombotic therapy and angioplasty with drug-eluting stent, without complications [11]. In diverse experiences (389 patients) [12-14] of affectation of distal anastomosis, treated with balloon and/or conventional stent, a primary success between 87% and 92% with low incidence of major complications and restenosis of 20% to 41% at 1-year follow-up was observed. In a cohort study of 52 patients [15] treated with balloon (29%), conventional stents (33%) and drug-eluting stents (38%), a primary success of 93% and revascularization of 17% to 1 year (without differences in the three groups) was observed. The impossibility of stenting due to severe tortuosity with dissection risk is 19% [16], being recommended the use of hydrophilic guide wires and drug-eluting balloons [17].

In the case of radial bridges, affection usually is due to arterial spasm, flow competence and intimal hyperplasia (they have a thickening of the middle muscle layer, vulnerable to the lack of vasa vasorum in explanted arteries).

Their incidence is of 1.7% in a study with 2.211 patients [18]. 22 patients [19] treated with balloon, conventional or pharmacological stent [20] with bypass occlusion due to flow competence of 6%, restenosis of 17% (balloon 11%), and 6% of non-cardiac mortality at 6-year follow-up have been reported. We wonder if we must use **protection systems**. The incidence of adverse events in venous bridges is of 20%, with mortality increase at 30 days of 15% in complex, extensive and friable lesions. Systems of distal protection are recommendation I-B class (ACC/AHA/SCAI) [21] and II-B (ESC) since they have proven to reduce AMI due to atheroembolism in 50% of the cases [21]. It is suggested in high risk patients, such as: aged, chronic kidney insufficiency, severe ventricular dysfunction and lesions with high risk of embolism (thrombus presence, extensive stenosis, and high degree of bypass degeneration). There is a degeneration score based on the relation between the length of the stenosis and the ectasia regarding the total length of the bypass (Grade 0: <25%, Grade 1: 26-50%, Grade 2: 51-75%, Grade 3: > 75%). The type of protection will depend on the anatomy and tolerance of the ischemia. In stenosis of distal anastomosis, proximal occlusion balloon system or systems with filters, and distal occlusion balloon in critical stenosis of proximal anastomosis, of the body or with severe tortuosity are recommended. Intra-stent restenosis would not require its use since they have low incidence of major cardiovascular events [22]. Protection systems may be: a) distal occlusion balloon (PercuSurge Guardwire® or TriActiv®) being its advantages, its low profile and the effectiveness in the preven-

tion of particle migration, and the disadvantages, ischemia induced by vessel occlusion and limitation in contrast injection. The SAFER trial has shown a 42% reduction in major events due to lower AMI rate and no-reflow, with lower hospital costs having used PercuSurge® distal protection system [23], b) proximal occlusion balloon (Proxis®) allowing to cross stenosis with stopped flow [24,25]. In the PROXIMAL trial significant differences were not observed in relation to PercuSurge®, c) filters: they have the advantage of avoiding ischemia due to preserve flow during the procedure and the disadvantages of embolism and difficulty in crossing the lesion in critical stenosis due to its higher profile. Among them are, Filter Wire®, Spider®, Emboshield® and Trap® with a major events rate similar to the occlusion balloon. The FIRE trial showed an ischemic events reduction [26], and in Blaze I and II registries, cardiovascular events higher than 10% were reduced (FIRE trial) to 5% (p = 0.03). However, in an analysis from the Society of the American College of Cardiology with 19,546 patients included, only in 22% was performed under distal protection system and with significant lower incidence of no-reflow but without impact in mortality [27].

Even if, **drug-eluting-stents** have won their place in coronary territory due to high success rate, less restenosis and better long-term results [28], in the DIVA trial [29] there were not significant differences between conventional and drug-eluting stents (15 %vs. 13% revascularization to 3 years, 19% vs. 17% mortality and 18% vs. 20% AMI). Nevertheless, in the SOS [30] with paclitaxel and RRISC [31] with sirolimus studies, it was demonstrated lower AMI incidence (17% vs. 46% - p < 0.01), restenosis and revascularization (10% vs. 41% - p< 0.004) at 3-year follow-up, and in the ISAR-CABG [32] (paclitaxel and sirolimus), BASKET-SAVAGE [33] (5-year follow-up) and meta-analysis (5.296 patients) [34] were significantly reduced: mortality, restenosis and with 0.7% incidence of thrombosis. At 10-year follow-up (3.063 procedures), restenosis and AMI were also significantly lower with this stent type [35]. In SOS-Xience V [36], with stents of the latest generation, it was observed 18% mortality, 8% AMI and 12% target lesion reintervention. In a comparative study between balloon and drug-eluting-stent there were not significant differences either in restenosis or in major cardiovascular events [37]. The MGuard® of cobalt chrome with a polyethylene terephthalate micronet mesh-covered stent has been used in plaques of high risk of embolism. The INSPIRE trial and its experience with limited number of patients reported low incidence of cardiovascular events (7% AMI and 20% restenosis) at 1-year follow-up [38]. The use of stents graft is not recommended due to the evidence in multiple trials such as: RECOVERS, BARRICADE, STING (balloon-expandable Jomed® stent) or the Symbiot® stent (self-expandable), because of higher incidence of AMI and restenosis than conventional stents [39-41], only indicated in perforation cases (0.5%) and in aneurism exclusion. There are few reports of angioplasty performed with bioabsorbable stent in venous bridges as was evidenced in 10 patients [44] with 20% (2 patients) of events greater than 2-year follow-up (1 patient with thrombosis at 15 months and 1 patient with restenosis), and a case without complications at 40-month evolution with Absorb stent, distal protection system and controlled by OCT [44].

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b) Diabetes. *Dr. Diego Grinfeld (Interventional Cardioangiologist)*with contributions from Dr. Walter Rodríguez (Cardiovascular Surgeon).*

Ischemic cardiopathy is one of the major causes of global morbimortality [(1)], affecting more than 1/3 of diabetic patients in whom it presents in early ages, causing 60% of deaths, and producing an event incidence 4 times more frequent than in non-diabetic patients [(2)]. Diabetes prevalence remains growing as a population of higher clinical risk, with more comorbidities (vascular peripheral disease, stroke, chronic kidney insufficiency, etc) frequently associated with AHT, dyslipidemia, obesity, endothelial dysfunction, platelet hyperreactivity, diminished fibrinolysis and hyperfibrinogenemy with higher thrombotic risk [(2)]. In this context, diverse studies have shown that the presence of diabetes mellitus (DM) is a risk factor independent of adverse clinical events in patients undergoing atherosclerotic coronary disease (CD), observing regular outcomes with surgical revascularization or endovascular especially if they are compared with non-diabetic patients [(3)]. In accordance with the results of various randomized studies (CARDia, FREEDOM, SYNTAX), guidelines of clinical management recommend myocardial revascularization surgery (MRS) as first line treatment in patients with DM and CD, especially in the subgroup with multi-vessel disease and insulin requesting. The BARI study was the only one that showed with a 10-year follow-up period, the superiority of MRS in relation to coronary angioplasty (TCA) in terms of longer survival. However, a contemporary analysis of DM impact in long-term survival of patients with CD with multi-vessel compromise has not been performed. The FREEDOM results [(4)], basis of the current clinical practice guidelines were taken into account to place MRS as IA indication in the treatment of patients with DM and multi-vessel CD [(5)]. In real life, more than half of the patients have not been eligible to participate in a clinical trial as FREEDOM trial. Given its profile, the mentioned patient prognosis is worse, with higher mortality and with more major cardiovascular events independently if the revascularization was complete or not. Such characteristics conduct cardiologists and members of the multidisciplinary team to recommend individually the most sui-

table strategy. A 30-40% of diabetic patients with multi-vessel disease (MVD) are not candidates for surgical treatment due to the presence of comorbilities or adverse conditions in the vascular bed which increase the risk of the procedure, becoming TCA a therapeutic alternative [6]. Currently, TCA is not similar to the one of the FREEDOM trial where first generation pharmaco-active stents (51% sirolimus and 43% paclitaxel) were used. The current platforms have overcome the stents with paclitaxel in numerous scenarios, including diabetic patients [5]. Pharmaco- active stents of ultra-thin strut have shown lower rate of adverse events than first generation ones (> 120 μm) [7]. This great improvement in stents technology, modification in calcified plaque techniques, and intracoronary image guided TCA (IVUS or OCT or with pressure guide (FFR) help to improve the TCA results. Comparing the SYNTAX II trial [8], after 5-year follow-up, the main study happened in a significantly lower manner in Syntax II group versus the TCA historical cohort (21.5% vs. 36.4%, HR 0.54, IC 0.41-0.71, p <0.001), including a lower incidence of all-cause mortality (8.1% vs. 13.8%, p=0.015) and cardiac death (2.8 vs. 8.4%, p< 0.001). It highlighted also, the significant lower incidence of periprocedural infarction, spontaneous infarction, new revascularization, and stent thrombosis. Regarding medical therapy, 80% of patients were receiving aspirin and statins at 5 years post procedure. Even if the comparison between both studies (SYNTAX I vs. II) would have some methodological mistakes, the SYNTAX II shows us changes which occurred in a short time not only related with technology evolution but also with a better knowledge of the root of the problem (atheroma plaque), and consequently with significant improvements in the treatment strategy which involve, pharmacotherapy, plaque assessment and endovascular revascularization planning avoiding involvement with more complex plaques and poor results in the follow-up.

In conclusion, the therapeutic approach of multi-vessel coronary disease in diabetic patients remains a challenge for current cardiology. While clinical trials are carried out in selected and low risk populations will be essential to complement them with data on the real clinical practice results. The resources optimization in the use of IVUS, OCT or FFR should be a priority in these patients and the use of latest generation pharmacoactive stents must be mandatory to perform adequate outcomes and low rate of events in the long-term. Undoubtedly, MRS still has a relevant role in this subgroup of patients.

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c) Revascularization in patients with immediate perioperative Acute Myocardial Infarction, cardiac and non-cardiac. *Dr. Arturo Fernández Murga (Interventional Cardioangiologist).*

1.- Perioperative Myocardial infarction, cardiac (PMIc).

The perioperative myocardial infarction after myocardial revascularization surgery (MRS) is one of the most serious and life-threatening complications associated with a substantial increase of in-hospital morbi-mortality. The rise of cardiac biomarkers (AMI type 5) is correlated with higher risk of death and long-term adverse results [1]. A variety of mechanisms related or not with the coronary bridge have been described [2]. The most common causes associated with the graft are: the occlusion due to acute thrombosis, the subtotal anastomotic stenosis, the excessive kinking or stretching, the spasm of graft. Among non-related etiologies are: inadequate myocardial protection due to technical mistakes in cardioplegia management, incomplete revascularization, and coronary microembolization.

Early graft failure seems to be an infrequent event. In a meta-analysis published in 2017 by Thielmann M et al, an incidence close to 3.5% was found, although it widely varies among the analyzed series (0.2 to 6.8%) also existing a bias linked to the non-report of emergency re-operated patients without coronary angiography (CCG). Besides, the AMI incidence type 5 was variable depending on the definition and diagnostic criteria used, so when the elevation of cardiac biomarkers and new Q waves or left branch complete block was used, the reported incidence was of 5 to 14%, but when incorporating NMR which identifies new losses of viable myocardium increased to 20-30%. Early clinical suspicion and a precocious CCG allow identifying patients who will be able to benefit from a coronary re-intervention strategy in order to save myocardium, preserve ventricular function and improve the prognosis [4]. Karhunen et al [5] proved that a CCG control policy in patients with PMIc suspicion was associated with a drastic reduction of post-operatory mortality in comparison with a historic control group without CCG (22.2% vs.46.1%, p=0.015). The knowledge of the coronary anatomy prior to surgery and the grafts performed will give us an idea of the magnitude of the problem and the feasibility of a possible new intervention. The coronary circulation and the regional myocardial perfusion after MRS is not always comparable with the basal situation, so, the time of window could be expanded for a new reperfusion treatment.

Emergency coronary re-intervention in the context of PMIc requires an integrated approach of the intervening medical team (heart team), and may conduct to a new paradigm in which the emergency cardiac catheterization is available routinely when acute ischemia is identified in early postoperative. Emergency coronary angioplasty post MRS would be reserved to treat the native coronary artery (with acute graft failure or if a bridge had not been received, in presence of incomplete revascularization), and to the arterial grafts, avoiding to treat the occluded venous grafts and anastomosis sites, being reserved for these cases the re-operation with revision of bridges in not favorable cases for TCA and with big area of ischemia.

Conclusion: The early clinical suspicion in the postoperative and the urgent angiography enable the identification of different underlying causes of the perioperative myocardial infarction. Patients with early graft failure may benefit from an urgent re-revascularization treatment, being TCA preferable in most patients.

2,- Perioperative Myocardial Infarction, non-cardiac. The peri-operative myocardial infarction of a non-cardiac surgery (PMInonC) is an infrequent complication (0.9%), but serious for more than 300 million patients worldwide who undergo a major non-cardiac surgery each year [(6)]. The efforts to prevent them through the different risk scores have been unsuccessful. In-hospital mortality was higher in patients undergoing PMInonC than in those without infarction 18% vs. 1.5% P <0,0001. The PMInonC occurs more frequently in patients undergoing vascular surgeries (2%), transplants (1.6%) and thoracic surgery (1.5%). The optimal treatment is uncertain due to potential complications and risk of bleeding or thrombosis; however, patients with an early invasive strategy had associated lower mortality than the conservative treatment (8.9% vs. 18.1%, p=< 0,001. Current guidelines of clinical practice recommend the regular treatment, and the type of surgery adapted or modified according to each patient.

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d Revascularization before TAVI. *Dr Alfonsina Candiello (Interventional Cardioangiologist)*

It is estimated that the significant coronary artery disease (CAD) is present in the 50% of the patients treated with TAVI reducing the prevalence as the patient's age and risk diminishes. Currently, the impact of the coronary revascularization in patients with asymptomatic CAD being under TAVI is not clear, that's why it remains a matter of discussion. The key question that is waiting for its answer with the clinical studies that are being carried out is if a transluminal coronary angioplasty (TCA) must be done before TAVI to all the patients, and if it must be done when the best moment to perform it would be. The latest Clinical Guidelines of Valvulopathies 2020 of ACC/AHA [(1)] and of ESC 2021 [(2)], based on observational studies, declare that in patients submitted to TAVI with significant CAD of left main coronary artery or proximal epicardiac vessel, with or without angina, it would be reasonable to make an TCA (IIa Class, C: Evidence Level). According to the updated evidence, a meta-analysis of observational studies with 5,000 patients compared patients with CAD submitted to TAVI with vs. without previous TCA and no benefits were found with the routine TCA previous to TAVI at the occurrence of MACE at 30 days or at the mortality at a year the follow-up [(3)]. The ACTIVATION trial, is the unique randomized clinical trial, of non-inferiority, made so far, which compared a TCA strategy vs. no TCA previous to TAVI. The observed death and re-hospitalization rates at 1 year were similar between both strategies; however, the margin of non-inferiority was not achieved, and the group submitted to TCA showed an increase in the bleeding rate [(4)]. The recent consensus of the European Society of Cardiology 2023 on the handling of patients with CAD submitted to TAVI establishes that the scarce evidence available so far does not support performing a routine TCA previous to TAVI in patients with asymptomatic severe CAD [(5)]. However, it is suggested that it should be considered in patients with severe CAD (obstructions ≥ 70% in proximal epicardiac vessels or ≥ 50% in left main coronary artery), especially in presence of acute coronary syndrome, angina or sub-occlusive lesions (>90%). As regards the moment of the TCA, there is no evidence which determines so. However, considering the possible difficulties to have access to the coronaries after TAVI, it seems reasonable to make it previous to the valve implant [(6)]. We must point out that considering the absence of current evidence regarding the decision of making TCA previous TAVI, the Heart Team must play a key role individualizing the indication or not of coronary revascularization considering the before mentioned recommendations and taking into account clinical variables such as the presence of angina, risk of bleeding and variables related to the lesion like severity, localization and anatomic complexity.

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3) REVASCULARIZATION MODALITY (ENDOVASCULAR VS. SURGERY)

a) **Left main coronary artery.** *Dr Juan Manuel Telayna (h) (Interventional Cardioangiologist) Dr Guillermo Gutiérrez (Cardiovascular Surgeon) Dr Guillermo Vaccarino (Cardiovascular Surgeon) Dr Ricardo Costantini (Interventional Cardioangiologist).*

In 3 to 5% of the coronariographies a severe obstruction of left main coronary artery (LMCA) is observed, which implies a higher quantity of myocardial at risk of left ventricle, especially in cases of dominant left circulation, considering severe obstruction with criteria for an intervention when: 1) the diameter of stenosis by visual estimation in the angiography ≥ 50%, or 2) minimum luminal area (MLA) is < 6 mm^2 and minimum luminal diameter (MLD) < 2.8 mm measured by IVUS or 3) an index of FFR ≤ 0.80. From the anatomic point of view, LMCA has special conditions such as: a) a higher diameter than the rest of the coronary territories (3.5 to ≥ 6 mm, b) in the aorto-ostial union fibers of the middle layer of the aorta are mixed up with the ones of the coronary, being in this localization its structure similar to the aorta and c) of variable length, from absent (birth in "pipe rifle") up to ≥ 15 mm. It is divided in three segments with implications for the interventional treatment: ostium, body and distal. Considering distal commitment Medina's classification allows to evaluate the complexity of the lesion in bifurcation and the planning of the procedure, without predicting the post angioplasty events, being considered as true bifurcations: 1,1,1; 1,0,1; and 0,1,1. In this way we could divide the lesions in bifurcation in simple and complex ones, which would determine the endovascular strategy. In the one hand, in the simple ones, the stenosis of the secondary branch is < 70% and the lesion length is < 10 mm, which can be approached with a unique stent. On the other hand, in the complex ones, the stenosis of the secondary branch is > 70% and its length is > 10 mm. With the presence of two of the following criteria, the lesion can also be considered complex: 1) moderate to severe calcification; 2) multiple lesions; 3) angle between DA and CX > 70%; 4) diameter of the vessel of main reference < 2.5 mm; 5) thrombus; 6) length of main lesion > 25 mm. These lesions usually require a two-stent strategy. For the isolated ostium lesions of DA, the provisiona stenting technique towards CX with POT (proximal optimization technique) is recommended. On the other hand, for the isolated lesions of the ostium of CX, the strategy of the two stents showed lower TLR and TLF than the treatment with only one stent.

The higher angulation at 70° between LMCA and the anterior descending artery (DA) was associated with less events due to the lower frequency of restenosis. However, the angulation between DA and circunflex (CX) did not predict events. As regards the surgical technique we suggested the preferential use of arterial conducts over vein bridges. Lytle et al., 1999 showed higher survival when using two mammaries instead of one in patients submitted to CRM. In turn, the surgery without using the extracorporeal circulation could be a protector of early mortality. However, the international publications are not decisive in this aspect, depending on many preoperative variables and the experience of each group in this subject. From the Veterans (Circulation 1976) and the CASS (Circulation 1995) trials the myocardial revascularization surgery (MRS) was established as class I for the LMCA treatment. With the advent and development of drug-eluting stents and intravascular images, the coronary angioplasty (TCA) has been winning its place. Currently, the guides recommend TCA in patients with LMCA disease and/or other coronary vessels in absence of diffuse or complex coronary lesions, the surgical therapy will predominate when they are present.

In diabetic patients there were no differences in terms of MACE (death + AMI + re-intervention + stroke) between the groups treated with TCA with stent or MRS in the evidence published in the last great randomized ones (Syntax 10 years - Excel - Noble), although there was a higher tendency to events, especially re-intervention in patients treated with angioplasty.

Although the trials published, as well as in the daily practice, the percentage of patients with kidney insufficiency is low, and the analysis of sub-groups is not performed in this scenario, we must emphasize that its presence implies more risk. In the analysis of the EXCEL subgroups at five years, the patients with ventricular dysfunction lower than 50%, did not show differences in terms of MACE for both treatments, with a tendency in favor of MRS. In most of the series published there is a higher tendency of events in the group of coronary angioplasty, in patients with higher anatomic complexity, assessed by the SYNTAX Score. However, when the SYNTAX Score is low or intermediate, it seems to be there are no differences in terms of MACE between both treatments. Finally, we can say that in presence of the ostium and LMCA body commitment, there are no differences between both treatments. But we should analyze the clinical and anatomical conditions in presence of bifurcation lesions. In the one hand, the greater anatomical complexity, the better long-term results would seem to have the a priori surgery, especially in the re-intervention. On the other hand, considering a high clinical risk, the coronary angioplasty has gained its place. If the endovascular treatment is chosen, it is compulsory to use intravascular images, due to the fact that its use has shown less mortality, infarction and re-intervention. The Heart Team should evaluate apart from mortality, the morbidity conditioned especially by AMI, CVA and re-intervention, all of them conditioning the quality of life. Finally, we would like to emphasize Dr Braunwald's phrase when referring to the Excel study in 2017: *"The message to take home of the EXCEL trial is that most of the patients with non-protected left main coronary artery disease, that was a very serious condition, which shortened life and disabled people at the beginning of my professional life, now it can be managed just as well through two strategies of revascularization if they are carried out by experts, like the ones who take part in the EXCEL trial".*

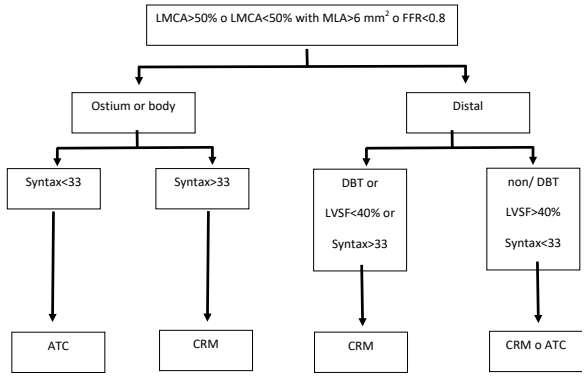

Figura 3. .

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b) **Multivessel disease.** *Dr. Guillermo R. Martino (Interventional Cardioangiologist) and Dr. Gustavo Bastianelli (Cardiovascular Surgeon).*

The multivessel disease is defined as a ≥70% stenosis in at least two coronary arteries or in one of them related to a ≥ 50% obstruction in the left main coronary artery. More than half of the patients to whom coronariography is performed undergoes multiple disease, which implies a three-time-higher risk compared to the ones who have only one epicardial vessel disease [1,2]. Advance in surgical techniques with smaller incisions, arterial conducts, surgeries without extracorporeal circulation and a better postoperative attention have led to a morbimortality reduction. Therefore, the technological advances and the technique refinement have also improved the TCA outcomes widening the scope of the treatment including patients with complex anatomy such as the multivessel disease with good immediate and long-term results [3]. Sometimes the decision of the best strategy is not easy. In the SYNTAX 1 [4] 1,800 patients were randomized, who had > 50% obstruction in vessels > 1.5 mm to MRS or TCA. In the one hand, the rates of adverse events higher than 12 months were significantly higher in the TCA group mainly due to higher need of revascularization repeated by restenosis (13.5% vs. 5.9%, p< 0.001). On the other hand, at 12 months, the rates of death and myocardial infarction were similar between groups, and the cerebrovascular accident was significantly more probable with MRS (2.2% vs. 0.6%, p = 0.003). At 10 years, the follow-up was completed in a very high percentage of these patients (93% angioplasty group and 95% MRS group) and there was no difference as regards mortality in favor of one or the other method [5]. With Syntax Trial, the classification of patients has been implemented according to the lesions anatomic complexity, its location, its quantity, etc. as Syntax *Score* (SS). It grants a score that has allowed us to separate 3 groups (a) < 22, b) 22 to 32 and c) > 32) with different complexity and different risk. In the ones of low score, the results are comparable to both methods (32.1% vs. 28.6% in composite endpoint); however, in the ones of moderate risk, although there were no substantial differences globally, when only the patients with multivessel disease are taken into account and the left main coronary artery disease is excluded, the outcomes are in favor of a higher surgical benefit, fact that is more marked when the patients are diabetic (37.9 vs. 22.6, p=0.0008); when the SS increases, the curves get separated in benefit of the surgical revascularization at 5 years. Although one of the main advantages of the surgery was the lower need of reinterventions, the TCA had lower stroke incidence at short-term. In spite of the fact that the SYNTAX Trial was performed with a paclitaxel eluting stent already out of service, the new studies

made with different drugs could not show the non-inferiority of the TCA either as regards MRS in the multivessel disease due to the need of reinterventions [6]. A detail to be taken into account is the proportion of complete revascularization obtained being 63% with MRS and 57% with TCA. In some sub-studies [7,8] the residual score was analyzed and defined as 0 in complete revascularization and > 0 in incomplete one, which was in turn stratified in terciles (>0-4, >4-8, >8) showing the increase of the anatomic and clinical complexity. A residual Syntax score > 8 was associated to a 35.3 % all cause-mortality at 5 years (p< 0.001). Banglatore et al [9] compared all cause-mortality, infarction, stroke and need of a new revascularization in patients with multivessel disease treated by one or the other method observing that who received stent with everolimus had less stroke, but higher incidence of infarction mainly in those to whom a complete revascularization had not been achieved; not like that in those to whom it could be achieved. Although we do not count on randomized studies, we have some information from registries. From the surgical point of view, in the Argen-CCV registry 1001 patients were incorporated to whom revascularization surgery, valve surgery, of the ascending aorta or combined were made in the Argentina Republic. 59% were coronary patients. In the immediate postoperative the following was observed: bleeding 10%, low expediture syndrome 16%, inotrope/vasopressor requirement 70%, prolongued ARM 18%, kidney failure 14%, haemodialysis 3.5%, Stroke 3%, psychiatric alterations 9%, postsurgical infection 6%, mediastinitis 1%. Average of hospitalization days: 8 days and global mortality: 11% (MRS: 8%, valvular: 9% and combined 18%) [10]. From the endovascular point of view in the RAdAC 2 (Registro Argentino de Angioplastia Coronaria–Argentine Registry of Coronary Angioplasty) from September 2019 to September 2020, 38 medical centers of 15 Argentine provinces included 2,256 patients with indication of coronary angioplasty. The clinical indication laid on: ACE: 14.85%, unstable angina: 30.46%, STEMI 26.44%, NSTEMI 18.37%, ICC 4.05%, Silent ischemia. Severe coronary obstructions were located in LMCA: 5.27%, being one vessel disease: 49.62%, 2 vessels: 29.49% and ≥ 3 vessels: 20.89%. 2.544 TCA were performed with a Global Primary Success of 92.93%. The number of necessary procedures in order to solve the cases were: 1: in 93.53%, 2: in 6.26% and 3: in 0.2%. The patients were treated with DES in 93.69%, BMS: 5.9% and DEB: 0.4%. The following were registered as periprocedure complications AMI type 4a: 0.53%, AMI type 4b: 0.04%, TIA: 0.08%, TIMI major bleeding: 0.35% (digestive 3points, femoral puncture 2 points, radial puncture 2 pts, urinary 1pts), stent thrombosis: 0.35% (Acute and Defined in 6pts, Sub-acute in 2pts being Possible 1 point and Probable 1point). An urgent MRS was not necessary in none of the patients. Global mortality was of 1.37% being the cardiovascular cause 1.24% and the non-cardiovascular cause 0.13% [11]. We believe that both registries show us a guideline on the strategies and possible results in the centers which participate in our field. TCA must be considered as first option in patients with moderate / low SYNATX *Score*, conserved ventricular function and non-dibetic, being able to think in MRS in more complex scenarios [12]. In selected cases the hybrid revascularization must also be evaluated [13]. Although SYNTAX *Score* is widely used, we must consider the subjectivity in the evaluation, having shown great intra variability in inter-observer [14]. In order to decide the best revascularization method in each case we must evaluate the anatomic characteristics, the ventricular function, the feasibility of complete revascularization, comorbidities and patient's preference. Before similar possibilities with both techniques (MRS or TCA) we must evaluate the alternative of staggered approach and eventual higher possibility of re-intervention in the one hand or take the post-operative risks involved, higher incidence of stroke, more in-hospital days with a more prolonged convalescence, higher possibility of kidney failure. Although the surgical technique of avoiding the aortic manipulation, aortic no-touch off pump technique, has shown a very low rate of neurological event (0.09%) it is not the most used strategy [15]. As a conclusion, we must say that each case is unique and therefore, the most appropriate behaviour must be decided in the consensus of the Heart Team who assesses risks and benefits of each tactic, the experience of the treating group and the patient's preferences.

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4) ENDOVASCULAR REVASCULARIZATION STRATEGIES

a) Thrombus containing lesions. *Dr. Alejandro Diego Fernández (Interventional Cardioangiologist).*

The evident angiographically thrombus is present in the 91.6% of the patients with acute myocardial infarction with ST elevation, and the intracoronary thrombosis defined as "massive" has been reported in 16.4% of the cases. (Sianos G, 2007). The primary angioplasty is today, the elective treatment for the acute infarction with ST elevation, and the presence of intracoronary thrombosis, especially in the cases with massive thrombosis, remains a challenge for the interventional cardiologist because, despite counting on powerful antiplatelet and anticoagulant drugs, the thrombus is still a factor of distal embolization risk, a phenomenon of "no clock", thrombosis stent and development of long-term adverse effects. **Quantification of intracoronary thrombus**. The most commonly used method for the thrombus quantification is based on the angiography. Angiographically, the thrombus is defined as the presence of a filling defect, with a density of reduced contrast also defined as "haziness" (from English "hazz" = "fog"). The TIMI score is the most widely used to quantify the intracoronary thrombus, and it is based on the relative size of the thrombus regarding the affected vessel, using a score that goes from 0 if there is no thrombus to 5 in case of thrombus of a great size with total vessel occlusion. (Gibson CM, 2001). In **Table 6** the Thrombolysis in Myocardial Infarction (TIMI) score can be observed. Some authors suggest that in the cases of thrombosis Grade 5 with total vessel occlusion, the thrombus should be reclassified after passing a wire or a balloon of small diameter to restitute the antegrade flow. Once the flow is restituted, it is recategorized as Grade 0: without residual thrombosis, grade 1-3: small residual thrombus and grade 4-5: great residual thrombus. (Sianos G, 2007).

Table 6. TIMI thrombosis score

Grade	Description
0	Without angiographic thrombus evidence
1	Possible thrombus: Reduction of the contrast density or ***"Haziness"***, a lesion with irregular outline
2	Thrombosis present in multiple projections, with a filling defect with a size ***lower than half of a vessel diameter***
3	Thrombosis present in multiple projections, with a filing defect with a size ***higher than half and lower than twice the vessel diameter***
4	Thrombosis present in multiple projections, with defect of filling with a size ***higher than twice the vessel diameter***
5	Thrombosis with ***a complete vessel occlusion***

HANDLING OF INTRACORONARY THROMBUS.

As we already mentioned, the current guides recommend the angioplasty as the chosen treatment in the acute coronary syndromes with ST elevation. Handling lesions with high thrombotic content during a coronary intervention implies a great challenge and in order to do so we have a wide range of tools either pharmacological or mechanical that we describe as follows.

Pharmacological Agents. The early administration of ***dual antiaggregant therapy*** is able to reduce the amount of the thrombus and to substantially improve the clinical results. The Aspirine, administrated orally or chewed in 150 – 300mg loading dose has an initial action of between 30-60 minutes, to this the administration of a P2Y12 inhibitor (Clopidogrel 600mg, Prasugrel 60mg o Ticagrelor 180mg) is added. Ticagrelor and Prasugrel have an initial action quicker than Clopidogrel and they have shown better clinical results in some comparative trials. There is a P2Y12 inhibitor for the intravenous administration (Cangrelor), which is not available in our country now (2023), and it is very useful to administer in the cath-lab especially in patients who cannot receive oral medicine such as for example those who are under respiratory assistance. (European Society of Cardiology, 2018). **IIb/IIIa Glycoprotein inhibitors** take to a quick and almost complete inhibition of the whole platelet response. These agents have shown an excellent capacity to dissolve the thrombus angiographically visible and to restore the flow. Most of the clinical evidence available is based on the use of Abciximab, but we can consider that there is certain effect of class and we can extrapolate this piece of information to other agents available in the market (Tirofiban and Eptifibatide). In contrast to its high efficiency in the treatment of patients with acute coronary syndrome, the high risk of bleeding is the weak point of these agents. In a meta-analysis of 10,123 patients to whom a primary angioplasty was made, the nonfatal infarction was reduced from 8.3% to 5.1% ($p< 0.001$) by using IIb/IIIa inhibitors, but there was a 3% bleeding increase vs. 1.7% ($p< 0.001$). (Winchester DE, 2011). That is why the current guides do not recommend the routine use of these agents and they only consider them for the cases in which the presence of a thrombus is observed, slow-flow or no-reflow or other thrombotic compilation (European Society of Cardiology, 2018). The classical via of administration of IIb/IIIa inhibitors is the intravenous one, although, in theory, the administration via intra-coronary could have some advantage, because a higher local concentration of the drug could be achieved and it could result in a higher receptor activity. In this sense, there are small studies and with controversial results because the AIDA-STEMI study did not show differences in the final point comparing the intra-coronary administration versus the intravenous

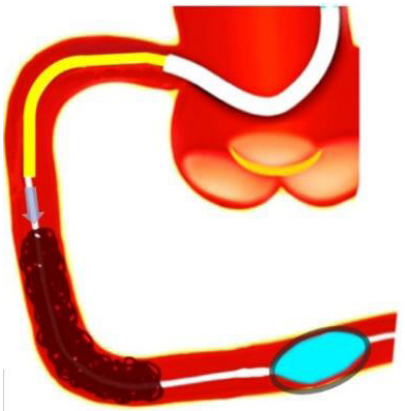

Figura 4. *"Marinado" technique. Taken from: Unzue L. 2022.*

one and, on the other hand, a meta-analysis of Shimada et al, showed a favorable effect of the intracoronary bolus in terms of final TIMI flow and short term mortality, without bleeding risk increase (Shimada YJ, 2012). The truth is that, as long as a final evidence does not appear, supported by higher importance studies, the administration via recommended for IIb / IIIa inhibitors is still the intravenous one. The ***Thrombolytics*** administered by intra-coronary via have shown a favorable result in small studies, in patients with high thrombotic burden where the aspiration methods have failed. The first randomized study on this matter was the DISSOLUTION trial, where a total of 102 patients were randomized in order to receive intracoronary Urokinase or saline solution as adjuvant treatment to the manual aspiration. This study showed a higher incidence of TIMI 3 flow and higher resolution of ST with urokinase without bleeding increase. Currently, there are two studies belonging to phase III, one with low dose of intracoronary tPA (STRIVE trial) and another one with intracoronary tenecteplase (RESTORE-MI trial) that wish to show, at a higher scale, the benefit of the intracoronary thrombolytics as therapy contributing to the aspiration. As an alternative to the intracoronary administration, the group of Eulogio García et al. proposes a technique of administration called "marinade technique". With this technique the thrombolytic is administered selectively through an extension of a guide catheter, while a distal balloon is insufflated to the thrombus, this guarantees a higher time of thrombus exposition to the thrombolytic agent. **(Figure 4)** (Unzue L, 2022)(J.I. Damonte, 2022).

Thrombectomy devices. The devices of thrombectomy are divided into two big groups: the *manual devices* and the *mechanical devices*. The first device of ***manual aspiration*** was developed by Auth in 1995, from that time up to now the devices through aspiration have turned into more friendly for their users, thanks to a higher flexibility, hydrophilic coverage and lower cross profile. All the systems of manual aspiration available nowadays use the same principle and have a catheter of quick interchange over cord 0.014", with its distal extreme bevel cutting and its proximal extreme connected to a vacuum syringe. The first study randomized of manual aspiration use in acute infarction was the REMEDIA Trial, which showed that the manual aspiration was related to a significant reduction in the incidence of No Reflow and of distal embolization with a ST higher resolution, although it could not show any clinical benefit. Then, the TAPAS trial which gathered 1,071 patients showed a reduction of higher events. In contrast to these results, when studies randomized at a higher scale were made comparing the systematic thrombus aspiration versus the angioplasty, such as the TASTE and TOTAL trials, it was observed that that practice did not show any benefit. Based on these results, the current guidelines do not recommend the thrombus aspiration as a routine practice in the primary angioplasty and they only recommend it for those cases where there was the presence of high residual thrombotic burden after opening the artery with a wire or a balloon. (Jolly SS C. J., 2018)(Jolly SS C. J., 2015). As regards the ***mechanical thrombectomy devices***, there are different principles of functioning, among which the most widely spread are: the rheolitical thrombectomy devices (Angiojet®), the by extraction devices (X.sizer®) and the thrombectomy through Excimer LASER. As regards ***Angiojet®,*** the principle of functioning is based on the injection of a saline solution at high speed, which generates thrombus dissolution and a great force of suction by Venturi effect. The JETSTENT trial compared the use of this device versus the primary stent implant in 501 patients and it could not find significant differences between both treatments in terms of resolution of ST or TIMI 3 flow incidence. However, the group treated with Angiojet® showed a better survival free of events at one year. Angiojet® could be a useful device in patients with high thrombotic burden, except for its use is limited to a total of 10 minutes maximum in order to prevent the appearance of hemolytic anemia as a complication (Migliorini A, 2010). The ***X-sizer®*** system has a catheter where a helical propeller is in its distal extreme and it is able to rotate at 2100rpm by means of a battery engine, whose proximal extreme is connected to a vacuum bottle. The X-TRACT AMI trial registered 216 patients and showed an improvement in the TIMI 3 flow rate and the X AMINE ST trial showed an improvement in the ST resolution and in the No reflow incidence, but none could show the clinical benefit. Finally, the use of ***Excimer LASER*** has also been proposed as treatment for cases with high thrombotic amount, although there are not randomized studies which guarantee so, there is only a multicenter file, the CARMEL registered 151 patients and it only showed an improvement in the TIMI 3 flow rate. (Kumar V, 2020).

Stenting. As regards the implant of stents in the thrombotic injury context, there are several possible strategies. On the one hand, the ***implant of a stent in a direct way*** without previous pre-dilation reduces the possibility of distal embolization when minimizing the manipulation of the lesion, the disadvantages that this technique can have are the underestimation of the vessel real size, an inadequate stent expansion or the appearance of the bad and late apposition. In a meta-analysis of 754 patients, the direct stent implant showed a significant improvement in the ST resolution and a reduction of in-hospital mortality (Aiman Alak, 2015). The

covered or self-expansible stents are another alternative proposal for the cases of lesions with high thrombotic content. In the case of covered stents, they are metallic stents covered with a fine metallic mesh able to capture the thrombus (MGuard®) and in the case of the self-expansible ones, they are nitinol stents (Stentys®) which are able to adapt themselves to the vessel wall, even once the thrombus stuck to the wall has been dissolved. Although in the MASTER I trial, the MGuard® stent showed benefit in terms of ST resolution and mortality at one year. The trial at higher scale, MASTER II, had to finish prematurely due to an increasing operators' preference for drug eluting stents. As regards Stentys®, the APPOSITION IV trial showed a lower percentage of struts badly positioned at 4 months compared to the stent expansible balloon, but in the follow up at 9 months the rate of badly positioned ones was similar in both groups. From what has been said, the conclusion that arises is that there is no evidence so far which can support the use of stents covered or self-expansible in the context of injuries with high thrombotic content. Finally, there is the strategy of ***differing the stent implant,*** giving from 24 to 48 hours of intense antithrombotic therapy with IIb/IIIa inhibitors and heparin. The angioplasty performed after this time usually shows a significant reduction of the thrombus, which would allow the stent placement with a minor risk of distal embolization. The DEFER-STEMI study showed a significant reduction in the rates of no reflow in the high risk population, using the strategy of a stent deferred. (Carrick, et al, 2014). However, the DANAMI 3-DEFER study could not show the significant clinical benefit with the deferred stent strategy. (Kelbæk, et al, 2016).

Conclusions. The presence of thrombus during the primary angioplasty is a challenging situation, due to the potential risk of embolization, slow flow and non-reflow. In general, the use of an optimal dual platelet anti-aggregation and anticoagulation is enough when the amount of the thrombus is small. The treatment of thrombus of higher quantity may be faced with the intravenous administration of IIb/IIIa inhibitors. In presence of massive thrombosis (degree ≥3) the manual aspiration can be considered and in case of not being successful with it let us consider the use of intracoronary thrombolytics. As regards the stent implant, the use of a direct stent is always convenient, if the presence of a residual thrombus is little (degree < 2), and when tortuosity or vessel calcification are absent.

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b) Calcified lesions. *Dr. Juan Manuel Ponce (Interventional Cardioangiologist).*

Calcification of coronary lesions is usually associated with complex lesions in patients with multiple co-morbidities (Diabetes Mellitus, Arterial Hypertension, Chronic Renal Insufficiency). Its presence forces us to develop a strategy for proper plaque preparation, which directly influences the outcome of coronary angioplasty (TCA) and long-term prognosis [1]. Calcium content is usually underestimated by coronary angiography, especially when it comes to assess the circumferential vessel involvement or the presence of calcium nodules, that is why intracoronary imaging, such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT), should be used [2-3]. Calcifications can be concentric/eccentric, superficial/deep and/or short/long, although nodular calcification is the most complex.

Intravascular imaging: IVUS shows calcium in the artery wall as an important ecorefringence (bright plaque) with an acoustic echo behind it that does not allow evaluating the depth of the plaque (in the case of very calcified plaques) or by reverberations with multiple oscillations of the ultrasound in the less calcified ones. It has a sensitivity of 86.7% and a specificity of 93.3%. When OCT is used, calcium is observed as an area of low signal intensity, with well-defined borders, which enables us to evaluate its depth. Compared to the information provided by IVUS, OCT allows us to evaluate the thickness, area and volume, which is very important to define a plaque preparation strategy [4, 5, 6]. In order to plan the best plaque preparation strategy, it is relevant to define how many quadrants (1 to 4) are involved.

Plaque preparation: to change vessel compliance and thus achieve adequate dilatation and subsequent stent apposition and symmetry (if used), proper plaque preparation is mandatory, for which we have different devices, namely:

Non-Compliant Balloons: these balloons can be pushed to high pressures (around 20 Atm) with minimal changes in diameter allowing to concentrate the forces on dilating, often achieving the rupture of the calcified plaque. They are also often used to post dilate stents and thus optimize their expansion and apposition.

Very high-pressure Balloons: these are non-compliant balloons of 2 or 3 layers that allow a uniform dilatation and can reach up to 35 Atm. They are usually used in both concentric and eccentric lesions. Due to their higher profile, they are not the first choice [7].

Cutting balloon®: are balloons with longitudinally arranged micro-blades on their surface (3 or 4 depending on the diameter), which allow micro-cuts to be made on the surface of the calcified lesion and optimize stent implantation by changing the compliance. Its limitations are its high profile and the risk of coronary perforation [8].

Scoring balloon: these balloons have nitinol filaments on their surface, having a mechanism of action like the Cutting balloon® with a better crossover profile, but a lower success rate. They are usually used in combination with other methods such as rotational atherectomy [2, 8].

High-speed ***Rotational Atherectomy:*** (RA) consists of an olive-shaped reamer with the distal part of its surface covered with diamond crystals. This olive is mounted on a special guide of 0.009/0.014 inches and rotates at high revolutions (from 135,000 to 180,000 rpm). Various diameters of olives are available and can be selected according to the case. RA obtains the best results in concentric plaques, with circumferential involvement and luminal area smaller than the available olives. In the case of eccentric plaques and tortuous segments, the risk of dissection and coronary perforation increases. The latter, together with olive entrapment, bradycardia and no-reflow phenomenon are the complications described for this procedure, though the risk is low if there is an adequate selection of patients [1, 9, 10, 11, 12,13, 14].

Orbital Atherectomy (OA): the device has an eccentric crown, whose surface is coated with diamond crystals, which rotates pneumatically (80,000 to 120,000 rpm) when mounted on a special 0.012/0.014-inch wire. Therefore, it achieves an elliptical rotation. This, due to the eccentric location of the crown, causes an anterograde and retrograde sanding of the vessel wall. The indications and contraindications are the same as for RA. As for complications, they are similar to the ones in RA, with a lower risk of crown entrapment due to the anterograde and retrograde effect, and as the particles released are smaller, the occurrence of No-reflow is lower [1, 15, 16, 17].

Excimer LASER (EL): consists of a catheter mounted on a 0.014" guide which, by applying high-energy light, pretreats the plaque by means of a photomechanical (bubbles generated in the liquid medium), photochemical (disintegration of the plaque) and photothermal (local temperature due to the high-energy light) mechanism. EL is not frequently used as the first option, being its main application when it is not possible to progress microcatheter or in the case of chronic occlusions. Complications are the same as for RA and AO, the most frequent ones are perforation and coronary dissection. [18, 19].

Coronary lithotripsy (CL): it is performed by means of a balloon with ultrasound emitters inside, which by means of small electric sparks generate vapor bubbles in the liquid medium of the balloon, which, when expanded, generate compression and decompression pulses on the calcified plaque, of approximately 50 atm. This fractures the calcium in the vascular wall [20]. Although it is used for circumferential calcium, good results have also been shown for eccentric calcium, tortuous vessels, calcium nodules and in the case of under-expanded stents due to severe calcification or calcified neoatherosclerosis, being the latter an off-label indication [21, 22, 23, 24]. Complications are not well defined, since there are no records or presentations with a large number of cases and long-term follow-up, and may present coronary dissection or perforation; it should be noted that, given the fragmentation of calcium caused by CL, the fragments do not migrate, there is a low risk of no-reflow, which makes it a safe and efficient treatment option [25, 26, 27].

Severe calcification of coronary lesions continues to be a challenge. It occurs in patients with co-morbidities, elderly, with difficult access, etc. This makes procedures more complex. We should be able to evaluate calcifications as accurately as possible with endovascular imaging and thus choose the best plaque preparation method in order to perform an excellent angioplasty, thereby guaranteeing adequate stent expansion and apposition, and the lowest incidence of events over time.

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c) Long lesions. *Dr. Sebastián Balestrini (Interventional Cardioangiologist).*

Although there is no universally accepted definition based on the ACC/AHA/SCAI classification and the development of the SYNTAX Score, we can define diffuse or long coronary lesions as those that are longer than 20 mm. When the length of the lesions exceeds 40 mm, they can be considered ultra-long lesions. Based on angiography, in the one hand, when there are multiple obstructions in the same coronary segment and the distance between them is less than 3 times the reference diameter of the vessel, they should be considered as "tandem" lesions; on the other hand, when the distance between the obstructions is greater than 3 times the reference diameter, they should be analyzed and considered as different lesions[1,2]. Diffuse long lesions comprise more than 20% of percutaneous coronary interventions and are an important determinant of unfavorable clinical outcomes. Although the use of drug-eluting stents (DES) has drastically reduced the rate of angiographic and clinical restenosis compared with conventional bare-metal stents (BMS), the occurrence of in-stent restenosis and remote ischemic events remains a problem[3]. By using pullback (manual or automatic) of pressure guides under both maximal (FFR) and instantaneous (iFR) vasodilation, functional patterns of disease can be found: A) a predominantly focal pattern with the greatest pressure drop localized within a given lesion segment, B) a predominantly diffuse pattern with a gradual and continuous pressure drop along the length of the lesion and C) a mixed pattern with balanced focal/diffuse distribution with multiple mild to moderate pressure drops in segments with diffuse disease[4,5]. Overall, hemodynamic measurements allow reclassification of the disease pattern in more than 35% of cases compared to angiography alone [4]. In long lesions, despite a successful angiographic result, a suboptimal physiological result (FFR or iFR ≤ 0.90) is observed in up to 30% of cases, mainly in the context of a diffuse pattern of disease[5]. In fact, in patients with long (30 mm) and ultra-long (> 50 mm) lesions, a satisfactory post-PTCA FFR value (FFR > 0.90) was achieved in only 26% of patients and about 20% of patients had FFR < 0.80 at late follow-up[5,6]. Percutaneous intervention of long stenosis with focal functional patterns provides greater late clinical (symptomatic) and anatomical (angiographic) benefits compared to vessels with diffuse disease patterns[5,7]. The use of intravascular imaging such as ultrasound (IVUS) has shown to reduce by approximately 55-60% the risk of cardiovascular death, combined major events (death, AMI or revascularization) and by 70% the risk of stent thrombosis. Therefore, the recommendation for the use of IVUS becomes mandatory in these lesions[8,9]. In this type of lesions, the direct stenting technique does not seem appropriate, and an adequate plaque

preparation is recommended[9]. Although the use of first-generation drug-eluting stents (DES) overlapping in order to cover a greater length showed a higher risk of adverse outcomes[10,11] due to persistent inflammatory reaction, fibrin deposit and delayed endothelialization, due to the higher concentration of drugs and stent polymer, such reaction is not seen with the new DES models, and the results are comparable to those obtained with a single stent[13-15].

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d) Ostial lesion. *Dr. Daniel Zanutini (Interventional Cardioangiologist).*

An ostial lesion of a coronary artery is the one located within the first 3 mm of its origin [1]. The ostium is rich in elastic fibers, so it is retractile and difficult to expand, especially in cases of aortic ostium where the artery wall is part of the aortic wall. They usually have a high rate of restenosis and calcification. After mechanical expansion, dissection can easily occur [2]. Since in most cases we work with angiographic equipment in a two-dimensional plane, it is often difficult to pinpoint the exact site of the ostium, which complicates the precise stent placement. In these cases, we must evaluate the plaque in multiple projections, which would allow us to "construct" the three-dimensional image in our mind. For an adequate plaque preparation, we must know the characteristics of the lesion and IVUS is more appropriate than OCT because it allows us to choose more accurately the best alternative method. When fibrosis is predominant or when faced with calcifications < 180° we will choose non-compliant balloons or cutting balloons (Cutting Balloon® or AngioSculpt®) and when faced with larger calcifications we will choose high speed rotational atherectomy or intravascular lithotripsy depending on the case. Incomplete expansion of the stent, poor apposition of the struts in the arterial wall and/or stent fracture are important risk factors for restenosis and/or thrombosis, so it is imperative an adequate preparation of the plaque and if possible subsequent evaluation with IVUS to evaluate it [3]. However, we must bear in mind that the most modern angiography equipment is provided with a software [4] (StentBoost®, StentViz®, etc.) that, through the radiological system, allows better visualization and evaluation of the expansion and symmetry of the stent. There is no single technique that allows optimal placement of the ostial stent so we must consider in each case the use of multiple angiographic views to assist in the implantation such as the use of the Ostial PRO® device, the aortic flow guide technique, the anchor guide technique (Szabo technique), the T-stent and/or small protrusion technique (TAP), as described in bifurcation lesions, and the new dedicated ostial stents. The Ostial PRO® device, designed for the treatment of coronary or renal aorto-ostial lesions, is introduced through the guide catheter's light (6, 7 or 8 F) and consists of 4 nitinol handles coated in gold for better visualization, which are evaginated when they come out. These handles rest on the wall of the aorta so the catheter is not in contact with the aorta. Thus, less trauma to the catheter and better objectification of the ostial geometry would be achieved [5]. The Szabo technique allows the stent to be adjusted to a coronary ostium or to the carina in bifurcation lesions; 2 coronary cords are used, one as usual and the second is passed through the last proximal cell; advancement is usually difficult and there is a risk of stent loss in recoil. There are only isolated reports, and due to the deformation generated in the stent there can be various inconveniences during implantation. The "floating stent" tactic consists in leaving the stent a few millimeters before the ostium (floating stent) without the possibility of apposition due to the diameter of the vessel. For example, if the ostium of the anterior descending artery was treated, the stent would remain a few millimeters inside the left main coronary artery "leaning out" into the ostium of the circumflex artery [7]. Another strategy consists in implanting a stent that simultaneously covers the ostial lesion of the AD, the origin of the Cx and, to a greater or lesser extent, the distal LMCA [8]. This involves further intervention to adapt the proximal portion of the stent to the bifurcation and the LMCA. In the vast majority of cases by simultaneous final inflation of two balloons (kissing balloon) and/or POT (proximal optimization technique). Another new technique is the use of real-time IVUS guide, which allows the precise placement of the ostial stent [9]. In relation

to stent design, although it is universally accepted that we should use DES because of the lower probability of restenosis at the coronary level, we must consider that for the aortic ostium there are models with a more variegated proximal mesh (Synergy Megatron®) that would allow greater support and less «recoil» than the usual ones, since we are partially supporting the aortic wall.

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e) **Non-left main coronary artery bifurcation lesions.** Dr. *José Oscar Gomez Moreno (Interventional Cardioangiologist).*

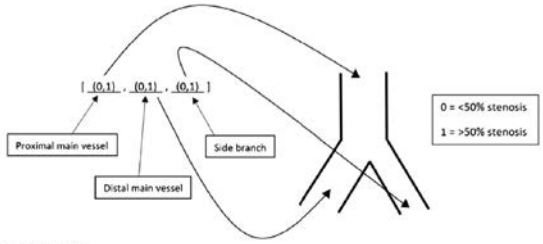
In recent years there has been a very rapid increase in the recommendations for therapeutic intervention by catheterization of coronary bifurcations that do not involve the left main coronary artery territory. There is a high prevalence of bifurcation lesions which reach 30% of cases in multi-vessel disease. Multiple strategies are available based on the analysis of the secondary branch according to its outflow angle, diameter and size of the vessel in relation to the potential ischemic amount.

The distribution of the coronary tree follows a physical concept of low-energy fluid distribution, i.e. it is designed to achieve maximum distribution of blood flow to the capillaries and to maintain a constant velocity during systole and diastole.

From a practical point of view, given this form of distribution based on the hydraulic physics of the coronary tree, we have tried to apply formulas such as Murray's law D^3mother = D^3daughter1+ D^3daughter2.

Or Kassab's law modifying Finet's law validated by IVUS Intravascular Ultrasound Dmother = (Ddaughter1 + Ddaughter2) x 0.678 [1].

The vessel diameter between the main branch and accessory branch is maintained in its first segment and then undergoes an abrupt change, so this concept leads Interventionists to use or apply this data to bifurcations and think like physicists in the aspects related to diameter and flow velocities, as well as abrupt diameter changes require optimization techniques as described below in order to preserve the continuous flow of the accessory branch and optimal stent apposition in the main vessel. Today there are many classifications of bifurcations, the simplest of which is that of Medina [2], which has been validated in many publications (**Figure 5**).



Medina 1 classification.

Figure 5.

It should be kept in mind that the area where the main vessel and the accessory branch divide is an area of high shear stress, which under normal conditions has a protective effect against the development of atherosclerosis. So that if an atherosclerotic plaque develops, it tends to be less voluminous, but the opposite wall of the vessel, with a low shear stress, is prone to develop more voluminous plaques with inflammatory characteristics that make it more vulnerable [3].

Bifurcation variables. The diameter and extent of the accessory branch are primary criteria for the definition given that only 20% of the non-left main coronary artery bifurcations involve 10% or more of the myocardial mass irrigation. Although the Medina classification is useful in showing the involvement of each zone with a binary concept, it does not provide other information no less useful such as the presence of calcification that predicts a high rate of major events (up to 36% of combined events such as infarction or death) in the follow-up [4].

An important detail to consider is the angle between the main vessel and the accessory branch; in the COBIS trial it was observed that when the angle was > 55° there was no greater occurrence of MACCE. The angle also partly determines the strategy to be used (T stent, Y stent, etc.) and if we are thinking of placing 2 stents in cases with an angle > 80°, we should take into account the potential deformation of the stent with the use of techniques such as culotte and perhaps prefer DK Crush which has greater complexity, but better evolution [5]. Studies with IVUS have shown that 85% of cases with accessory branch loss are due to carina deformation during stent implantation in the main branch, this is due to what we consider plaque displacement during stent implantation in the main branch. The V Resolve study demonstrated

Figure 6. *Variables to take into account when choosing a bifurcation technique. Modified from David Hildrick et al. EuroIntervention 2022.*

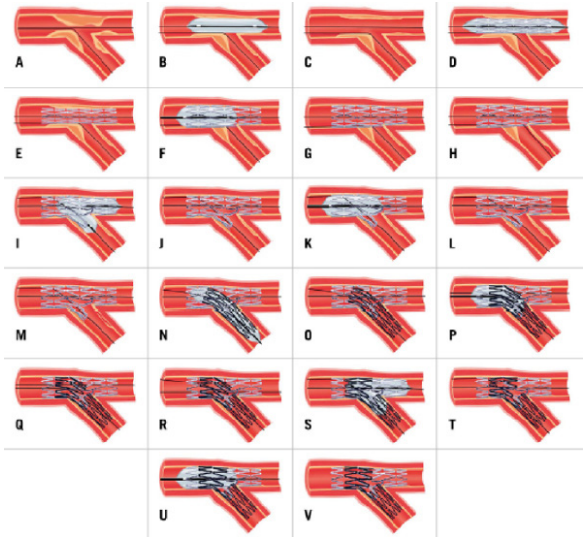


Figure 7. *Each one of the potential scenarios for provisional stenting technique is evidenced, being from the scheme, E,F, GH the preferred technique by EAPCI in its current recommendations. Modified from David Hildrick-Smith MD. EuroIntervention 2022.*

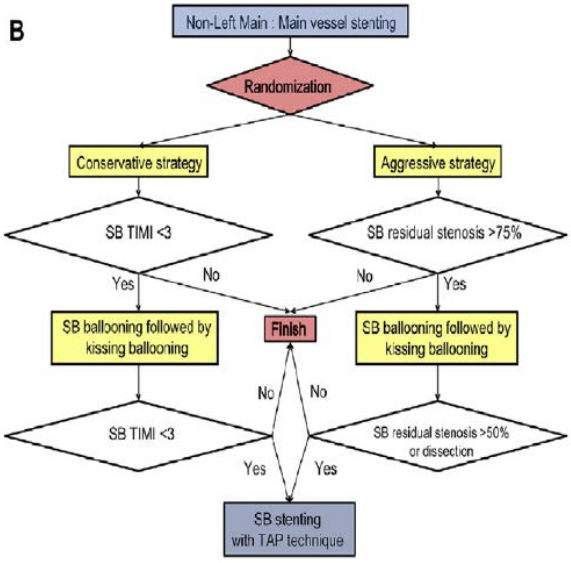


Figure 8. *Modified from Young Bin Song et al. Smart Strategy Trial. JACC Interventions 2016. Currently, there is another approach, it has been recently published by Mattia Lunardi el al. (9). The Bifurcation Academic Research Consortium (Bif-ARC) Project.*

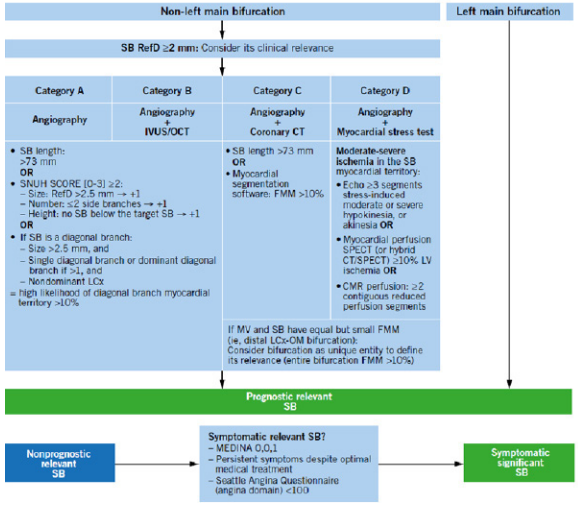


Figure 9. *In Non-Left Main Bifurcation lesions are the Bif ARC Project criteria. EuroIntervention 2022.*

independent predictors of accessory branch occlusion: a) Plaque distribution from the main branch to the accessory branch, b) TIMI flow 2 or less after plaque preparation or stent implantation, c) Bifurcation angle > 70° d) Main vessel to accessory vessel ratio greater than the accessory branch [5], occlusion was observed in 26% vs. 3% at low risk. Evaluation with imaging such as IVUS and/or OCT reduces the event rate demonstrated in the DK Crush II studies to DK Crush VIII or the IVUS-guided Ultimate with significant reductions in MACCE and mortality. **(Figure 6).**

Endovascular tactics in coronary artery bifurcations

Provisional Stent. For the treatment of bifurcations in all techniques, a 0.014" wire is passed "initially" in each vessel (main and accessory), the plaque of the main vessel is prepared and not the accessory vessel if there is one due to potential dissection and possible occlusion of the branch (recommendation of the European Bifurcation Club). After placing the stent over the main vessel, POT (Proximal Optimization Technique) is performed and the stent is recrossed with another guidewire to the accessory branch over the distal strut, the trapped guide is removed and once the stent is opened to the branch it is optimized again with re-POT. When we must recross the stent to the accessory branch, we must bear in mind the usefulness of hydrophilic and/or heavier guidewires (Pilot® 50 to 200), especially in the case of severe calcification. Although controversy persists about the value of kissing balloon in this technique, the Nordic Baltic study showed no differences between performing it or not **(Figure 7).**

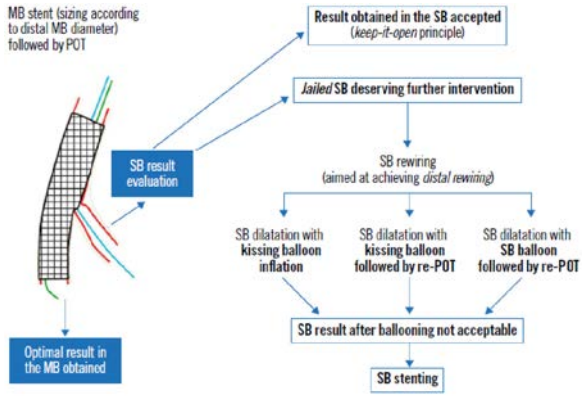


Figure 10. *Possible strategies in provisional stenting technique POT (Proximal Optimisation Technique). Modified from David Hildick. EuroIntervention 2022.*

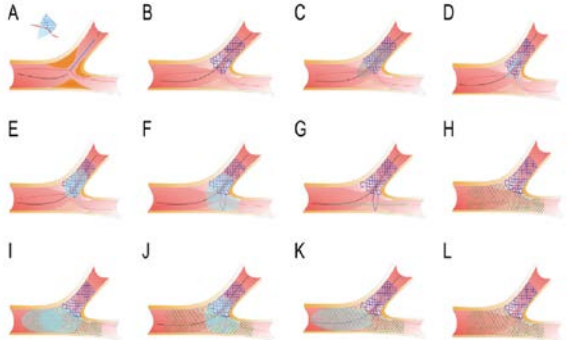


Figure 12. *Step by step Nano Culotte technique. Kahraman S. et al, 2023.*

In the provisional technique it is important to implant the stent in the appropriate vessel axis, by measuring the diameters and the area preferably with IVUS and/or OCT, thus this enables an adequate apposition to be made. Deformation of the bifurcation carina is a frequent occurrence that can change the outcome of an intervention, so it should be very clear that in this technique it is crucial to maintain the Bay Window of the implant site in order to improve the removal of the cord for proper opening of the balloon and the strut with subsequent POT. While the use of imaging techniques is preferable, optimization of the accessory branch can be performed using IFR or FFR. In the single-center work of Bin Song MD et al, a simple scheme was evaluated that is very useful to apply to daily practice [7] **(Figure 8 y 9).**
Clearly, decisions must also be made in the context of each operator's experience and the percentage of myocardium that is irrigated by the accessory vessel. It is mandatory to achieve proximal optimization with POT, a residual stenosis < 50% and TIMI 3 type flow.

2-STENT STRATEGIES. Multiple techniques which include dedicated stents have been tested in the non-left main coronary artery bifurcation, the most commonly used are DK Crush and Culotte.

Culotte technique. It has been designed for complete coverage of the bifurcation that requires adequate pre-

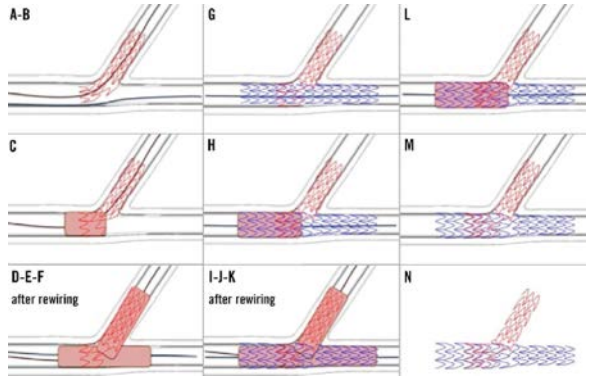


Figure 11. *Modified from Gabor G. Toth et al. EuroIntervention 2020.*

dilatation and performance of Proximal Optimization (POT) **(Figure 10).** Rewiring of the accessory branch cell and placement of the stent within the main branch toward the distal branch axis is required. The stent is released and rewiring of the stent cell in the main branch and subsequent re POT is required. **(Figure11).**
There is discussion about the performance of the Double Kissing outflow and the possible re POT that is still a subject of debate because of the amount of metal in the bifurcation. Recently, the Nano Culotte technique has been published by the group of Kahraman et al [10] with the aim of minimizing metal apposition in the neocarina **(Figure 12).**
This 12-step technique is quite complex in terms of materials and accuracy of recrossing the last cell of the stent strut in the accessory branch. The results should be compared against nano crush and DK Crush. What is important in these techniques is the performance of an adequate double kissing balloon and a re-POT. There is still no conclusive data. In our daily practice the most important thing is to evaluate whether the Provisional Technique requires a possible second stent or a drug-eluting balloon (DEB) would be enough. Currently angiographers present software with radiological systems for stent optimization (e.g. Stent Boost®) that help to see quite clearly the correct apposition, but do not allow, as in the case of CTO, to see the area of the neocarina and the correct apposition of the stent layers.

DK Crush technique. It is a complex technique that requires a precise follow-up of the steps in order to perform a correct apposition of the stent layers in the accessory branch and at the ostium level. As shown in the graph, it requires a release and crush of the stent in the accessory branch and subsequent rewiring through the stent to which the crush was performed. Once the side branch is recrossed, initial double kissing (DK) and release of the stent in the main branch is performed. Then, proximal optimization POT and double balloon kissing are performed and finally the re-POT. As in any crush technique, there is a possibility that the rewiring and opening of the double stent layer is not easily achieved, so it is a time and material demanding technique, which is the release 2 mm from the ostium of the accessory branch. The balloon kissing technique should be performed with non-compliant balloons (NC) to achieve an adequate opening of the cell; the proximal optimi-

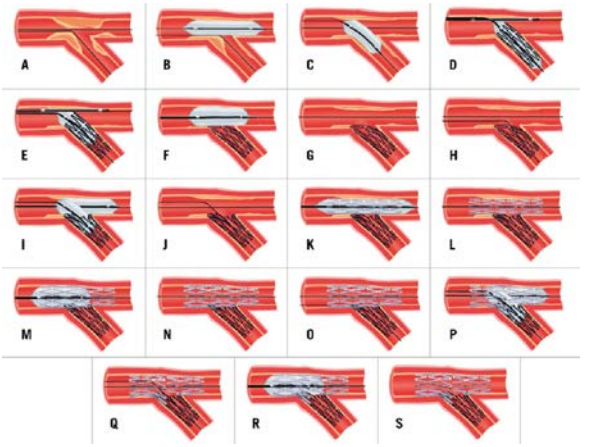


Figure 13. *Step by step DK Crush technique. Modified from D. Hildrick et al. EuroIntervention July 2022.*

Trial/Registry (Ref. #)	Study Design	Years of Procedure	Number of DK Crush Procedures	Comparator Group (for RCT)	sLMS, %	Follow-Up Time	ST
DK crush							
DKCRUSH-I (14)	RCT	2005-2006	155	Classic crush	15	8 mo	2 (1.3)
DKCRUSH-II (20)	RCT	2007-2009	185	PS	0	1 y	4 (2.2)
Ye et al (34)	RCT	2008-2009	38	PS	0	8 mo	0 (0)
DKCRUSH-III (4)	RCT	2009-2011	208	Culotte	100	1 y, then 3 y	1 (0.5)
DKCRUSH-V (3)	RCT	2011-2016	240	PS	100	1 y, then 3 y	1 (0.4)
DEFINITION-II (7)	RCT (1 vs 2 stents)	2015-2018	235	PS	29	1 y	2 (0.9)
Mini-crush							
MITO (12)	Registry	2002-2013	135	–	100	5 y	0 (0.0)
Freixa et al (35)	Registry	2003-2007	304	–	4	4.1 y	5 (1.7)
Yang et al (33)	Registry	2005-2009	111	–	22	3 y	2 (1.8)
PERFECT (36)	RCT	2007-2013	213	PS	0	1 y	1 (0.5)
FAILS-2 (21)	Registry	2007-2015	104	–	100	2.3 y	0 (0)
Yurtdaş (37)*	Registry	2015-2016	125	–	0	2 y	–
Nano-crush							
Rigatelli et al (38)	Registry	2014-2017	205	–	35	1.3 y	0 (0)
Classic crush							
Ge et al (9)	Registry	2002-2004	181	–	27	9 mo	5 (2.8)
CACTUS (10)	RCT	2004-2007	177	PS	0	6 mo	3 (1.7)
DKCRUSH-I (14)	RCT	2005-2006	155	DK crush	16	8 mo	5 (3.2)
Nordic Bifurcation Study (38)	RCT	2005-2007	209	PS	10	3 y	6 (2.9)
Yang et al (33)	Registry	2005-2009	69	–	25	3 y	2 (3.0)
Zheng et al (39)	RCT	2013-2014	150	Culotte	9	1 y	4 (2.7)

Figure 14. *Different Crush techniques in Trials and Registries for non-Left Main Bifurcation Lesions.*

zation with NC balloon of larger diameter in a ratio 1/1 of the axis diameter should be done correctly in the window of the implant bay. Subsequently, double balloon kissing is performed and finally a re-POT. This technique is the preferred technique by many Asian operators and centers, but it requires a much longer learning curve than the provisional stent technique [11]. These DK crush data are supported by the DK Crush I to IV studies **(Figure 13).**

Comparison of Non-Left Main Coronary Artery Bifurcation techniques.

Non-left main coronary artery bifurcation techniques have been compared since the BBC ONE, Cactus Trial, Definition Trial I and II, Nordic Baltic trials. In our daily practice, it is absolutely advisable to have a good strategy when approaching non-left main coronary artery bifurcation lesions. There is much evidence that favors the provisional stent technique, but new data tell us that the provisional technique could mutate to a 2-stent technique due to technical difficulties and involvement of the accessory branch. Therefore, whoever chooses either technique should be prepared to make a modification to the mini crush or nano crush and/or provisional T or provisional Y techniques, certainly as described in the 16th European Bifurcation Club Consensus. Bifurcation techniques will continue to evolve, the debate will persist as to which is the least complex and the one that gives satisfactory long-term results **(Figures 14 and 15).**

Finally, it is crucial to have an outline to discuss in advance as a team.

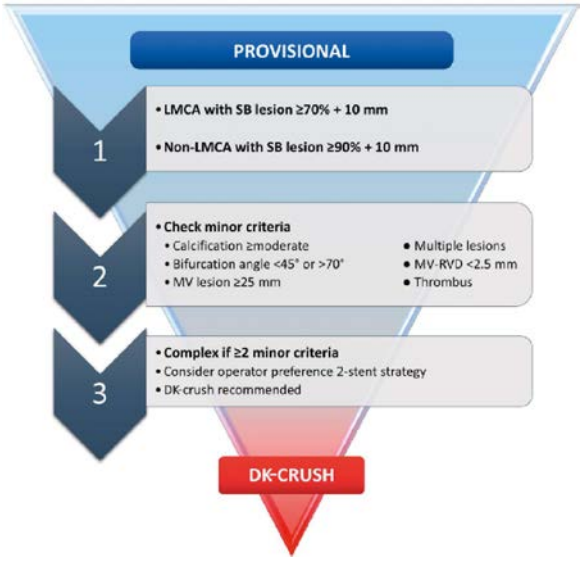


Figure 15. *The Definition trial criteria. David Hildrick et al. EuroIntervention 2022.*

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f) Chronic Total Occlusion (CTO). *Dr. Arturo Fernández Murga (Interventional Cardioangiologist).*

CTOs are defined as lesions in which there is angiographic documentation of interruption of antegrade coronary flow (TIMI 0 type) of ≥ 3 months of evolution. Although there are some angiographic parameters that make it possible to distinguish acute occlusion ("champagne glass" image, absence of collateral circulation, etc.) from chronic occlusion ("bridged" collateral circulation, etc.), it is often difficult to establish the time of occlusion. The prevalence varies from 18 to 52% of diagnostic angiographies [1-2]. Currently, angioplasty of these lesions is only performed in 5 to 22% of cases, [3] and there is a marked variability between different groups of interventionalists (6-9% in the United States and up to 60% in Japan) [4]. Although angioplasty of a CTO is a very challenging procedure in coronary interventionism, considerable technical advances together with expert hands have increased the success rate to over 80% [5]. The main objective is symptom relief and thus improvement of quality of life, and the prognostic impact on hard points such as mortality is a matter of controversy. Adequate patient selection is fundamental, eligible are considered those with persistent symptoms despite optimal medical treatment (OMT) and evidence of extensive ischemia/viability (>10%), [6] as they usually have a worse prognosis with medical treatment [7]. Retrospective studies suggested better clinical outcomes (improvement in anginal status, normalization of functional tests and improvement in left ventricular function) for those patients in whom successful recanalization was achieved compared to those in whom it failed [8,9]. The 30-day mortality rate after TCA by CTO is 1.3%, with an occurrence of perforations in 4.8% of cases [10]. However, some studies have not demonstrated an improved function (REVASC study) [11] and have been equivocal with regard to symptoms [12]. The EURO CTO [13] and EXPLORE trials [14] demonstrated a greater reduction in angina frequency and improved quality of life with TCA, but a much larger trial, the DECISION-CTO trial [15] has not confirmed these results, with no differences in symptoms or clinical outcomes found between TCA vs. OMT. The mortality benefit is controversial. Analysis from the UK database (14,000 angioplasties of CTO) showed that successful TCA was associated with an improved outcome in terms of survival [16]. A Japanese registry (1,424 patients) reported a decrease in mortality when recanalization was associated with the anterior descending artery and right coronary artery but not in the circumflex artery. Multiple variables should be taken into account when deciding on TCA of CTO, such as: clinical picture (frequency of symptoms and anti-ischemic medication), age, comorbidities, angiographic characteristics and anatomical feasibility, where imaging methods (SPECT, ECO, coronary Angio tomography, NMR, etc.) play a fundamental role. As it is a challenging and complex procedure, careful planning is of utmost importance, possible changes in strategies should be considered, as well as being prepared for any contingency that is why all the materials must be available both for the procedure itself and in case of complications (dissection, perforation or rupture of the vessel). It is beyond the scope of this document to discuss the details of different strategies, but in general it is useful to follow the algorithm of Brilakis et al. to plan the available techniques to be used in each particular case, called the hybrid approach, [17] which suggests three specific techniques to cross a CTO: antegrade approach with staggered coronary guides, antegrade approach with dissection/reentry strategy and retrograde approach. All this has allowed for greater effectiveness, safety and optimization of the procedure time as well as a decrease in the radiation and contrast doses used.

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g) Restenosis. *Dr. Jorge Iravedra (Interventional Cardioangiologist).*

Definition. The definition of restenosis has been the subject of constant debate over the years. The methods to evaluate it have been very different, although from a practical point of view, we should consider invasive angiography with subjective evaluation as the "gold standard", due to its universality of use, even considering intra- and inter-observer variability as limiting factors. Of the numerous definitions proposed, the most widely accepted is the one that establishes a diameter reduction ≥ 50% of the reference diameter (binary restenosis) [1]. This includes, in the case of stents, the 5 mm proximal or distal to their edges. In fact, the definition of restenosis (whichever is adopted) inevitably implies the therapeutic decision to be made, and the clinical context of the patient should be considered. Restenosis as an angiographic finding in an asymptomatic patient is different from its detection in the presence of symptoms compatible with ischemia and/or its demonstration by noninvasive methods. The appearance of physiological invasive methods opens a new scenario, given the prognostic correlation of their results, at least in stable clinical conditions. The conclusion is that restenosis with associated angina or ischemia should be treated [2].

Types of Restenosis. The characterization of in-stent restenosis has evolved from the first angiographic classifications at the end of the last century (focal, diffuse, diffuse proliferative, occlusive) [3] to the current evaluations with intravascular imaging. In addition to the already established neointimal hyperplasia characteristic of drug-free stents, as an anatomical substrate of restenosis, in the second decade of this century the concept of neoatherosclerosis appeared that is defined fundamentally by CTO criteria, with visualization of greater or lesser heterogeneity of the observed tissue, fibroatheromas with different thicknesses of fibrous sheath and lipid content, as well as the presence of calcium inside the struts, and the presence of calcium inside the stents [4]. From restenosis due to neointimal hyperplasia being considered a "benign" entity, although relatively frequent (approximately 15% occurrence in the first 12 months), a later appearance of restenosis and thrombosis phenomena has been observed in the latest generation of drug-eluting stents after 12-24 months after implantation, with an average occurrence of revascularization of the lesion of 2% per year. "Modern" restenosis is also associated with a higher incidence of acute coronary syndromes, with or without ST-segment elevation, and is a predictor of greater occurrence of major cardiac events and new restenosis during follow-up [5].

Mechanisms. Different mechanisms may be responsible for the development, severity and presentation patterns of in-stent restenosis [6]. Patient-related factors include the presence of diabetes mellitus, chronic renal insufficiency, older age, female sex and increased body mass index. There could be some biological factors, such as individual resistance to anti-proliferative drugs (genetically determined) or development of hypersensitivity, with consequent inflammatory response to the polymer or metallic platforms used. Among the anatomical factors, the size of the vessel to be treated stands out, with an inverse relationship between restenosis and diameter. Other factors to consider are the presence of a significant thrombotic burden that could hinder normal diffusion of the antiproliferative drug to the vessel wall and/or significant parietal calcification that would prevent adequate stent expansion. Let us also consider as predisposing anatomical factors the treatment of bifurcations, ostial lesions, long or diffuse obstructions, chronic occlusions or venous bridges. In relation to the factors related to the procedure, one could summarize the situation with the concept that stent implantation should be optimal, which entails adequate expansion, good apposition of the struts to the wall and absence of segments with significant uncovered atherosclerotic disease ("geographical loss"). Finally, in relation to the factors that depend on the stent, we will consider whether the stent is antiproliferative drug-eluting, the type of drug used, the thickness of the struts and the possibility of stent rupture, which could be related not only to its structural characteristics but also to aspects related to its correct implantation (absence of overexpansion).

Management strategies. Restenosis management is a challenge itself, given the heterogeneity of its causes. Since most patients present with a stable clinical picture, intervention can be appropriately planned. When the assessment of severity is uncertain, the use of invasive physiological methods (with or without vasodilatation) should be considered. The possibility of having information on previous procedures (type of stent and technique used) is of utmost importance in order to determine potential restenosis mechanisms, as well as the availability of intravascular imaging methods (IVUS and OCT) to characterize the anatomical substrate. Current European guidelines establish as a class I indication, with level of evidence A, the use of both drug-eluting stents and drug-eluting balloons in the treatment of in-stent restenosis [2]. The factors that favor the use of stents would be: restenosis with an "aggressive" anatomic pattern (diffuse or occlusive), restenosis of previous drug-eluting stent (single layer), stent-related mechanisms (rupture or uncovered atherosclerotic segments), and suboptimal expansion due to poor plaque preparation. Meanwhile, the factors associated with good evolution with the use of drug-eluting balloons would be: "focal" anatomical pattern with good expansion in predilatation, restenosis of metallic stents without drug release, restenosis with several layers of previous stents, patients at high risk of bleeding who would not tolerate prolonged double antiplatelet therapy, and special anatomical situations (such as the emergency presence of a secondary branch already "imprisoned" with the previous stent) [6,7]. According to these European guidelines, the use of intracoronary imaging with IVUS or OCT to determine the restenosis mechanisms is also a class IIa indication with evidence level C [2]. Lesion preparation is crucial for the treatment and good outcome of in-stent restenosis. The use of cutting balloons (Cutting Balloon® /AngioSculpt®) may be useful to avoid balloon displacement (watermelon seed effect) of predilatation outward from the stent and propensity to dissection. The use of "high pressure" with non-compliant balloon may also be indicated, especially in cases of lack of previous stent expansion. "Resistance" to the drug used in the previous stent has been mentioned as a possible cause of restenosis. However, there is no evidence that the use of a different drug alters the course of a possible new restenosis [7]. The use of "atheroablative" techniques has also been proposed as an addition for a good preparation of the restenosis to be treated [7]. Rotational atherectomy has been used for more than three decades. The best indication for its use in this context would be the presence of neointimal hyperplasia. Ideally, the use of in-

travascular imaging would help to individualize cases with poorly expanded stents, where there is a greater risk of olive entrapment although metal ablation is possible. Even though the use of laser and brachytherapy has shown promising results in literature, they have their use has not been developed in our setting. The appearance of intravascular lithotripsy raises expectations about its usefulness, especially in cases where the stent has been implanted and its adequate expansion is not achieved. For the moment it is an "off label" indication [8]. One limitation is the possible need to adequately predilate the lesion to be treated, given the profile of the lithotripsy balloon. We should mention that the use of medical treatment to reduce restenosis has had limited results although poor control of the patient's lipid profile is associated with a higher risk of restenosis [9] and the use of PCSK9 enzyme inhibitors has shown some favorable effects in reducing stent restenosis or thrombosis [10]. Finally, the use of myocardial revascularization surgery should not be ruled out in cases of recurrent restenosis (especially in lesions of the main coronary artery or multiple vessels), after an adequate individual analysis of each case [11].

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h) Spontaneous Coronary Artery Dissection. *Dr. Ernesto M. Torresani (Interventionist Cardioangiologist).*

Arterial dissection is defined as the separation of the layers of its wall, with the formation of a new lumen between them (false), communicated or not with the true lumen, in the latter case due to the development of intramural hematoma. The most common cause is followed by to rupture of an atheroma plaque with the consequent development of an acute coronary syndrome in which different degrees of dissection are usually seen [1], the best-known categorization of which is based on dissections generated during plaque preparation in angioplasty, these range from an intraluminal radiolucent image to vessel occlusion in the F type [2]. We must take into account that it overlaps with the angiographic definition of thrombus (occluded vessel: convex margin, "cup image"; permeable vessel: intraluminal globular filling defect) [3] with which it usually coexists and where it is not always easy to differentiate one from the other. It is also possible the development of coronary dissection (CD) due to chest contusions caused by trauma caused by traffic accidents, sports (rugby, boxing, etc.), etc. and produced by the acceleration and deceleration forces involved [4]. Another possible situation is during aortic dissection, which can present as acute coronary syndromes, most commonly inferior infarctions due to involvement of the right coronary ostium. However, it is possible that in anterior infarctions [5] the aortic hematoma obstructs the coronary ostium, but it is also possible that the dissection extends into the interior of the vessel as it usually does in splanchnic arteries. Finally, the subject that concerns us is spontaneous CD (SCD) not caused by any of the previously mentioned factors and which coexists with arteries of "normal" angiographic appearance and in which there are two possible mechanisms: a) rupture of the intima or b) hematoma in the tunica media due to rupture of the vasa vasorum with or without rupture of the intima. [6]. We should think of this entity when in the angiography we see arteries of normal appearance associated with any of the following characteristics, type 1: typical localized dissection (staining of the wall with contrast and radiolucent images in the light), type 2: predominantly hematoma (narrowing > 20 mm of smooth walls of varying degrees) and type 3: usually confused with atherosclerosis (focal or tubular stenosis) [7]. Imaging methods such as IVUS or OCT can be helpful in identifying dissection and hematoma. An angiographic detail to be taken into account is the presence of tortuosity [8], which compared to a control group, in patients with SCD had a high impact that increases with age, is less frequent in peripartum cases and is a predictor of recurrence. Another noteworthy aspect of angiography is the possibility of simultaneous involvement of more than one vessel in 10 to 20% of cases [9]. It has a high prevalence in the female sex (more than 90% of those affected are women) with an average age of 50 years, although it can affect older people [6,7]. There are predisposing or associated factors (it is not entirely clear) such as Fibromuscular Dysplasia (FD), pregnancy, connective tissue diseases, systemic inflammatory diseases or hormonal therapy. It can be stated that more than 60% are associated with FD, about 30% are idiopathic, and 25% of all of them are related to obstetric aspects [6]. In the diagnostic suspicion of SCD and in the search for FD, we should study other vascular territories such as the renal, iliac arteries, neck and intracerebral vessels that could also be involved [7]. The condition is usually precipitated by intense exercise, emotional stress, activities that involve the Valsalva maneuver, drug use or hormone therapy, developing as an acute coronary syndrome with or without ST [6]. Occasionally it could be confused with Takotsubo syndrome [10]. Although there is no specific treatment for patients with SCD and the usual treatment methods for acute coronary syndromes are used, the use of beta-blockers seems to be mandatory with a favorable impact on the prevention of recurrences in the follow-up [7]. The Canadian Registry of SCD [11] shows that the «current» indication for revascularization does not usually exceed 20%, due to the poor results obtained with angioplasty [6]. In case

studies from the Mayo Clinic, [6] they performed a retrospective analysis of what was done between 1984 and 2014, classifying patients between those who had undergone TCA versus those who had undergone conservative treatment and whether their arteries were occluded or permeable. In the cases of patients treated with TCA, the success rate when the artery was occluded was 54% and the success rate when the artery was permeable was 50%, with a high rate of referral to emergency coronary-artery revascularization surgery MRS[11]. From this analysis the following information arose: 1) TCA in spontaneous coronary artery dissection is associated with a high rate of complications and emergency surgery, even in cases with a permeable vessel. 2) In selected cases of spontaneous coronary artery dissection, MRS confers excellent immediate follow-up. 3) Conservative therapy is associated with favorable in-hospital evolution, but it should be kept in mind that there are cases that experience progression of the dissection during the first week.4) Revascularization does not reduce the risk of recurrence of the dissection or the need for new revascularization. Close follow-up and the development of new therapeutic strategies are necessary [12].

The challenges of TCA are related to: (a) risk in inducing iatrogenic dissection with the catheter due to the particularities of the wall, (b) difficulty in properly placing the wire in the true lumen, (c) spread of intramural hematoma with dilatation, (d) tendency for dissection to extend over distal vessels, (e) the potential need to place stents in very long segments increase the probability of restenosis and (f) subsequent resorption of hematoma generate conditions for late malapposition [6]. A detail to take into account is the recurrence that occurs in 10% of cases, which has as predictors being female, young, with FD and/or migraine, and severe tortuosity of the coronary arteries [8]. It is important to highlight that patients in whom blood pressure is adequately controlled have a greater survival free of new episodes of CD, so it is relevant in cases of fibromuscular dysplasia to know the situation of the renal arteries that could benefit from angioplasty [7]. To conclude, and by way of summary, we should consider a high index of suspicion of this entity in young women with ACS, without traditional risk factors, who have coronary arteries without atheromatous appearance, in peri-partum situations, with FD, or history of connective tissue disease, or systemic inflammatory condition, that has been triggered after intense exercise or emotional stress [13]. Non-invasive medical treatment should be considered as the first choice [11].

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i) Tortuous vessels. *Dr. Jorge Baccaro (Interventional Cardiologist).*

The endovascular approach to tortuous vessels represents a challenge that should be considered by the medical team as an additional difficulty and risk when deciding on the intervention. There is no single definition, and it can be described as the presence of 2 or more curves ≥ 75° or at least 1 curve > 90°, or the presence of a "significant" curvature, prior to the lesion to be treated. Others have attempted a classification considering the number of curves with angles ≥ 45° prior to the lesion to be treated as a) mild 1 curve, b) moderate 2 curves, or c) severe 3 or more curves [1]. From the tactical point of view, it is important the adequate selection of materials and planning of the procedure for each case.

Guiding catheter: Larger diameter catheters (7 and 8 F) are more rigid due to their greater structural strength which provides greater support, essential for approaching these vessels. However, their use entails the risk of complications in vascular access (bleeding, pseudoaneurysm and ischemia) or the probability of dissection of the coronary ostium, and it is also essential to monitor pressure to avoid dumping. By femoral route the support can also be reinforced using long introducers ≥ 45 cm. Thinner catheters, especially 5F, give the possibility of deep intubation, advancing them directly over the guide, or balloon, or with balloon anchoring in the vessel to be treated or in a branch. This makes it possible to negotiate the proximal curves, increasing the thrust force exerted on the device to be used. It is usually preferable to start with the classic JR, JL or EBU, and then change to another if they are not efficient, bearing in mind that those with a more sophisticated shape, although they allow catheterization of the ostium more efficiently, entail the difficulty of deep intubation and perhaps a greater risk of ostial dissection.

Support or extension catheter: With the "mother in child" technique [2] guide catheter extension systems have been designed to achieve greater intubation depth. The most common in our country are Guidezilla II® (Boston Scientific), Telescope® (Medtronic) and Heartrail II® (Terumo) but there are others such as Guideliner V3® (Teleflex), Trapliner® (Teleflex), Guideplus® (Nipro Corp) and Proxis® System (St Jude). Most of them are monorail systems and in sizes compatible with guide catheters from 5 to 8F [3].

With them, a greater depth of intubation is achieved, thereby increasing the thrust force and being able to "negotiate" proximal curves and the presence of superficial calcium, two

reasons for failure in the advancement of the stents. For advancement, the predilatation balloon is almost always used as an internal tutor, or its distal anchor, since advancement alone can cause disengagement of the guiding catheter. Recently, two models compatible with the 5F guiding catheter have been developed for use from the radial approach, while maintaining the advantages of the radial approach and with excellent support. The first one is the Kiwami lock® (Terumo) [4] with a 0.050» central lumen, which can be used with 5 or 6 F guiding catheters, and a second guidewire can also be placed in a collateral branch or as a "Buddy wire". If a 6 or 7 F guiding catheter is used or if another guiding catheter is placed for a second puncture (Fig. 1), an anchoring balloon can be placed on a second parallel guidewire to achieve a much higher thrust force (Fig. 2) [5].
Another support catheter is the Guideplus® 5F compatible with the 5F Heartrail® guidewire (both from Terumo), [6] which has an external diameter of 1.48 mm. Its internal diameter allows the passage of most of the current ultrathin stents up to 3.0 mm diameter, the Coroflex® (Braun) is the only one that can pass in the 3.5 and 4.0 mm sizes **(Figure 16).**

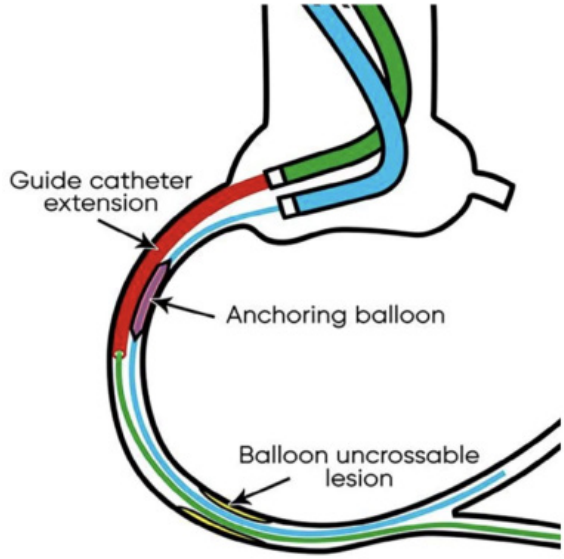

Figure 16.

Microcatheters: Initially, those designed for other territories were used [7] (cerebral or peripheral for radiological use), but currently others have been developed for specific use in coronary arteries. Although they have common properties, some are more useful in chronic occlusion, others in tortuosity or for navigating collateral vessels. The internal diameter must be considered for the appropriate choice of the cord, the length and flexibility of the distal end, which allows to circumvent curves or give more support depending on the case. Its end can be straight or at different angles (60°, 90° or 120°) so as to increase its penetration or to allow access to the lumen by re-entry when generating proximal dissection or to branches in cases of retrograde access. The external diameter varies between 1.3 – 1.8 F and the internal diameter for chordae from 0.014 to 0.021". Radiopacity is low, but all have distal tip marking, which helps to work more precisely on the termination of the true lumen. Displacement is facilitated by all having hydrophilic coating. There are those with **a single light:** FineCross MG® (Terumo), Caravel® (Asahi Intecc Co.), Mcath® (Acrostak), Tornus® (Asahi), Corsair®/Corsair Pro® (Asahi), SuperCross® (Teleflex), Turnpike® (Vascular solution), Mamba® (Boston Scientific), Teleport® (Cardiovascular Systems), Microcross® (Roxwood Medical), and with double lumen: Twin-pass® (Teleflex), Sasuke® (Asahi), Crusade® (Kaneka Medix), Fineduo® (Terumo), Recross® and NhancerRx® (IMDS, Roden).

Guidewires: Although hydrophilic coated guidewires are usually preferred, in some cases, Teflon-coated or silicone-coated guidewires may be useful. In relation to the support, although those with a harder core provide a greater possibility of thrust, in certain situations it can be negative, generating an accordion effect with eventual compression of the balloon or stent against one of the curves. Those with higher torque are those with a Nitinol core from proximal to distal end. They are also designed with different support segments from proximal to distal. Those of smaller diameter (0.010 or 0.012") have potentially lower resistance in critical lesions, and lower torque capacity. Those that vary in diameter from proximal to distal, with taper from 0.014 to 0.009" are very useful for crossing microchannels and extremely closed lesions, while retaining good proximal torque (e.g. Fielder XT®).
A tactic that could help in situations where we are unable to advance balloons and/or stents is the "Buddy Wire", placing a second parallel guidewire.
Tortuous vessels provide us with an additional challenge in angioplasty, for which we must adequately select the access route, the diameter and curve of the guiding catheter, considering the possibility of being able to use a catheter extension and that good support is crucial. We must have appropriate microcatheters and guidewires and evaluate in each case the real possibility of being able to advance different plaque preparation devices if necessary. In selected cases, shorter stents may allow a more user-friendly navigation.

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j) Vascular ectasia and coronary aneurysms. *Dr. Alejandro Cherro (Interventional Cardioangiologist).*

Coronary artery ectasia (CAE) is defined as a diffuse dilatation with an increase in diameter ≥ 1.5 times the normal diameter of the major vessel involving at least one third of its length; on the other hand, aneurysms are focal dilatations and can be saccular (longitudinal diameter < transverse diameter) or fusiform (longitudinal diameter > transverse diameter). Ectasia or aneurysms are present in 0.15% to 5% of patients undergoing diagnostic angiography [1, 2], with 75-80% of cases being ectasia, 15% fusiform aneurysms and 5% saccular. Described by Morgagni in 1761, they were diagnosed by coronary angiography by Munker two centuries later. According to the American Heart Association, a giant coronary aneurysm is defined as that > 8 mm in diameter, most frequently affecting the right coronary artery, followed by the anterior descending and circumflex arteries, being less common in the left main coronary artery. It tends to be more prevalent in men. It may be secondary to atherosclerosis in 50 to 80% of cases, connective tissue diseases such as Ehler-Danlos or Marfan syndromes, Kawasaki disease, and less common congenital, traumatic, infectious or tumor diseases [3]. It may have a higher impact in cases of familial hypercholesterolemia and in cocaine users, and an inverse correlation with diabetes. Marquis et al. [4] developed a classification relating the number of vessels involved with the extent of ectasia (focal or diffuse) **(Table 7)**, and they concluded that in patients with more affectation the event possibIlities are increasing.

Table 7. Classification relating the number of vessels involved to the extent of ectasia

CAE	Number of vessels involved	Extent
Type 1	Two or more vessels	Diffuse
Type 2	Two vessels	Diffuse in a vessel, focal in other
Type 3	One vessel	Diffuse
Type 4	One vessel	Focal

Abnormal dilatation of the lumen of coronary arteries has been attributed to several processes that would cause excessive expansive remodeling of the vessel wall, which would arise in response to the release of lytic enzymes that produce enzymatic degradation of the extracellular matrix as well as the tunica media, causing thinning and chronic inflammation. High levels of C-reactive protein, homocysteine and vascular endothelial growth factor have been associated with CAE, suggesting that they may play a role in inflammation and neovascularization. Another theory states that increased nitric oxide levels could cause vasodilatation and relaxation of ectatic areas. Genetic factors such as angiotensin-converting enzyme DD, genotype polymorphism, abnormal lipoprotein metabolism associated with hypercholesterolemia, potassium voltage-dependent channel H subfamily member 1 (KCNH1) mutation, and autophagy-related 16 like 1 (ATG16L1) gene mutations have previously been linked to CAE [5-7]. To this date, 50 genetic variants associated with coronary artery disease have been identified, but none appear to be strongly associated with ectasia. The most frequent clinical manifestation is angina pectoris [8] caused by slow coronary flow, which occurs even in the absence of associated coronary obstructions. Within the clinical spectrum we find asymptomatic patients, patients with functional tests that reveal myocardial ischemia and patients whose diagnosis is an acute coronary syndrome (ACS) that may be caused by the development of an occlusive thrombus or distal embolization. In the treatment spectrum there are no evidence-based management guidelines. With regard to pharmacological therapy, antiplatelet agents are the usual therapy. Although the pathophysiology is still not entirely clear, there are studies that show an increase in platelet activity, higher levels of P-selectin, beta-thromboglobulin and platelet factor 4 compared to a control group of patients with normal coronary arteries. An increase in mean platelet volume has also been demonstrated, which suggests that the platelet thrombotic effect may play an important role in the pathophysiology of CAE [9-11]. In symptomatic patients with significant coronary stenosis associated with aneurysm, surgical intervention or angioplasty with covered stent, when anatomy allows it, could be a therapeutic option with a good medium-term evolution, taking into account that patients treated conservatively have an occurrence of events close to 50%. It is worth mentioning that in cases of isolated coronary aneurysms without associated stenosis the evolution is less predictable. In these cases (giant aneurysms discarded) therapy is based on antiplatelet therapy and anticoagulation, evaluating the thrombotic load and ischemic vs. hemorrhagic risk. [13]. From a 10-year cohort of 1698 patients with AMI monitored by Doi et al. [14], 51 patients had CAE; their presence was associated with higher cardiovascular mortality and nonfatal AMI. Those treated with Warfarin and with adequate anticoagulation range did not show new events in contrast to those who did not take the drug (33%) or did not reach adequate levels of anticoagulation (p=0.03). Patients with ACS associated with CAE represent a high-risk group for new events in which oral anticoagulation is an effective therapeutic alternative. In ACS associated with Markis grade I-II CAE, the double and triple therapeutic schedule should be taken into account according to the balance of ischemic risk vs. bleeding risk **(Figure 17).**

A fact to always keep in mind is that patients who must undergo coronary angioplasty have greater complications than those without CAE.

In conclusion, we can say that the treatment of coronary aneurysms and CAE remains challenging, and it is necessary to individualize each case always considering the clinical condition, anatomy, size and growth over time, location, presence of concomitant atherosclerotic lesions and comorbidities, without neglecting the experience of the operators in the case of inclining the treatment towards an endovascular or surgical resolution. The vast majority of published cases have been treated with dual antiplatelet therapy, oral anticoagulation or a combination of both, taking into account all the factors mentioned above. Although rupture is possible, it is exceptional in coronary arteries.

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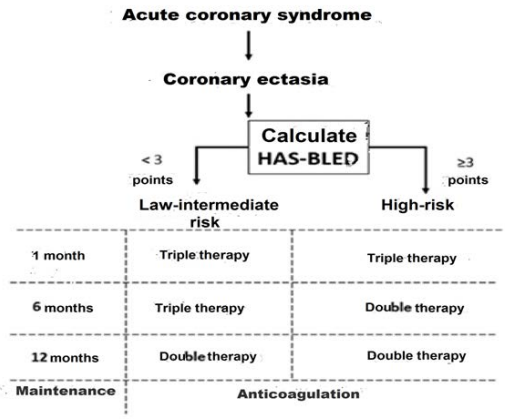

Figure 17. *(Double therapy= ASA + P2Y12 inhibitor) // (Triple therapy= ASA + P2Y12 inhibitor + OAC).*

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5) MISCELLANEOUS

a) Drug-coated Balloon. *Dr Alejandro Goldsmith (Interventional Cardioangiologist)*

A Drug Coated Balloon (DCB) consists of a semi-compliant balloon coated with an anti-proliferative agent encapsulated in a polymer matrix that when insufflated contacts the vessel intima, fixing itself to the vessel and allowing homogeneous drug release. The concept arises from the possibility of "implanting" an anti-proliferative drug without requiring metal (stent) and inhibiting the process of myointimal hyperplasia and negative remodeling. The idea of the strategy of using DCBs is based on "leave-nothing-behind strategy", but only in selected patients after an optimal result ("stent like"). Patients with small vessel disease, restenosis, myocardial infarction, bifurcation or high risk of bleeding have been treated with good results. Several studies have demonstrated its efficacy and safety in the treatment of both de novo lesions and in-stent restenosis. In a recently published meta-analysis [1] with more than 2400 patients, the comparison of DCB vs. DES had similar results in terms of severe adverse events (cardiac events, thrombosis of the treated vessels, cardiovascular mortality and Target Lesion Revascularization: TLR) and a lower incidence of vessel revascularization (TLR) and restenosis (Late Lumen Ross: LLL) compared to BMS (drug-free stents). However, DCBs were associated with a lower occurrence of myocardial infarction (RR, 0.48; 95 % CI, 0.25-0.90) and all-cause mortality (RR, 0.45; 95 % CI, 0.22-0.94) irrespective of DES generation. A potentially ideal scenario for its use could be that of small caliber vessels, since if stents were used, the thickness of the struts would condition the minimum luminal diameter (Minimun Luminal Diameter: MLD), and the use of DCB has been associated with similar TLR to DES. Extrapolating the concern [2] (under review) of the DCB mortality associated with the treatment of peripheral vascular disease is beyond the scope of this paper, but the absence of correlation in the coronary scenario could be demonstrated. We should ask ourselves why use DCBs knowing that DESs are the gold standard strategy? DCBs would provide us with a stentless strategy, without the increased potential risk of remodeling phenomena with late recovery or stent thrombosis. The potential benefits [3] of DCB could be: a) a larger contact surface and more uniform drug transfer, b) improved arterial restoration due to the absence of a long-term inflammatory source, c) preservation or early restoration of normal vessel anatomy and function, and d) application in scenarios where stent implantation may not be ideal.

Which to choose, sirolimus or placlitaxel? There are few comparative studies between these two technologies. Although no significant differences were observed in the SIRPAC study [4], "a priori" there would not be a class effect, we must bear in mind that the differences between the DCBs are not only based on the drug (Placlitaxel or Sirolimus) but also on the association with the different polymers. In this regard, comparative studies in different scenarios are necessary. The combination of BMS with DCB has not been shown to be better than DES. In de novo lesions the use of DES remains the gold standard. The use of DCB as the only tool without DES requires careful and adequate preparation of plaque with a "stent like" result and is an interesting strategy in view of the need to shorten the time of double platelet antiplatelet aggregation, restenosis, in small vessels and bifurcations as the only potential alternative for the secondary branch. The use of DCB is another strategy for our usual practice, with adequate results in specific clinical and angiographic scenarios.

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Table 8. Covered stents available in Argentina. Coronary covered stents. EuroIntervention 2016; 12:1288-1295.

					
	GRAFTMASTER**	Direct-Stent	BeGraft**	PK Papyrus**	Aneugraft Dx
Manufacturer	Abbott Vascular	InSitu Technologies	Bentley Innomed	Biotronik	ITGI Medical
Graft material	ePTFE	ePTFE	ePTFE	Electrospun polyurethane	Processed equine pericardium
Stent material/ design	Stainless steel (316L) Sandwich design	Stainless steel (316L) Sandwich design	Cobalt-chromium (L-605) Single layer	CoCr (L-605) with amorphous silicon carbide coating Single layer	Stainless steel (316L) Single layer
Guide catheter compatibility	6 Fr (≤4.0 mm) 7 Fr (4.5 and 4.8 mm)	6 Fr 7 Fr	5 Fr	5 Fr (stents <4.0 mm) 6 Fr (stents ≥4.0 mm)	6 Fr
Crimped profile	1.63-1.73 mm	1.2-1.8 mm	1.1-1.4 mm	1.18-1.55 mm	1.26-1.41 mm
Stent diameter (mm)	2.8-4.8	2.25-6.0	2.5-5.0	2.5-5.0	2.5-4.0
Stent length (mm)	16-26	10-38	8-24	15-26	13-27
Nominal implantation pressure	15 atm	8 atm	11 atm (2.5-4.0 mm) 10 atm (4.5-5.0 mm)	8 atm (2.5-3.5 mm) 7 atm (4.0-5.0 mm)	5 atm*

Information obtained from product catalogues. *Nominal pressure. Full stent opening requires ≤9 atm. CoCr: cobalt-chromium; ePTFE: expanded polytetrafluoroethylene

b) Covered stents. *Dr. Dionisio Chambre (Interventional Cardioangiologist).*

Since the beginning of percutaneous angioplasty, different difficulties have been resolved. In 1986, the stent was developed to deal with dissection and thrombosis; in 1999, the drug-eluting stent was developed to deal with restenosis. Already in those stages, covered stents had been devised to correct these problems. First, by suturing a vein or autologous pericardium to the stent was tried, but it represented a technological problem, and the stent had an interesting profile. We have tried a freeze-dried collagen coating, which solved the rejection issue, but the profile was still not the desired one. Increased procedural complexity led to the observation of a higher rate of coronary perforation[1]. This made it necessary to implement more standardized solutions. One of the first experiences was in 1996 with a stent covered with a plastic membrane [2]. This has led to the development of new stents and materials [3].

There are different stent types and coverage: **(Table 8)**

- *Graftmaster®* (formerly Jostent® by Jomed) by Abbott. The stent is made of 316L steel, sandwich type, two stents and an ePTFE interlayer. It is the first to be produced and already has an older stent material (steel) and higher profile and hardness.
- *Direct® stent* (not marketed in Argentina) is also based on a 316L steel sandwich stent.
- *Aneugraft DX®* (not marketed in Argentina), also based on a 316L steel platform and 90 µ thick equine pericardium coating.
- *Bentley's BeGraft®* is made of chrome-cobalt, single layer and ePTFE. This allows it to have a better crossover profile and greater flexibility, allowing it to "navigate" complex and distal anatomies.
- *Papirus PK®,* from Biotronik, is also made of Cobalt-Chromium, but with a polyurethane layer that covers the stent by deposition. This allows it to have a very low profile and excellent navigability. Polyurethane has already been used in peripheral stents and has demonstrated good biocompatibility.

Indications. Perforation induced by the material in an angioplasty, such as that of a guidewire lodged distally and not seen during the procedure, or by an overexpanded stent, or by a balloon exceeding in diameter, that would be the moment when one should have these stents available in the inventory. As for the treatment of aneurysms, these devices are very useful, considering the overlap of stents when we do not have the necessary length. Degenerated saphenous vein bridges are another indication to take into account, since they imprison the fragile material. The situation would be different when facing a coronary fistula (e.g. Anterior Descending Artery-Pulmonary Artery) where it is still under discussion, because we face the possible effects of a proximal stent in the Anterior Descending Artery (greater thrombosis and greater restenosis, since they are not drug) versus a direct exclusion treatment (coils) that do not concern the artery**.**

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c) Dual antiaggregation strategies. *Dr. Guillermo Migliaro (Interventional Cardioangiologist).*

Dual antiplatelet therapy (DAPT) implemented with aspi-

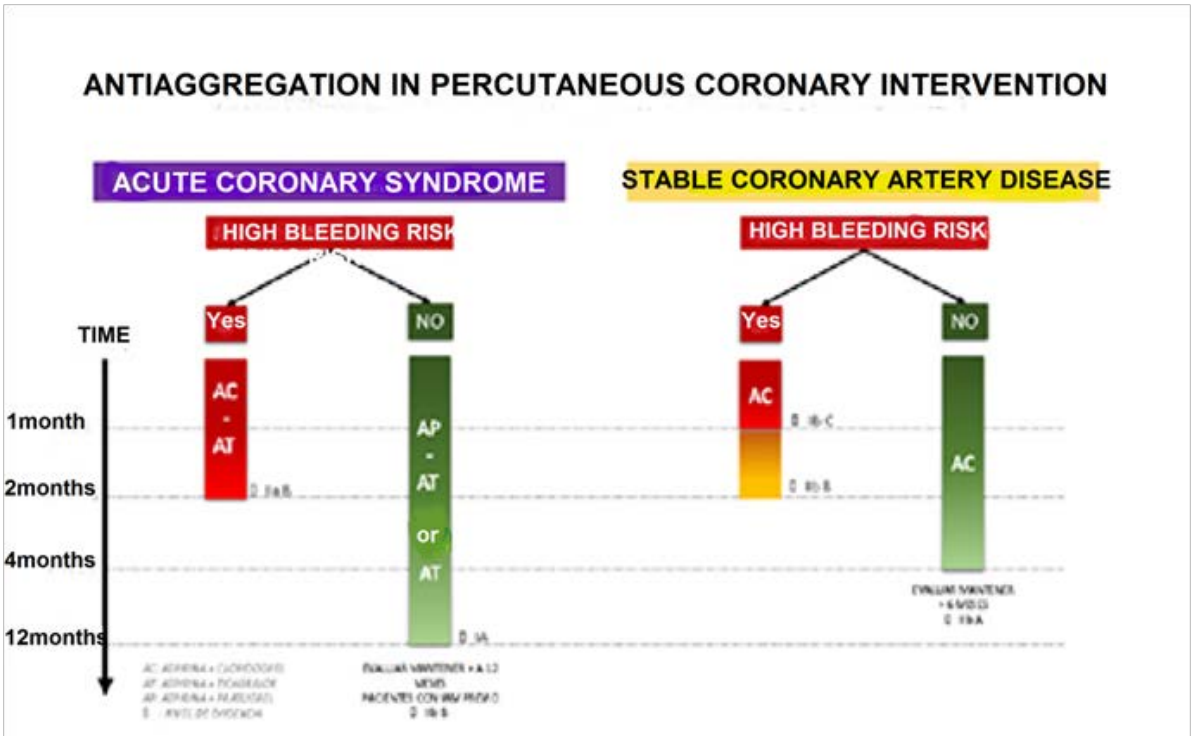

Figure 18.

rin (ASA) plus a P2Y12 receptor inhibitor is the standard treatment after coronary angioplasty (TCA). The choice of the best DAPT strategy (in terms of the selection of the second antiplatelet agent) and the optimal duration of DAPT aims to reduce both thrombotic complications at the stent level and new ischemic events, minimizing the risk of bleeding, which is the main complication of this treatment. Once the second antiplatelet agent is discontinued, monotherapy (generally with ASA) is continued indefinitely [1-3]. The recommended doses of ASA are a loading of 160 to 325 mg orally or 200 to 500 mg intravenously followed by maintenance doses between 75 and 100 mg per day. As for P2Y12 inhibitors the recommended doses are for clopidogrel loading with 600 mg, followed by maintenance dose of 75 mg per day or prasugrel loading of 60 mg, followed by maintenance dose of 10 mg per day or ticagrelor, loading dose of 180 mg per day followed by 90 mg twice per day [1,2]. The second antiplatelet should be initiated as soon as possible in the case of clopidogrel and ticagrelor in acute coronary syndrome (ACS) and in the case of prasugrel only when an indication for TCA is established (i.e. with known coronary anatomy) [1,2]. In patients with stable coronary artery disease in whom TCA was performed regardless of the type of stent implanted, the use of DAPT, ASA plus clopidogrel for 6 months is recommended (class I A) [1]. In patients at high bleeding risk (with PRECISE Score DAPT 25), consideration should be given to shortening the DAPT to 3 months (Class IIa B), although in the subgroup of patients at higher bleeding risk, who have been treated with stents with ultrathin struts, consideration could be given to reducing it to 1 month (Class IIb C) [1]. In the subgroup of patients with high thrombotic risk and low bleeding risk, the duration of DAPT can be extended up to a maximum of 30 months (Class IIb A). In patients with ACS, DAPT with ASA plus ticagrelor or ASA plus prasugrel for 12 months is recommended. In the case of contraindications to prasugrel (age over 75 years, weight less than 60 kg and/or history of stroke) or intolerance to ticagrelor (dyspnea or bradycardia), the ASA plus clopidogrel schedule can be used (Class I A) [1,2]. In patients at high thrombotic risk and without bleeding complications, prolongation of DAPT beyond 12 months can be considered (Class IIb A). In these patients with a history of myocardial infarction, ticagrelor is preferred over clopidogrel and prasugrel (Class IIb B)[1]. In patients at high risk of bleeding, the recommended combinations are ASA plus clopidogrel or ASA plus ticagrelor for a period of 6 months (Class IIa B)[1]. In the case of conventional balloon-only TCA, there are no current recommendations regarding either the selection of the second antiplatelet agent or the duration of DAPT[1]. In the case of TCA with drug-eluting balloons, both the duration and drug selection are homologous to that of the stent, according to the clinical condition (class IIa B). In the case of bioabsorbable platforms, dual antiplatelet therapy with ASA plus prasugrel, ticagrelor or clopidogrel is recommended, according to bleeding risk for at least 12 months, regardless of clinical condition (Class IIa C) [1]. The following algorithm summarizes the evidence on the selection of the DAPT strategy according to clinical condition and bleeding risk **(Figure 18).**

When TCA has been performed and treatment with oral anticoagulation (OAC) is also indicated, a triple schedule with ASA, clopidogrel and new oral anticoagulants or anti-vitamin K is recommended for 1 month, followed by OAC plus clopidogrel or aspirin for 1 year (class IIa B). Consideration may be given to extending the triple schedule to 6 months in patients with ACS or other anatomic or procedural features that exceed the bleeding risk (Class IIa B). When the bleeding risk is very high, the double schedule, anticoagulation with clopidogrel or ASA, can be considered from the beginning (Class IIa A) [1,2]. Double antiplatelet the-

rapy with prasugrel or ticagrelor (Class III C)[1] is not recommended in the context of anticoagulation.

Special considerations. Among the strategies that can be applied in patients at high thrombotic risk in order to reduce new ischemic events are the following:

- Extend the time of DAPT. Within this strategy there is evidence for the use of monotherapy with ticagrelor 60 mg twice daily for a extended period of time in patients with acute myocardial infarction [4].
- Switch to more potent P2Y12 inhibitors, from clopidogrel to ticagrelor or prasugrel, which is called escalation (a new loading dose is always used in ACS, but not in chronic coronary artery disease). Given that clopidogrel can present variability in platelet reactivity in up to 30% of cases, studies were performed with platelet aggregation tests and genetic studies without conclusive results due to the lack of statistical power [5]. Results of a recent meta-analysis show a 26% reduction in ischemic end points with the use of these techniques without increased bleeding [6].
- The use of new low-dose oral anticoagulants (rivaroxaban 2.5 mg twice daily) plus ASA as a replacement for DAPT showed a 24% reduction in major cardiovascular events. There is still no recommendation in the guidelines for preference over DAPT[7].

Among the strategies that can be used in patients at **high risk of bleeding** are:

- Reduce DAPT time to 1 month and continue aspirin monotherapy [8].
- Reduce the time of DAPT but continue monotherapy with a P2Y12 inhibitor. There is evidence for the use of both clopidogrel and ticagrelor [9,10].
- Perform "de-escalation" of the P2Y12 inhibitor, i.e., switch to a less potent inhibitor (from prasugrel or ticagrelor to clopidogrel) to mitigate bleeding effects. Although the strategy guided by aggregation testing or genetic testing has not been shown to be statistically superior to unguided de-escalation, the result of a meta-analysis demonstrates a 19% reduction in bleeding with no increase in ischemic events [6].
- It is recommended to accompany dual antiplatelet therapy with proton pump inhibitors (there is no evidence against the use of omeprazole) [1-3].

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d) Stents with evidence of dual antiplatelet therapy for 1 month. *Dr. Ernesto M. Torresani (Interventional Cardioangiologist).*

The effectiveness of antithrombotic treatment depends on a delicate balance between the reduction of ischemic events and bleeding, and their prevention is an essential objective. In the first 24hs of TCA there is a certain balance (1) between ischemic and bleeding risk, then, and during the first month, the benefits of intensive antithrombotic treatment generally outweigh the increased bleeding risk. However, this benefit dissipates with additional time, favoring a therapeutic approach that considers the risks of both bleeding and thrombosis (2). Bleeding (3) is related in the first hours to the access site and the antithrombotic drugs we have used, further influenced by age, weight, renal function, patient frailty, predisposing comorbidities and the need for post-CTA anticoagulation.

It is interesting to note that there are several bleeding scores (GUSTO, TIMI, ACUITY, BARC, etc.), which may show a different occurrence in the same study (4) depending on how it is defined, but it is certain that bleeding is an indicator of high risk and a predictor of mortality. In the Consensus for the Prevention and Management of Bleeding of the Argentine Society of Cardiology (5), it is suggested that the risk of bleeding should be evaluated in all patients before receiving antithrombotic treatment, emphasizing that no risk score replaces the clinical evaluation of the individual patient and recommending the use of the CRUSADE or OASIS 5 scores for Acute Coronary Syndromes and the HAS-BLED for patients with Atrial Fibrillation.

From the interventionist's point of view, we must consider some aspects in order to help reduce the possibility of bleeding, such as: approach route and size of access, anticoagulation, choice of stent, need for the use of IIb-IIIa inhibitors and, finally, in some cases, offer the possibility of closing the femoral access by endovascular stitches, closure of the left atrial appendage or therapy by vascular occlusion (embolization of the bleeding site) depending on the case.

Drug-eluting stents have demonstrated their effectiveness in reducing restenosis and have a class I indication. However, due to the need for prolonged dual antiplatelet therapy, they have been questioned, especially in patients with a higher risk of bleeding. In BMS, dual antiplatelet therapy can be maintained for only 1 month (6) and with 1st generation DES it should probably never be discontinued, this being related to the rapid endothelialization of the former and the probable absence of complete endothelialization of the latter, probably linked to the polymer used in these stents. Therefore, if we were to use a stent without polymer or a biodegradable one, this could change. In the LEADERS FREE study (7) patients at high risk of bleeding were randomized

to the use of the BioFreedom® stent with Biolimus A9 on the abluminal surface without polymer or the Gazelle® stent (Bare Metal Stent). The inclusion criteria used in this study (patients at high risk of bleeding from multiple causes) are usually exclusion criteria in the design of most studies 2,466 patients were randomized to one or the other stent. At discharge, more than 96% had double antiplatelet therapy, 35% were anticoagulated and 32% had triple therapy. A lower rate of combined events and the need for revascularization of the culprit vessel was observed, which gave DES greater safety and efficacy over BMS. A detail to be taken into account is that it is not that the patients did not bleed (7% of severe bleeding was recorded) but that it has been shown that drug-eluting stents can be used with equal risk and greater future benefit in all cases; the potential benefit will begin to be obtained after the first month and probably not before. At one month, in 75% of cases, antiplatelet therapy was continued with aspirin alone.

The LEADERS FREE trial has been taken as the gold standard and used in new studies to compare it with other stents such as the Onyx Resolute® in the ONYX ONE trial [8] and later by the MASTER DAPT [9,10] with the Ultimaster® stent where the possibility of 1 month double antiplatelet therapy was also proven. It is worth mentioning that the polymer of the Onyx Resolute® stent is non-biodegradable and that of the Ultimaster® stent is, so the possibility of rapid endothelialization or not is evidently a phenomenon that requires a more complex analysis, and the drugs released are all different (Biolimus A9, Zotarolimus and Sirolimus).

Very recently the T-PASS study [11] was presented in which 2,850 patients were randomized after having undergone TCA and using Orsiro® stents (60 µ struts, cobalt chromium, biodegradable polymer, Sirolimus) to DAPT with ticagrelor and aspirin, suspending aspirin after one month in one group and in the other group continuing with DAPT for 1 year. It is worth mentioning that patients at high risk of bleeding were excluded. The strategy with 1-month DAPT followed by ticagrelor monotherapy reached a threshold of noninferiority and provided evidence of superiority at 12 months for combined events (death, AMI, stent thrombosis, CVA, and major bleeding) due to a significant reduction in bleeding events.

The current guidelines (2023) of the European Society of Cardiology [11] recommend aspirin and prasugrel or ticagrelor as the first-choice dual antiplatelet therapy in most cases but consider that in patients with a higher risk of bleeding this should be replaced by aspirin and clopidogrel. In those with a need for associated anticoagulation, it is necessary to weigh up whether we are more concerned about ischemia or bleeding, in which case we will perform a triple scheme for the shortest possible time and safely post-TCA (with aspirin, clopidogrel and the anticoagulant), and then discontinue an antiplatelet agent, preferably aspirin, and continue with the anticoagulant and clopidogrel association.

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e) Circulatory Support Systems. *Dr. Carlos Miguel Fava (Interventional Cardioangiologist).*

Cardiogenic shock (CS) associated with AMI occurs between 5% to 12% [1], being more frequent in older patients, with a higher incidence of comorbidities and complex anatomies [2], and mortality is currently between 50% to 80% [3]; in an attempt to improve survival, different ventricular assistance devices (VAD) have been developed which have shown benefits under certain conditions. It is currently proposed that patients with AMI complicated by cardiogenic shock should be referred to centers with a "Shock Team" trained in VAD, and initial analyses have shown a decrease in mortality [4].

Intra-aortic Balloon Pump Counterpulsation (IABP). It is the most accessible VAD in the world, easy to use and low cost compared to the rest. Multiple investigations have been carried out without demonstrating a real benefit, but the most important study is the IABP-SHOCK II [5], in which 600 patients were randomized to IABP vs. conventional treatment. At 30 days, 6 months, 12 months and 6 years there was no difference in mortality, infarction, stroke, new revascularization, rehospitalization for heart failure, functional class or quality of life. Currently the guidelines place it in Class III A [6], and its use can be considered in the initial phase of CS or in the presence of acute mitral insufficiency, septal wall rupture or in those who present CS without availability or access to more advanced VADs.

ECMO (extracorporeal membrane oxygenation). This VAD began to be used in the 1960s [7] and has been increasingly used in recent years [8]. The device has shown,

in different series, lower mortality, fewer hospitalizations for heart failure, lower incidence of neurological complications and fewer days of hospitalization compared to the conventional strategy and IABP, but on the other hand, it presents a greater presence of bleeding and ischemic compromise of the limb, which makes a very rigorous management of anticoagulation imperative. An important factor is the timing of its use. An analysis of the RESCUE registry [9] evaluated its early use during CS, showing lower in-hospital, 30-day and 1-year mortality, as well as fewer readmissions for heart failure, with no difference in the presence of bleeding (gastrointestinal or not), limb ischemia and stroke.

Impella®. This device is an axial centrifugal pump based on the rotation of a micro-helix (incorporated in the catheter tip) that is positioned in the left ventricle crossing the aortic valve and providing a minute volume between 2.5 to 5 L. At present, it is the one that provides the greatest hemodynamic support accompanied by good myocardial protection compared to the rest of the ventricular assist devices. The USpella registry [10] showed a decrease in mortality with its use, especially if it was used before starting TCA, also favoring the possibility of revascularization of multiple arteries due to hemodynamic stability. In patients with peripheral vascular disease, the INTERMACS II registry demonstrated that axillary access is feasible and safe, facilitating early mobilization [11]. One of the frequent complications in infarction with cardiogenic shock is the presence of renal failure. This device has been shown to reduce deterioration and the need for dialysis, as well as the presence of lactate and elevated cardiac enzymes, ensuring better mean arterial pressure [12]. Its early use, especially in infarctions with unprotected left main coronary artery involvement, has shown lower mortality and cerebral hypoxia or anoxia [10]. We can conclude that at present, in AMI complicated with cardiogenic shock, the IABP is not very useful, except, according to some authors, in the very early stage or at the onset of shock prior to TCA, but once advanced it is not a useful device and may be related to some complications such as bleeding. The Impella® is the one we should use, but it is not available in most medical centers in the world. It is important that high complexity centers be organized in the health system to treat AMI complicated with cardiogenic shock, ensuring early transfer, a strategy that would reduce complications and mortality in this complex scenario.

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A randomized pilot study of the Amicath® II microcatheter use for the intralesional infusion of drugs in patients with STEMI to improve microcirculation and ventricular function. AMIway study

Estudio piloto aleatorizado del uso del microcatéter Amicath® II para la infusión intralesional de fármacos en pacientes con STEMI para mejorar la microcirculación y la función ventricular. Estudio AMIway

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ABSTRACT

Background. ST-elevation acute myocardial infarction and its reperfusion continues to be a topic of debate in clinical practice, without a doubt the method of choice is primary percutaneous coronary intervention, although it is still not clear how to improve microcirculation. Intralesional drug treatment has been used to improve results.
Purpose. Two objectives were established in the study, firstly, to evaluate the feasibility of using a microcatheter assessed for its ability to cross the lesion, show the distal territory and allow the injection of drugs, and the second objective was to assess the improvement in LVEF between 3 and 6 months of evolution analyzed by baseline echocardiography and follow-up.
Methods. The AMIway is a randomized pilot study of two arms with patients with STEMI with a high thrombotic burden such as TIMI Thrombus ≥ 3 to be treated with primary PCI with intralesional Adenosine and Tirofiban infusion through the Amicath® II Catheter, IHT, Barcelona, Spain, compared with patients treated with primary PCI with placebo infusion through the same microcatheter within 12 hours of STEMI, in both groups treated with stents. Amicath® II is a rapid exchange micro perfusion catheter for intracoronary use, combines a single lumen in its proximal section (Teflon-coated stainless steel hypo tube). The outer lumen of the distal section ("Dotter" tube, made of flexible polymeric material, Pebax), has a progressive diameter, to obtain a cross ability effect and presents four distal holes, to measure distal perfusion pressure and infuse drugs. The other fast exchange lumen is for the 0.014" wire. It also presents 5 radiopaque marks with a distance of 10 mm between them.
Results. In three centers in Buenos Aires, Argentina, between October 2019 and March 2022, 50 patients were included, who were randomized into two groups with 25 patients in each. There were no significant differences between the two groups in baseline clinical and angiographic characteristics, the majority of patients were male, and diabetes was present in one third of both groups. The vessels treated were the Anterior Descending and Right Coronary Arteries, most were by radial approach. In all patients the microcatheter could be used without difficulties or complications; the lesions were crossed without difficulty and the distal vessel to the occlusions were observed and the infusion of drugs (adenosine and tirofiban) was carried out ultra-selective in the active group and placebo in the control group, it was possible to measure the length lesion in the culprit vessel compared with angiographic quantification. Seven patients in the placebo group underwent a crossover to the active treatment. LVEF improved at 223 days of follow-up±195 days from a baseline of 50.6±8.8 and increased to 59.5±9 at follow-up with a p=0.02, while in the control group it improved from 50.7±10 to 56.6±9.7 with a p=0.07. Three patients died of non-cardiac death associated with the SARS-CoV-2 virus, two patients in the control group.TIMI 3 flow was similar and myocardial Blush was better in the active group.
Conclusions. In this pilot study it was possible to observe that the Amicath® II catheter was able to cross the lesion in all the patients that was attempted, being able to observe the vessel of the involved territory and infuse the study drugs without complications. LVEF improvement was observed in the medium term in patients where microcirculation was treated ultra-selective in patients with a high thrombotic burden.

Keywords: *Amicath, STEMI, LVEF, primary PCI, adenosine, tirofiban.*

RESUMEN

Antecedentes. El infarto agudo de miocardio con elevación del ST (IAMST) y su reperfusión continúa siendo un tema de debate en la práctica clínica. Sin duda, el método de elección es la intervención coronaria percutánea primaria (ATC), aunque aún no está claro cómo mejorar la microcirculación. Se ha utilizado tratamiento farmacológico intralesional para mejorar los resultados.
Propósito. En el estudio se establecieron dos objetivos. En primer lugar, evaluar la viabilidad del uso de un microcatéter según su capacidad para atravesar la lesión, mostrar el territorio distal y permitir la inyección de fármacos; y el segundo objetivo fue evaluar la mejora en FEVI entre 3 y 6 meses de evolución analizada mediante ecocardiografía basal y seguimiento.
Métodos. El AMIway es un estudio piloto aleatorizado de dos ramas con pacientes con IAMST con alta carga trombótica como TIMI Thrombus ≥ 3 para ser tratados con PCI primaria con infusión intralesional de adenosina y tirofibán a través del catéter Amicath® II, IHT, Barcelona, España, en comparación con los pacientes tratados con ATC primaria con infusión de placebo a través del mismo microcatéter, dentro de las 12 horas posteriores al IAMST, en ambos grupos tratados con stents. Amicath® II es un catéter de microperfusión de intercambio rápido para uso intracoronario, combina una única luz en su sección proximal (hipotubo de acero inoxidable recubierto de teflón). La luz exterior de la sección distal (tubo "Dotter", de material polimérico flexible, Pebax), tiene un diámetro progresivo, para obtener un efecto de cruzabilidad y presenta cuatro orificios distales, para medir la presión de perfusión distal e infundir fármacos. La otra luz de intercambio rápido es para para la guía coronaria de 0,014". Presenta además 5 marcas radioopacas con una distancia de 10 mm entre ellas.
Resultados. En tres centros de Buenos Aires, Argentina, entre octubre de 2019 y marzo de 2022, se incluyeron 50 pacientes, quienes fueron aleatorizados en dos grupos de 25 pacientes en cada uno. No hubo diferencias significativas entre los dos grupos en las características basales clínicas y angiográficas, la mayoría de los pacientes eran hombres y la diabetes estaba presente en un tercio de ambos grupos. Los vasos tratados fueron la Descendente Anterior y la Coronaria Derecha, la mayoría fue por abordaje radial. En todos los pacientes el microcatéter pudo utilizarse sin dificultades ni complicaciones; las lesiones se atravesaron sin dificultad y se observó el vaso distal a las oclusiones y la infusión de fármacos (adenosina y tirofibán) se realizó ultraselectiva en el grupo activo y placebo en el grupo control, se pudo medir la longitud de la lesión en el vaso culpable en comparación con la cuantificación angiográfica. Siete pacientes del grupo de placebo se sometieron a un "cruzamiento" al tratamiento activo. La FEVI mejoró a los 223 días de seguimiento±195 días desde un valor inicial de 50,6±8,8 y aumentó a 59,5±9 en el seguimiento con una p=0,02, mientras que en el grupo control mejoró de 50,7±10 a 56,6±9,7 con p=0,07. Tres pacientes murieron por muerte no cardíaca asociada con el virus SARS-CoV-2, dos pacientes del grupo de control. El flujo TIMI 3 fue similar y el Blush miocárdico fue mejor en el grupo activo.
Conclusiones. En este estudio piloto se pudo observar que el catéter Amicath® II logró atravesar la lesión en todos los pacientes que se intentó, pudiendo observar el vaso del territorio involucrado e infundir los fármacos del estudio sin complicaciones. Se observó una mejora de la FEVI a mediano plazo en pacientes en quienes la microcirculación se trató de forma ultraselectiva, en pacientes con una alta carga trombótica.

Palabras clave: catéter Amicath, SCACEST (síndrome coronario agudo con elevación del ST), FEVI (fracción de eyección ventricular izquierda), ATC primaria (angioplastia coronaria percutánea), adenosina, tirofibán.

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TABLE 1. Angiographical and clinical basal characteristics.

	Control, % (n=25 patients)	Amicath, % (n=25 patients)	p Value
Age	59.8+/-11.6	58.7+/-9.8	0.71
Sex	88 (22)	72 (18)	0.157
Smoking	68 (17)	68 (17)	1.00
Dyslipidemia	72 (18)	92 (23)	0.066
Diabetes	36 (9)	32 (8)	0.76
HBP	64 (16)	64 (16)	1.00
CKF	8 (2)	0 (0)	0.149
pre PCA	20 (5)	12 (3)	0.44
pre CRM	0 (0)	4 (1)	0.31
Radial access	88 (22)	80 (20)	0.53
DA	48 (12)	40 (10)	0.56
RC	36 (9)	48 (12)	0.39
CX	16 (4)	12 (3)	0.68
Reference diameter	3.21+/-0.43	3.26+/-0.28	0.63
Distal lesions	36 (9)	16 (4)	0.10
Tortuosity	32 (8)	40 (10)	0.55
Severe calcification	32 (8)	24 (6)	0.52
Adenosine infusion	40 (10)	100 (25)	<0.001
Tirofiban infusion	32 (8)	100 (25)	<0.001
Cloridogrel	56 (14)	28 (7)	0.045
Ticagrelor	28 (7)	48 (12)	0.145
Prasugrel	16 (4)	16 (4)	1.00

HBP (high blood pressure), CKF (chronic kidney failure), PCA (percutaneous coronary angioplasty), DA (anterior descending artery), RC (Right Coronary), CX (Circumflex artery).

TABLE 2. Patients grouped in the control group and active treatment with Amicath® II catheter, with their echocardiographic follow-up, in their basal state and in the follow-up.

By intention of treatment (follow-up 223 +/- 195 days)			
N	Basal LVEF	Follow-up LVEF	P
Control group (25)	50.7+/-10	56.6+/-9.7	0.07
Pharmacological group (25)	50.6+/-8.8	59.5+/-9	0.02

LVEF (Left Ventricular Ejection Fraction)

INTRODUCTION

The myocardial reperfusion via catheter is still the treatment chosen by patients with STEMI[1], and LVEF in the long-term follow-up is the most efficient method of evaluating the prognosis in patients[2]. The impact of the microcirculation in these patients and their treatment is a challenge[3]. Prior studies with the treatment with adenosine systematically had promising results[4,5]. We conducted a pilot study, randomized in order to evaluate the feasibility of the use of a micro-catheter of quick interchange, devoted to the infusion of drugs in the invasive treatment of STEMI, the Amicath® II (IHT, Barcelona, Spain), and to evaluate medium-term LVEF, in patients treated with the infusion of adenosine and a Glycoprotein IIb IIIa inhibitor (GPI) ultra selectively in the infarct area.

MATERIAL AND METHODS

STUDY DESIGN

AMIway is a randomized, prospective pilot study where patients with STEMI were included within the 12 hours once the pain began in three centers with cath-labs in the Buenos Aires Metropolitan Area in Argentina. The centers were approved by the Ethics and Research committees. This study evaluated the feasibility of the use of a micro-catheter designed for the infusion of liquids or pharmacological drugs as they contribute to the myocardial mechanical reperfusion to improve the microcirculation and, thus, to achieve a higher recovery of the infarcted area. In order to do so, we designed a strategy of primary revascularization with stents in all the patients according to the standards of each interventional laboratory, where previously an adenosine infusion and an Inhibitor of GPI, the tirofiban (Agrastat, Patheon Manufacturing Service, Greenville, USA), took place directly in the affected area through the Amicath® II catheter in the active group compared with the placebo infusion in the other group with the same catheter. At the same time, in order to evaluate the acute myocardial infarction (AMI) size, LVEF was used, measured by a Doppler echocardiogram immediately post procedure and in the follow-up at three to six months after the primary angioplasty.

SELECTION AND RANDOMIZATION

The patients who underwent a STEMI were chosen to take part in the study. These patients had to be within the criteria of inclusion and they did not have to present any contraindication to enter. The details of the inclusion and exclusion criteria are shown in the Appendix of the study. The randomization was performed in blocks and by sealed envelopes which were pre-established before beginning the study. The researcher had to open those envelopes after including the patient and had to follow their instructions.

All the patients were previously evaluated by a Cardiology staff and the standards of STEMI treatment were followed.

All the events were evaluated by an independent safety committee.

The study was ruled by the good clinical practices and Helsinki principles.

REVASCULARIZACIÓN, PHARMACOLOGICAL TREATMENT AND FOLLOW-UP

All the patients were submitted to a primary coronary angioplasty performed according to the technical standards either by femoral or radial via according to the patient and operator's preferences. All of them received a 600 mg clopidogrel dose, a 60 mg prasugrel dose or 180 mg ticagrelor dose and a 300 mg aspirine dose. Intra- procedure: all of them received 100 U/kg of heparin. After positioned a coronary guide in the index vessel, a microcatheter of rapid exchange with marks of distance, Amicath® II, was passed where contrast was infused which indicated the size of the distal bed, the length of the lesion. After that, in the active group 2000 µg of adenosine and 2.5 mg of tirofiban (Agrastat) were passed slowly, and in the control group two syringes with 10 ml of physiological solution each one. Next, in both groups pharmacological stents were implanted according to the need to cover all the lesion to obtain a final TIMI III (**Figure 1**).

The treatment of the other vessel with severe lesion was left to the operator's criterion, although the treatment by stages was strongly recommended if it was necessary.

Post-procedure: all the patients were submitted to an

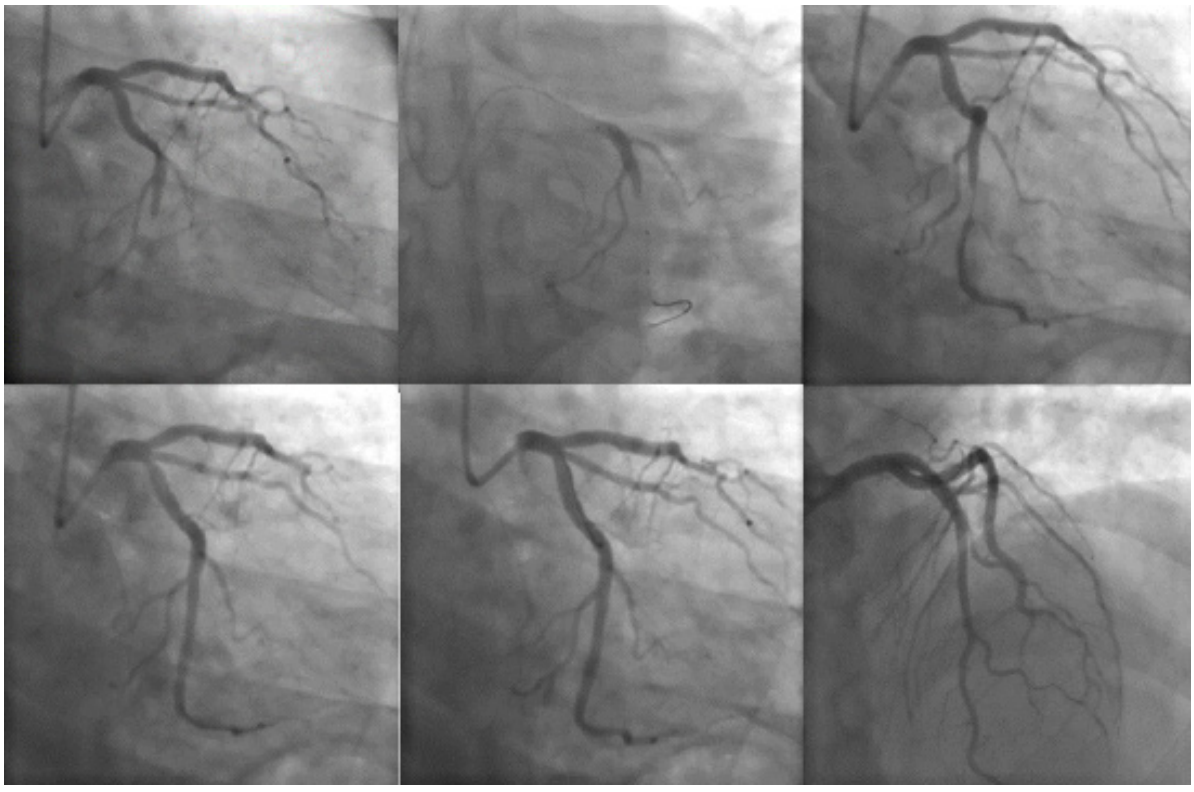

Figure 1. *A) Patient STEMI of lateral territory, with 100% total occlusion TIMI 0 of the circumflex artery. B) The Amicath® II catheter is observed where through its holes the drugs of the study are injected, after that. C) the lesion can be clearly observed and the distal bed can be quantified, D) in this image the immediate post-timplant of the stent which still has the coronary wire can be seen, E) and finally without the coronary wire and F) in the final axial view in front of TIMI III and BLUSH 3.*

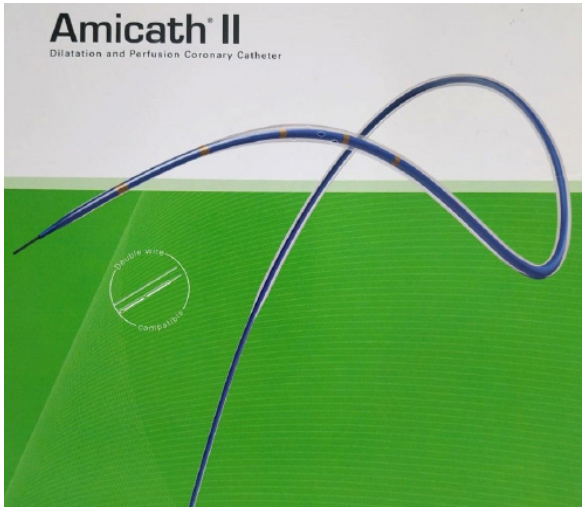

Figure 2. *Amicath® II is a rapid exchange coronary perfusion microcatheter.*

echocardiogram with LVEF measurement with Simpson´s method and at six months of follow-up.
All the data and their analysis obtained were monitored by the CECI (Centro de Estudios en Cardiología Intervencionista)

DESCRIPTION OF AMICATH® II

Amicath® II is a rapid exchange coronary perfusion microcatheter with 5 (five) radiopaque marks at a 10 mm distance among each other used in the intracoronary procedures of angioplasty during acute myocardial infarction.. It combines an only lumen in its proximal section (a stain steel hypo-tube covered by Teflon). The external lumen of the distal section ("Dotter" tube, of flexible polymeric material, Pebax) has a progressive diameter to be able to cross easily through dilatation ("Dotter") and it has four distal holes to measure distal perfusion pressure and pass drugs (saline solution, vessel-dilating drugs, glycoprotein inhibitors, thrombolytic, etc.). The other lumen (double lumen) of rapid exchange allows the passage of a coronary guide of 0.014" to ease and allow the progress of the catheter through the occlusion to be treated **(Figure 2).**

PRIMARY AND SECONDARY OBJECTIVES

The study primary objectives are to evaluate the feasibility of the use of a microcatheter designed for drug infusion in STE-ACS and to test if the adjuvant treatment of adenosine and tirofiban injected ultra selectively in STEMI index vessel improves the microcirculation, which would suppose a LVEF improvement in patients at six months under treatment compared with the post-procedure immediate results.
The secondary objectives are the major cardiovascular events and their components such as death, AMI, stroke and a new intervention of the vessel treated. The stent thrombosis was also analyzed.

STATISTICS

We calculated the sample size according to pilot studies similar to ours and to what García-García et al[6] state on this issue. For pilot studies we used a sample of 25 patients in each group. A level of significance of a $p< 0.05$ and a power of 80% were considered.

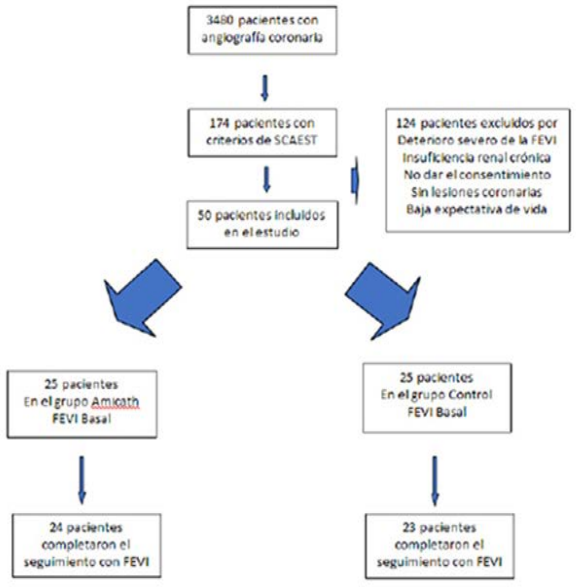

Figure 3. *Study flow diagram*

We calculated the averages and standard deviations (SD) of the continuous variables in both groups and we analyzed them with the test of the t-Student. The binary variables were reported as percentages and they were analyzed with the Chi2 test or the exact Fisher test.

RESULTS

Three centers of the Buenos Aires Metropolitan Area in Argentina which had the capacity of performing primary angioplasty took part in the study. Between October 2019 and March 2022, 3480 patients were admitted for a coronary angiography. Among them, 174 patients had STEMI, of them, 50 patients who qualified for the inclusion were accepted for the study and they were randomized in two groups of 25 patients in each one. **(Figure 3).**

Both groups were similar as regards clinical and angiographic basal characteristics, without significant differences among the analyzed variables **(Table 1).** Between both groups, most of the patients were male and diabetics was present in a third in both groups. The predominant vessels of treatment were the anterior descending and the right coronary. Most of the patients were approached through radial access.

In all the patients the Amicath® II microcatheter could be used without difficulties or complications related to it. The lesion could be passed through and the distal bed to the occlusion could be shown. The infusion of drugs (adenosine and tirofiban) could also be carried out ultra selectively in the active group and the placebo in the control group. Besides, the length of the lesion could be measured in the culprit vessel compared with the online coronary angiographic quantification.

There were 7 (seven) patients in the placebo group who made a crossover to the active treatment.

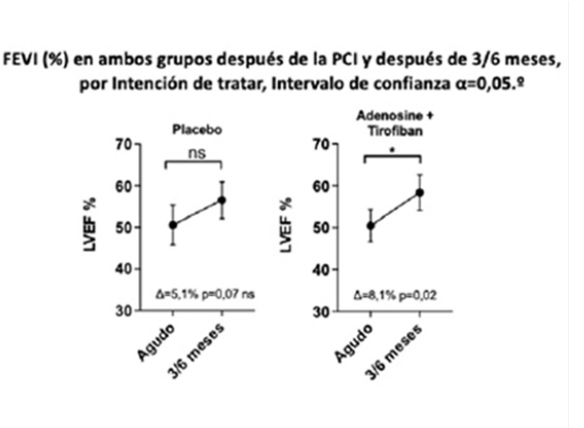

Figure 4. *LVEF improvement between both groups, between basal measurements and in the follow-up.*

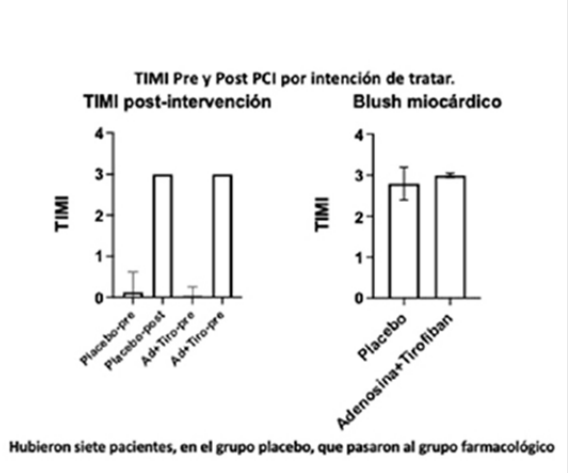

Figura 5. *Evaluación de la perfusión miocárdica a través del flujo TIMI y el blush miocárdico.*

All the patients were analyzed by treatment intention where it was observed that LVEF improved after 223 ± 195 follow-up days: from a basal of 50.6 ± 8.8 it was increased to 59.5 ± 9 during the follow-up with a p=0.02, while in the control group it improved from 50.7 ± 10 to 56.6 ± 9.7 with a p=0.07 **(Figure 4, Table 2).**

During the follow-up, probably due to the pandemic, three patients died due to a non-cardiac death related to the SARS-CoV-2 virus, two patients were in the control group and the other one in the pharmacological group.

As regards the TIMI flow and the myocardial blush, it is observed that there were no differences between the final TIMI between the two groups, but a slight improvement of the myocardial blush was observed in the active group **(Figure 5).**

DISCUSSION

In this pilot study we could see that the Amicath® II microcatheter has an excellent profile because in the 100% of the cases it could pass through the lesion without difficulty in all the patients where the primary TCA was performed, the vessel and its distal bed could be dyed being able to observe the lesion in detail and the adenosine could also be injected at high dose without obser-

ving in the majority of the patients the pauses frequently related to the infusion of the adenosine systematically plus the GPI in the form of intralesional bolus. Besides, in the active group an improvement of LVEF evaluated immediately after AMI could be seen and in the follow-up between 3 and 6 months, improvement that was significant.

The primary TCA has turned into the treatment chosen by the STEMI patients[1], and the evaluation of the ventricular function on the mid-term sets its prognosis[2].

The preliminary studies on the intracoronary adenosine in animal samples of myocardial ischemia indicate that it protected from the vascular injury[7].

The adenosine also present powerful anti-inflammatory effects like the adhesion inhibition of neutrophils to endothelium, the release of cytokines of the mononuclear cells, the release of radicals free from oxygen and the apoptosis of cardiomyocites[8]. Its antiplatelet effect has been also shown, which could limit the thrombus burden and allow the vessel permeability[9].

In the AMISTAD I[4] study where the adenosine infusion was used for three hours in patients with STEMI who received fibrinolytics, a reduction of the infarct size could be seen in the patients who presented infarct of the anterior face and did not present it in the other territories. Next, the AMISTAD II[5] study was performed; the adenosine infusion at 50 and 70 gammas to these same patients with STEMI, but infarcts of the descending anterior territory were only included. Benefits with higher infusion dose could be observed, which suggests that high dose of adenosine are needed in the infarct site as we could infuse our patients with Amicath® II catheter super selectively.

The GPI are very powerful drugs which inhibit the platelet aggregation immediately through the fibrinogen inhibition and von Willebrand factor related to the platelets[10], and they help to quickly reduce the thrombus size which is exaggerated in these patients.

In order to boost the beneficial effects of the adenosine we add to the GPI, that we know they are very good as contributors in the STEMI since the publication of the last meta-analysis of the GPI use in STEMI with 21 trials and more than 8500 patients, 10 trials with tirofiban, 9 trials with abcximab, one with eptifibatide and one mixed of tirofiban plus abcximab, only one trial used ticagrelor or prasugrel; all the cardiovascular events were reduced and the higher and lower bleeding was significantly higher in the GPI group, but not the intracranial[11] . In order to mitigate the latter and its potential danger, the concept of its intracoronary application was born. Small trials were made quickly which are summarized in the first meta-analysis: between the GPI injection by intravenous or intracoronary via there was a reduction of events in favor of the intracoronary strategy, although there was heterogeneity of the trials[12]. More recently, a new meta-analysis was carried out with 14 ttials with more than 3000 patients where LVEF, TIMI and the resolution of the ECG were better in the intralesional treatment than the systemic one, but without differences in the MACCE on the long-term, without differences in bleeding [13].

A recent review has revived this concept of intralesional application especially to patients with a high thrombotic burden creating an algorithm of treatment in these patients [14].

We believe that in these patients undergoing STEMI the aggressive treatment on the thrombus and the microcirculation can generate a better and higher recovery of LVEF at first instance and after the long-term events.

LIMITATIONS AND STRENGHTS

This is a study with a small sample size correlated with the fact that it is a pilot study. It tests strongly the use without complications of a microcatheter designed for drug infusion. Regarding the LVEF recovery, it seems promising, although a high scale trial is missing to be evaluated. Finally, an evaluation of cardiovascular events on the long-term must be carried out.

CONCLUSIONS

First of all, this study showed the feasibility of using accurately the Amicath® II catheter in all the patients to whom it was tried. It did not show complications during its usage and it demonstrated that it is able to indicate the lesion adequately allowing the drug infusion through it.

The administration of drugs, adenosine and intralesional tirofiban, did not show adverse effects and a LVEF mid-term improvement could be observed.

Being a pilot study, it leads to potential hypothesis for greater magnitude studies.

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Percutaneous closure of coronary-pulmonary fistula with microvascular plug in an adult patient: case report

Cierre percutáneo de fístula coronario-pulmonar con plug microvascular en paciente adulto: reporte de caso

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ABSTRACT

Coronary fistulas are rare anomalies that can be asymptomatic or cause serious complications such as myocardial ischemia or heart failure. In the presence of complications, their closure is indicated, either by surgical or percutaneous approach. We present the case of an adult patient with a coronary-to-pulmonary artery fistula, complicated by myocardial ischemia and ventricular arrhythmia, in which percutaneous closure with a Micro Vascular Plug (Medtronic®) was chosen. This is the first report on the use of the device in this clinical scenario in an adult patient in our setting

Keywords: coronary fistula, percutaneous closure, microvascular plug.

RESUMEN

Las fístulas coronarias son anomalías poco frecuentes que pueden cursar asintomáticas o generar complicaciones graves como isquemia miocárdica o insuficiencia cardíaca. En presencia de complicaciones está indicado el cierre, ya sea por abordaje quirúrgico o percutáneo. Presentamos el caso de un paciente adulto con una fístula coronario-pulmonar complicada con isquemia miocárdica y arritmia ventricular, donde se optó por el cierre percutáneo con un plug microvascular (Medtronic®). Se trata del primer reporte de utilización del dispositivo en este escenario clínico en un paciente adulto en nuestro medio.

Palabras clave: fístula coronaria, cierre percutáneo, plug microvascular.

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INTRODUCTION

The coronary fistulas are rare abnormalities, whose incidence varies between 0.1 and 0.2% of the patients to whom a cineangiocoronarygraphy[1] is made. They are defined as abnormal communications between the coronary arteries and the cardiac chambers or great vessels. They are usually congenital malformations, although they can also be acquired after the cardiac surgery, thorax trauma, endo-myocardial biopsy, surgical myomectomy or percutaneous coronary interventions[1,2]. The most frequent place of origin varies in the different series. The usual drainage place are the right cavities or the pulmonary artery [2,3].

The most frequent is that patients have them asymptomatically, although in many cases they can generate myocardial ischemia due to the coronary steal, which is one of the main closure indications[3,4]. The available therapeutic strategies are the direct surgical ligation or the percutaneous closure with diverse devices (removable balloons, coils, Amplatzers)[5,6]. The Micro Vascular Plug (MVP, Medtronic®) are devices that are mainly used for the closure of pulmonary arterial, splenic or renal malformations[7]. They have been used for the coronary fistula closure in children [8-10], but for the time being there are no reports of use of this device for the coronary fistula closure in adults in our place.

There is a case of a patient with a coronary-pulmonary fistula which caused myocardial ischemia and ventricular arrhythmia where it was closed successfully by percutaneous via with an MVP as occluder device.

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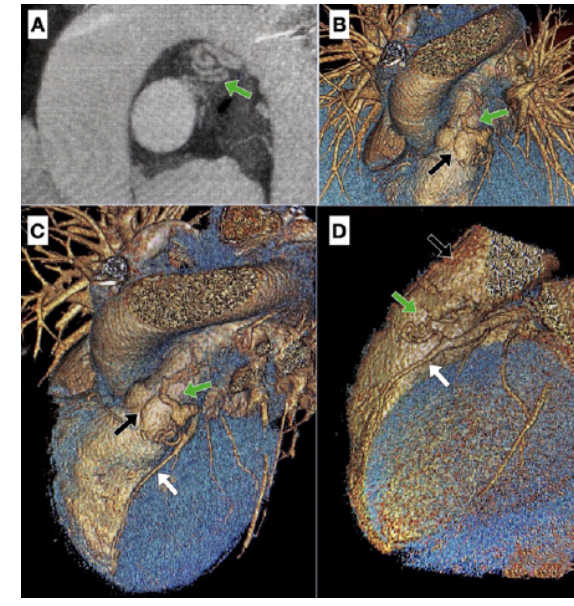

Figura 1. *Coronary tomography and 3D reconstruction showing the ADA-PA fistula from different angles. Green arrow: ADA-PA fistula (anterior descending artery, pulmonary artery). Black arrow: pulmonary artery trunk. White arrow: distal anterior descending artery.*

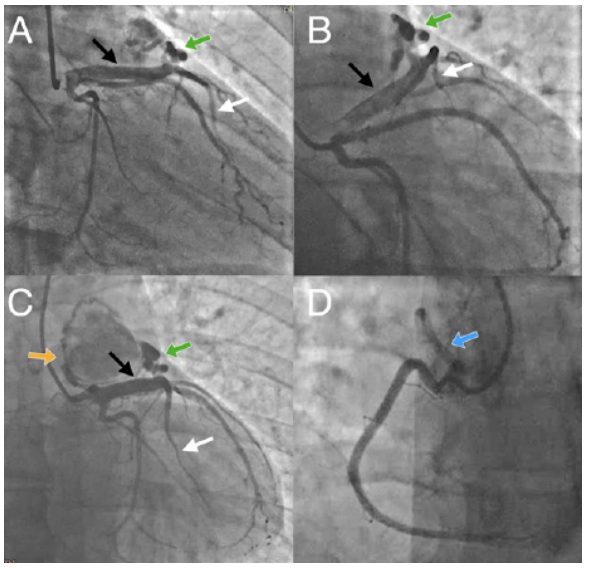

Figure 2. *Diagnostic coronariography. A, B and C. Left coronary artery. D. Right coronary artery. Black arrow: great caliber proximal ADA. White arrow: thin caliber distal ADA. Green arrow: ADA-PA fistula. Yellow arrow: LMCA-PA fistula (left main coronary artery). Blue arrow: RCA-PA fistula (right coronary artery).*

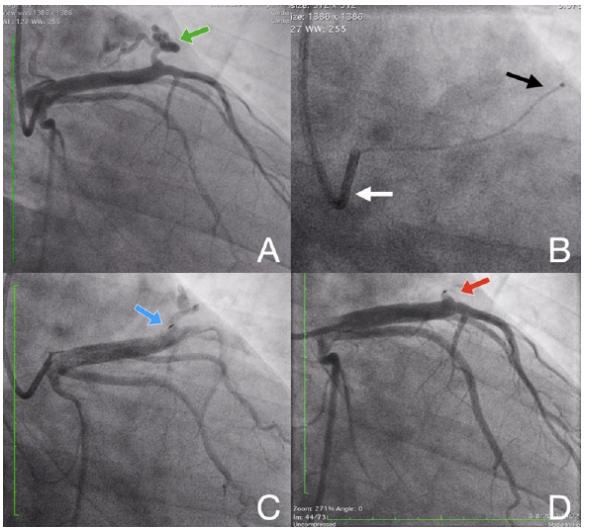

Figure 3. *Procedure of ADA-PA fistula closure. A. Initial image. B. Micro-catheter passing through the fistula. C. MVP released. D. Final result. Green arrow: ADA-PA fistula. White arrow: SBS 3 6 Fr catheter. Black Arrow: 2.8 Fr micro-catheter (Medtronic®). Blue arrow: MVP released. Red arrow: ADA-PA occluded fistula.*

A CLINICAL CASE

A 44-year-old patient, male, obese and hypertensive. History of atypical angor, without other cardiovascular symptoms. The electrocardiogram and the echocardiogram were normal. In the ergometry the patient presented an episode of non-sustained monomorphic ventricular tachycardia. A cardiac computed tomography **(Figure 1)** and a cineangiocoronarygraphy **(Figure 2)** were performed that showed the three coronary fistulas which drained in the pulmonary artery trunk: from the left main coronary artery (LMCA-PA), from the anterior descending artery (ADA-PA) and from the right coronary artery (RCA-PA). Coronary arteries did not show angiographically significant stenosis.

Due to the fact that the fistula ADA-PA was the largest (3.5 mm) and it had suggestive signs of coronary steal (great proximal caliber of ADA and reduction of distal flow to the fistula origin), its closure was decided. The use of an MVP as occlusor device was chosen.

The procedure **(Figure 3)** was performed in a coordinated way, under local anesthesia and through radial access. A SBS 3.5 6Fr guide catheter was used in order to cannulate the ostium of the left coronary artery, and a 0.014" coronary guide was crossed through the fistula. After that, a 2.8 Fr (Medtronic®) micro-catheter was positioned in the neck of the fistula and a MVP 5Q (Medtronic®) was released. An angiography of control was made and it proved the total occlusion of the fistula. There were no complications and the patient was discharged from the hospital 24 hours later.

DISCUSSION

Coronary fistulas are rare abnormalities that communicate the coronary arteries with the cardiac chambers or the great vessels. They can be originated by one or both coronary arteries, and in most of the cases they drain into the right cavities or in the pulmonary artery[2,3]. Its structure is tortuous.

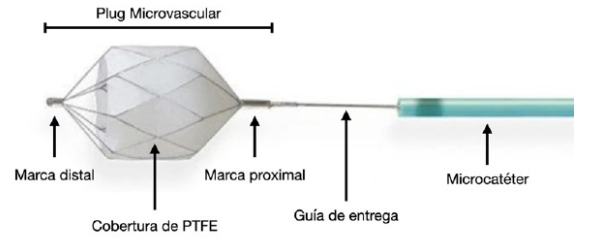

Figure 4. *Structure of microvascular plug and its release system (Medtronic®).*

The more proximal its origin is in the coronary artery, the higher its dilation degree is[1].

Most of the coronary fistulas are congenital although they can be also acquired[1]. They are usually asymptomatic and in some cases they can close spontaneously[3]. When this does not happen, they generate a shunt between both cavities, whose size depends on the caliber of the fistula and on the pressure between both extremes [3]. In these cases, the symptoms can be from dyspnea by cardiac failure with high effort up to angor or malign arrhythmias by secondary myocardial ischemia up to a coronary steal[3]. Other less frequent complications are thromboembolism, breakage, dissection or infection (endarteritis)[3].

The gold standard for the diagnosis of the coronary fistulas is the coronarygraphy. It contributes anatomic and hemodynamic data, such as size, place of origin, place of drainage and its own course. These data are useful to define the closure indication and to plan the best treatment strategy.

The importance of the coronary fistulas lies on the complications that they can cause, which in case they occur, they are a closure indication. The size, the hemodynamic impact and the presence of a myocardial ischemia are the main indicators [1,3]. The symptomatic or the ones which cause the

ventricular dysfunction have a formal indication of closure. However, it is contraindicated in asymptomatic and small fistulas [4]. Based on the evolutionary characteristic of the fistulas, the periodical re-evaluation is recommended.

The surgical closure through direct ligation has been the most used method for many years. It has 0-6% morbimortality rate and a probability of success higher than 95%[3]. The percutaneous closure is an efficient and safe alternative which was first introduced in 1980[2,6], whose probability of success is comparable, reducing time of recovery and of hospitalization[3]. This approach is preferred in those patients with proximal fistulas with a unique drainage site or with high surgical risk[1,6].

There are several devices of mechanical occlusion which can be used for the percutaneous closure: removable balloons, coils, Amplatzers[5,6]. Coils are the most usually used devices, but its main disadvantage lies on the eventual need of several coils to achieve a successful embolization, which extends the procedure. Removable balloons are practically not used these days and the vascular Amplatzers are little used in our place because they are very expensive.

MVP (**Figure 4**) are devices composed by nitinol and covered by a polytetrafluoroethylene (PTFE) membrane, which are delivered by a micro-catheter and they generate immediate occlusion of the vessel[7]. As they come in different sizes, they have been used in different clinical scenarios (pulmonary, renal, splenic, gastroduodenal, peripheral embolizations). Its main advantage is that a unique device can achieve the successful occlusion, with the resulting saving of time and money. In spite of its multiple advantages, the experience regarding its usage for the closure of coronary fistulas is little for the time being and it mainly predominates in children [8-10].

There was a clinical case of an adult patient with three coronary fistulas, one of them was identified as the cause of the myocardial ischemia by coronary steal, and its closure was decided. As there was a proximal fistula and it was easy to reach through percutaneous way, this approach was chosen. The occlusion device chosen was an MVP, being the first report of usage of this device on this clinical scenario in an adult in our place.

CONCLUSIONS

Coronary fistulas rarely occur and they usually happen asymptomatically. They can sometimes appear with secondary symptoms such as myocardial ischemia and malign arrhythmias. When these complications take place, its closure is decided. A percutaneous approach is practicable, having a low probability of complications and a high effectiveness rate. The use of MVP in this scenario is a novel alternative and it is highly favorable.

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Letter from the President of CACI

Carta del Presidente de CACI

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Dear colleagues, not only another year finishes, but also another management finalizes, in a country context where uncertainty controls the scenario and we are immersed in a very difficult situation regarding health. Professionals were forced to generate alerts, to get involved so that both patients and government become aware of the critical condition in which we find ourselves.

Considering the professionals who leave the country searching for better future prospects for professional and economic growth, young people who do not consider as option to invest 14 or 15 years of your life in order to specialize without the guarantee of a future economic well-being, with residence slots which are not filled, the obvious question is: Who is going to care for our children or grandchildren?

Therefore, the scientific societies must compromise with this type of problem, we must enhance and assert our work so as to ensure the patients to be provided with a quality care for which we were trained.

From our College we continue trying to fight for the defence of worthy fees for our medical practices, focusing on our Trade Union Commission that must be an autonomous one going beyond the Boards of Directors on duty, since it will be the only way to achieve that goal once and for all.

I would like to take this opportunity to thank everyone who collaborated and supported my management, the outgoing Board of Directors, the different working commissions, CACI permanent staff, and each member who provided voluntary cooperation with our College during these two years.

My best wishes and full support for the incoming Board that undoubtedly will work for all of us.

It was an honour to hold this position.

Martín Cisneros
President CACI 2022/2023

Reglamento de Publicaciones de la *Revista Argentina de Cardioangiología Intervencionista*

Publications rules Argentine Journal of Interventional Cardioangiology

La *Revista Argentina de Cardioangiología Intervencionista* (RACI) es una publicación trimestral editada por el Colegio Argentino de Cardioangiólogos Intervencionistas (CACI) con objetivos asentados en la divulgación de material científico y educativo para la especialidad. La distribución nacional es gratuita y está dirigida a cardioangiólogos intervencionistas, cardiólogos clínicos y pediátricos, radiólogos, neurólogos, técnicos en hemodinamia y especialidades afines. La publicación es de tipo impresa y electrónica (www.caci.org.ar).
Los principios editoriales de la revista se basan en las recomendaciones para manuscritos enviados a revistas Biomédicas *(Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals)* redactados por el Comité Internacional de Editores de Revistas Médicas *(International Committee of Medical Journal Editors - ICMJE)* en su más reciente actualización, disponible en www.icmje.org.

A partir del número 2 volumen 9 año 2018, por razones editoriales, los elementos gráficos (figuras, tablas, fotos) se editan a lo sumo en dos colores (azul y negro). Aquellos que los deseen a todo color deberán pagar un costo adicional por el trabajo de 200 US$.

Los artículos enviados deben ser originales. El Comité Editorial evaluará los trabajos y luego de un primer análisis sobre si el artículo sigue las normas Editoriales de la Revista, el Director y/o Directores Asociados serán los encargados de enviarlos a un arbitraje externo, que será simple ciego, que significa que los autores no conocen el nombre de los revisores y los revisores a su vez no conocen el nombre de otros revisores. Esta política del RACI se hace siguiendo los mismos criterios empleados por el Comité de Revisión y Editorial del *J Am Coll Cardiol* (JACC), que es la revista de cardiología de mayor factor impacto. La decisión final quedará en manos del Comité Editorial de acuerdo con las conclusiones del arbitraje. Asimismo, el Comité Editorial tendrá la facultad de introducir, con el consentimiento de los autores, todos los cambios editoriales exigidos por las normas gramaticales y las necesidades de edición de la revista. Los artículos de Revisión y Editoriales también serán objeto de la misma revisión. Los artículos Editoriales son usualmente pedidos por el Comité Editorial.

Luego de la primera revisión, los trabajos pueden ser aceptados en la forma en que fue incialmente enviado; Revisiones Menores es cuando si bien el trabajo tiene aportes importantes existen limitaciones menores que deben ser corregidas antes de su eventual publicación; Revisiones Mayores es cuando el trabajo es inaceptable para publicar de acuerdo a como fue presentado. Sin embargo, el Comite Editorial consideraría un posible nuevo envío, tambien llamado *de novo submission*, si el trabajo es modificado sustancialmente; Rechazo, es cuando los revisores y el Comité Editorial consideran que el trabajo es inapropiado para publicar en la Revista RACI
En casos especiales de consensos de diagnóstico y/o tratamiento realizados en conjunto entre el CACI y sociedades científicas afines, tal consenso, de común acuerdo entre las mismas y con conocimiento del Comité Editorial, podrá ser publicado en forma excepcional por las revistas oficiales de ambas sociedades en forma simultánea.

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Todos los autores así como los miembros del Comité Editorial deben declarar conflictos de intereses, en caso de que existan, con las publicaciones.

Cada artículo debe ser presentado con una primera página que debe contener: (a) el título, informativo y conciso; (b) los nombres completos de los autores y de las instituciones en que se desempeñan; (c) un título abreviado para cabeza de página; (d) el número total de palabras del artículo, sin las referencias bibliográficas; (e) el nombre y dirección completa, con fax y dirección electrónica, del autor con quien se deba mantener correspondencia. La segunda página debe incluir el resumen (abstract) en español y en inglés, con 3-6 palabras clave al final de éstos con términos incluidos en la lista del Index Medicus *(Medical Subject Headings - MeSH)*. Luego, en la tercera página, se debe desarrollar el contenido del manuscrito (véase Preparación del manuscrito), iniciando una nueva página para cada sección. Todas las páginas deben ir numeradas desde la portada.

El envío del artículo (texto, tablas y figuras) debe realizarse por correo electrónico a revista@caci.org.ar, con una nota firmada por todos los autores (véase modelo página web), con la indicación de la sección a que correspondería el manuscrito y la aseveración de que los contenidos no han sido anteriormente publicados. Una vez recibido el material, el Comité Editorial iniciará el proceso de incorporación que tiene una duración media de cinco semanas.
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Son trabajos científicos o educativos de investigación básica o clínica original. Condiciones: a) texto general, hasta 5.000 palabras, incluidas las referencias; b) resumen, hasta 250 palabras; c) tablas + figuras, hasta 8; e) autores, hasta 10.

Comunicaciones breves
Los trabajos de esta sección cumplen con los lineamientos de Artículos originales, pero no tienen la suficiente cantidad de pacientes como para ser considerados como tales.

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Son artículos sobre temas relevantes de la especialidad solicitados por el Comité Editor a autores de reconocida trayectoria (nacionales o extranjeros). Puede ser escrito por diferentes tipos de médicos (no más de 3 autores). Condiciones: ídem Artículo Original.

Educación básica
Son artículos sobre el manejo racional y protocolizado de diferentes circunstancias que se presentan en la práctica diaria. Son revisados y consensuados previamente con especialistas en el tema, y se culminan con un diagrama de flujo sobre el manejo diagnóstico y terapéutico de la patología. Es solicitado por el Comité Editor. Condiciones: a) texto general, hasta 2.500 palabras excluyendo referencias; b) resumen, hasta 150 palabras; c) tablas + figuras, hasta 6; d) referencias, hasta 20; e) autores, hasta 4.

Caso clínico
Es la descripción de un caso clínico de características inusuales, con su abordaje diagnóstico y terapéutico y su resolución final. Debe acompañarse de una breve discusión bibliográfica. Condiciones: a) texto general, hasta 1.200 palabras; b) resumen, hasta 100 palabras; c) tablas + figuras, hasta 4; d) referencias, hasta 10; e) autores, hasta 5.

¿Cómo traté?
Bajo el título "¿Cómo traté?" los autores presentarán un caso desafiante y la descripción del tratamiento realizado. El título deberá estar incluido al comienzo del texto, por ejemplo "¿Cómo traté un aneurisma en la descendente anterior?". Luego se incluirán los nombres, apellidos, títulos y lugar de trabajo de los autores. Deberá indicarse el autor que recibirá la correspondencia, incluyendo su dirección postal y e-mail. Todos los autores deberán declarar sus conflictos de interés y, en el caso de no tenerlos, indicarlo. Texto, figuras y referencias seguirán los criterios del Caso Clínico

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Se aceptarán para publicar imágenes de casos excepcionales, ilustrativas, y que el Comité Editorial y los revisores externos consideren de sumo interés para su publicacion en la revista. Deben ir acompañadas de una leyenda explicativa y un breve resumen de historia clínica. Condiciones: a) texto general, hasta 300 palabras; b) solo 2 figuras originales; c) referencias, hasta 3; d) autores, hasta 5.

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Como artículos especiales la Revista aceptará la publicacion de Protocolos de Investigacion Clinica, preferentemente multicéntricos y siempre que los mismos no hubiesen reportado antes los resultados parciales o totales del estudio.

Editoriales
Son análisis y/o comentarios de temas relevantes de la especialidad o de la Cardiología General que tuviesen relación con nuestra especialidad. Siempre serán solicitados por el Comité Editor a un experto en el tema. Asimismo, pueden solicitarse comentarios sobre temas no relacionados a un artículo en particular. Condiciones: a) texto general, hasta 2.000 palabras; b) referencias, hasta 40.

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Es una opinión sobre un artículo publicado en el último número de la revista, el cual requiere un arbitraje realizado por miembros del Comité Editor. Condiciones: a) texto, hasta 250 palabras; b) se podrá publicar una tabla y/o figura; c) referencias, hasta 5. Se aceptarán solo aquellas cartas enviadas dentro del mes de haber salido la versión impresa del número de la revista donde se publicó el artículo original.

PREPARACIÓN DEL MANUSCRITO

El artículo debe estar escrito en castellano, en un procesador de texto Word (Microsoft®) y guardado con extensión *.doc. El tamaño de la página debe ser A4 o carta, con doble espacio interlineado, márgenes de 25 mm con texto justificado y con tamaño de letra de 12 puntos tipo Times New Roman o Arial. Las páginas se numerarán en forma consecutiva comenzando con la portada. El manuscrito (artículo original) debe seguir la estructura «IMR D», es decir, Introducción, Material y métodos, Resultados y Discusión (véanse las normas de publicación ICMJE). Además, debe incluir Título, Resumen, Conclusiones, Conflicto de Intereses y Bibliografía. Al final de cada artículo original, antes de las referencias, deberá hacerse como una tabla destacada de los puntos relevantes del trabajo que se llamará Resumen de Puntos Salientes.

En estos 4 o 5 renglones se deberán señalar los problemas y el conocimiento que hay en el tema tratado hasta el momento y además cuáles serían los interrogantes.

En los dos últimos renglones se destaca el aporte y/o los aportes del trabajo más relevantes sobre este tema. Al final de las referencias se escribirán los Agradecimientos y un Apéndice Suplementario cuando correspondiese en estudios aleatorizados o registros multicéntricos que necesiten reportar todos los investigadores incluidos en el estudio.

Como unidad de medida se utilizará el sistema métrico decimal, usando comas para los decimales. Todas las mediciones clínicas, hematológicas y químicas deben expresarse en unidades del sistema métrico y/o UI. Solo se utilizarán las abreviaturas comunes, evitándose su uso en el título y en el resumen. La primera vez que se empleen irán precedidas por el término completo excepto que se trate de unidades de medida estándar.

Las tablas deben presentarse en hojas individuales, numerándose de forma consecutiva utilizando números arábigos (0, 1, 2, etc.) según el orden en que fueron citadas en el texto, con un

título breve para cada una de ellas. Todas las abreviaturas de la tabla no estandarizadas deben explicarse. Las notas aclaratorias deben ir al pie de la misma utilizando los siguientes símbolos en esta secuencia: *, †, ‡, §, ¶, **, ††, ‡‡, etc.

Las figuras deben tener formato TIFF, PSD o JPEG e ir, cada una, en un archivo aparte a 300 dpi en formato final. Cada una de ellas tiene que estar numerada de forma correlativa junto a la leyenda explicativa en archivo aparte. El tamaño usual de las fotografías debe ser de 127 x 173 mm. Los títulos y las explicaciones detalladas se colocan en el texto de las leyendas y no en la ilustración misma.

Las referencia s bibliográficas se enumerarán de manera consecutiva con números arábigos entre paréntesis. Se incluirán todos los autores cuando sean seis o menos; si fueran más, el tercero será seguido de la expresión «, et al.». Los títulos de las revistas serán abreviados según el estilo empleado en el Index Medicus. Ejemplos:

1. *Registro de Procedimientos Diagnósticos y Terapéuticos efectuados durante el período 2006-2007. Colegio Argentino de Cardioangiólogos Intervencionistas (CACI). Disponible en http://www.caci.org.ar/addons/3/158.pdf. consultado el 01/01/2009.(Página Web.)*
2. *Magid DJ, Wang Y, McNamara RL, et al. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. JAMA 2005;294:803-812. (Revistas en inglés.)*
3. *Aros F, Cuñat J, Marrugat J, et al. Tratamiento del infarto agudo de miocardio en España en el año 2000. El estudio PRIAMHO II. Rev Esp Cardiol 2003;62:1165-1173. (Revistas en español).*