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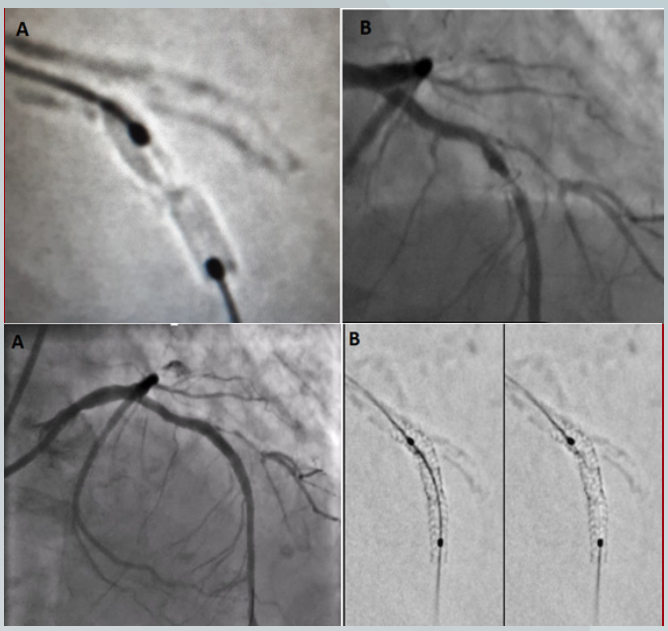

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[1] Laird JR. IN.PACT SFA 5-year Results. Presented at VIVA 2018; Las Vegas, NV, USA.

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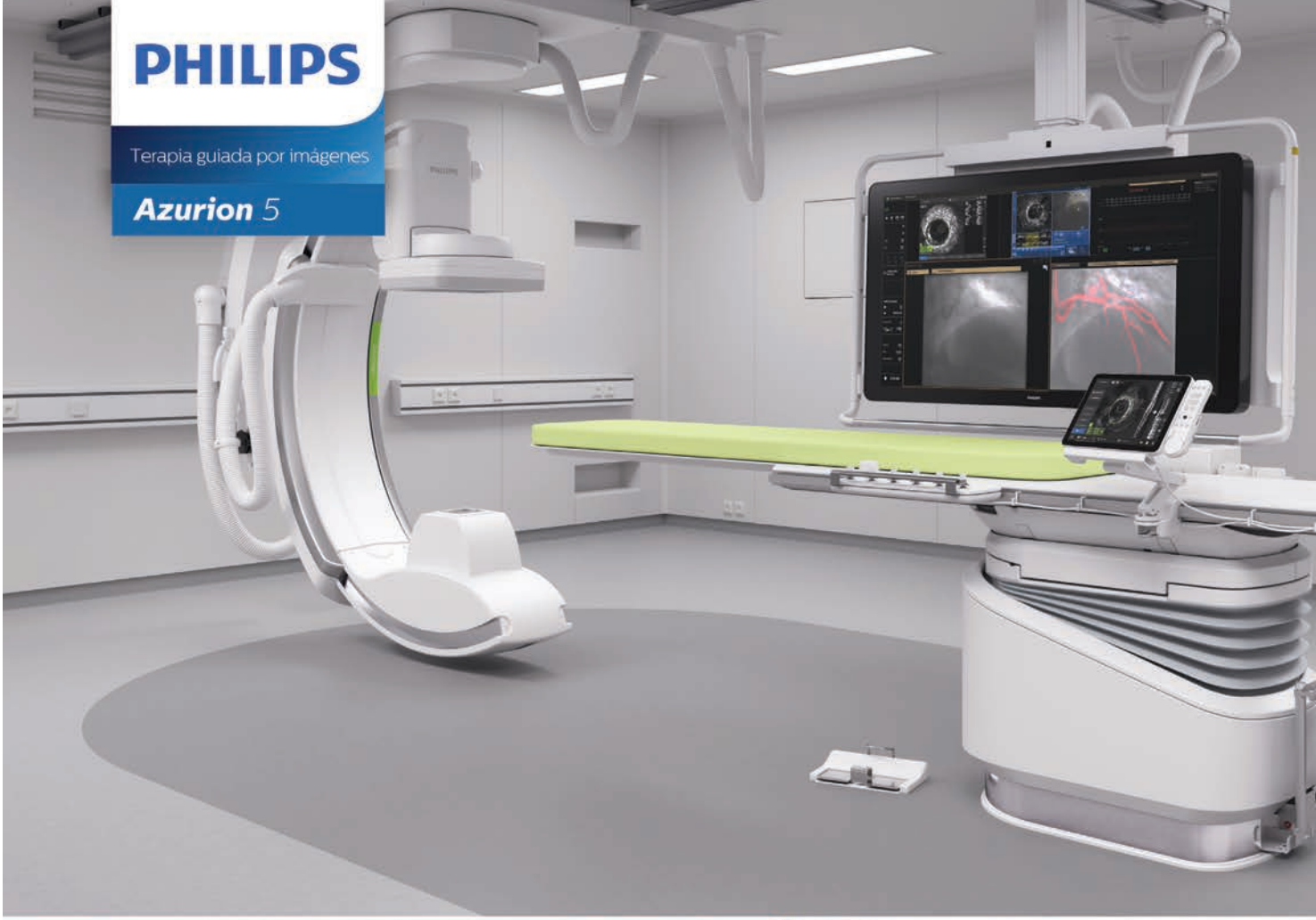

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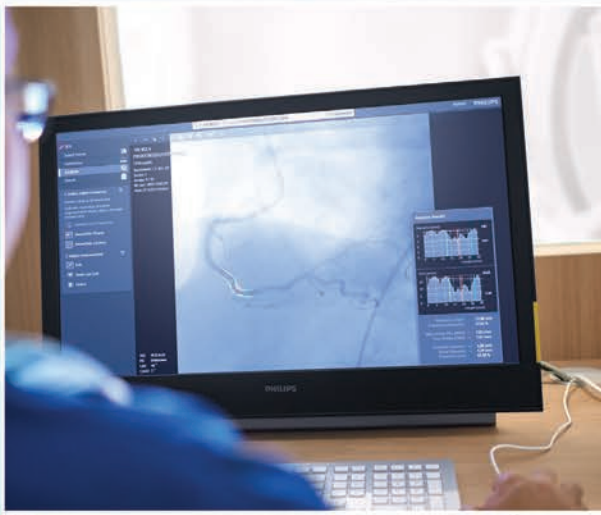

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EDITORIAL / EDITORIAL

SOLACI/CACI CONGRESS: A LONG JOURNEY IS FINALLY AND SAFELY COMING THROUGH

Alfredo E. Rodríguez

Once again, this year our country will be holding the most important interventional cardiology congress in Latin America. This congress has been hosted by the Argentine College of Interventional Cardioangiologists (CACI) since the first one held back in 1997.
The congress was scheduled to be held a year ago, but it had to be postponed because of the situation caused by COVID-19 both worldwide and in our region waiting for a better epidemiological situation that, unfortunately, has not come to our country yet.
For this reason, the congress will be held online. However, this does not mean that the scientific quality of the sessions and/or of the topics of discussion will be lower. The congress, that will be held from August 2nd through August 6th will be holding sessions on topics that have to do with interventional cardiology, angiology, pediatric cardiology, structural heart procedures, innovations, and clinical cardiology.
Added to the relevant joined sessions we will have with our partner international societies that have traditionally participated in our congress, this time we'll be holding other sessions with very important scientific societies from the United States and China that will be present in this congress for the very first time.

ARTÍCULO DE REVISIÓN / REVIEW ARTICLE

REPETITIVE AND OUTPATIENT INFUSIONS OF LEVOSIMENDAN TO TREAT ADVANCED HEART FAILURE. CLINICAL CASE REVIEW

Florencia Noutary, Sandra Swieszkowski

Advanced heart failure is defined as a clinical condition characterized by persistent symptoms (NYHA FC III-IV) despite the optimal medical therapy including cardiac resynchronization therapy, when indicated, in patients with severe ventricular dysfunction. The prognosis of these patients is poor, and the mortality rate and the rate of rehospitalizations are both high.
Recently, a new drug has been proposed for this stage of the disease: levosimendan. The intermittent infusions of levosimendan brought different clinical benefits to these patients including improved cardiac biomarkers, symptoms, quality of life, lower hospitalization rates, and lower heart failure-induced mortality rates.

ORIGINAL ARTICLE / ARTÍCULO ORIGINAL

NEUTROPHIL-TO-LYMPHOCYTE RATIO TO PREDICT ADVERSE EVENTS AFTER PERCUTANEOUS CORONARY INTERVENTION

Suilbert Rodríguez Blanco, Marleny Cruz Cardentey, Abel Y Leyva Quert, José M. Aguilar Medina, Alain Gutiérrez López, Mirta Pérez Yánes

Introduction. The neutrophil-to-lymphocyte ratio is an inflammatory marker associated with cardiovascular risk. Objective: To determine the value of the neutrophil-to-lymphocyte ratio (NLR) to predict major adverse cardiovascular events (MACE) in patients treated with percutaneous coronary intervention. Methodological design: prospective study including 101 patients. A binary logistic regression model was applied (P values = .05 were considered statistically significant and a 95% confidence interval). Results: a total of 29.7% developed adverse events,and the need for new target lesion revascularization (16.8%) was the most common finding. MACE kept a statistically significant association with: reduced left ventricular ejection fraction (P = .021), multivessel coronary artery disease (P = .030), SYNTAX score (P< .001), multivessel procedure (P = .024), thrombus in the lesion (P = .004), true bifurcation lesion (P = .001), complex bifurcation technique (P = .044), number of implanted stents (P = .016), non-type A lesion treated (P = .011), absolute number neutrophils (P = < .001), and NLR 6 hours after the procedure (P = < .001). In the multivariate analysis, this ratio (P = .010, OR, 2.254; 95%CI, 1.217-4.178) was an independent predictor of major adverse cardiovascular events. Conclusions: In percutaneous coronary interventions, the neutrophil-to-lymphocyte ratio is an independent predictor of major adverse cardiovascular events.

CLINICAL CASES AND LITERATURE REVIEW /
CASOS CLÍNICOS Y REVISIÓN DE LA BIBLIOGRAFÍA

ANGIOPLASTY IN HEAVILY CALCIFIED CORONARY LESIONS. EARLY EXPERIENCE WITH CORONARY INTRAVASCULAR LITHOTRIPSY

Sebastián Peralta, Carlos Fernández Pereira, Carla Agatiello, Juan P. De Brahi, Juan Mieres, Horacio Medina de Chazal, Martín Bodoira, Marcelo Bettinotti

The presence of heavily calcified coronary lesions has been our main public enemy for some time now because it affects the results of the angioplasty by initially preventing balloon crossing, complicating the proper passage of the drug from the surface of the stent to the vascular wall, and reducing stent expansion and

apposition. These effects keep a direct correlation with the short and long-term progression of these patients. Different devices have been created like noncompliant balloons, cutting balloons, rotational and orbital atherectomy, and intracoronary laser with different crossover profiles and results. A new alternative is coronary lithotripsy, capable of achieving the circumferential fracture of calcified plaques without changing the flow after the procedure. The early outcomes of cases performed with the Shockwave 2 C IVL system are presented here.

CLINICAL CASES / CASOS CLÍNICOS

TRAUMATIC ARTERIOVENOUS FISTULA. ENDOVASCULAR RESOLUTION

Esteban M. Quarchioni, María C. Licheri, Luis Gerardo, Alberto Licheri

Vascular trauma is present in approximately 10% of all lesions affecting the extremities. The inadequate management of these lesions causes serious consequences such as death or loss of limb functionality. Vascular lesions due to firearms are one of the leading causes of the appearance of arteriovenous fistulas. This is the case of a 76-year-old male patient with a past medical history of gunshot wound to his right calf. The patientpresented to his GP 6 months after sustaining the trauma due to claudication at 100 m, pain, and coldness at rest. Additional methods were used to finally achievea diagnosis of arteriovenous fistula that was resolved via endovascular approach. The medical literature was reviewed to update the information on this regard.

CARDIAC HAMARTOMA: ROLE OF ENDOMYOCARDIAL BIOPSY IN THE DIAGNOSIS OF CARDIAC NEOPLASM

José María Milanesi, Agustín Ignacio Hauqui, Juan Andrés Scaglia, Raúl Solernó, Ricardo Aquiles Sarmiento

Cardiac neoplasms are a rare entity. Due to the low specificity of imaging modalities in thisclinical setting, the surgical resection of tumors with subsequent microscopic evaluation is the technique of choice in most of the cases to achieve a definitive diagnosis. However, in selected cases, diagnosis can be achievedthrough an endomyocardial biopsy. We present a case of a cardiac neoplasm on which an endomyocardial biopsy was performed that resulted in a diagnosis of hamartoma of mature cardiac myocytes.

CORONARY STENTING IN THE RIGHT VENTRICULAR OUTFLOW TRACT

Jorge Gómez, Andrea Hozbor, Andrés Lucas, Manuel Porto, Carlos Vázquez, Ramiro Pelliciari

Three-month-old patient diagnosed with Down syndrome, tetralogy of Fallot with hypoplastic pulmonary branches, hypoxia, and a past medical history of prematurity, sepsis, infective endocarditis, protein-losing enteropathy, and respiratory distress syndrome. Stent implantation in the rightventricular outflow tract was decided as an alternative to surgical treatment. After the interventional procedure the properoxygen saturation was achieved. Technical details of the case and indications of this intervention are discussed in this clinical case.

ENDOVASCULAR THERAPEUTIC OPTIONS FOR VASCULAR LIVER LESIONS. CASE REPORT

Daniela Battisti, Julián Dalurzo, Rubén Retamar, Oscar Birollo

Benign vascular lesions of the liver are being observed more frequency; in many cases the resolution is complex given the vital importance of the organ and the possibility of failure of the different therapeutic approaches classically described. We present a case where endovascular treatment offers different possibilities for the management of trauma-induced vascular liverlesions.

CARTA DEL PRESIDENTE / LETTER FROM THE PRESIDENT

THE IMPORTANCE OF CARDIOVASCULAR INNOVATION AND DEVELOPMENT

Diego Grinfeld

The arrival of new medical technologies in prevention, diagnosis, and recovery of the patient is directly associated with the result indicators of the health status and with the increased hope, quality of life, and safety of the healthcare processes.

Medical innovation touches everybody on this planet. This innovation promises new ways to prevent, diagnose, and monitor health issues while the new drugs and devices available are intended to treat and eventually cure diseases. Medical innovation also enriches knowledge while transforming the entire healthcare process..

SOLACI/CACI Congress: a long journey is finally and safely coming through

Congreso SOLACI/CACI 2021: una larga jornada está llegando a buen puerto

Revista Argentina de Cardioangiología Intervencionista 2021;12(2):73. https://doi.org/10.30567/RACI/202102/0073-0073

Once again, this year our country will be holding the most important interventional cardiology congress in Latin America. This congress has been hosted by the Argentine College of Interventional Cardioangiologists (CACI) since the first one held back in 1997.

The congress was scheduled to be held a year ago, but it had to be postponed because of the situation caused by COVID-19 both worldwide and in our region waiting for a better epidemiological situation that, unfortunately, has not come to our country yet.

For this reason, the congress will be held online. However, this does not mean that the scientific quality of the sessions and/or of the topics of discussion will be lower. The congress, that will be held from August 2nd through August 6th will be holding sessions on topics that have to do with interventional cardiology, angiology, pediatric cardiology, structural heart procedures, innovations, and clinical cardiology.

Added to the relevant joined sessions we will have with our partner international societies that have traditionally participated in our congress, this time we'll be holding other sessions with very important scientific societies from the United States and China that will be present in this congress for the very first time.

Therefore, added to the traditional joined sessions we have always had with TCT and PCR in the ***main arena*** we'll be holding joined sessions with CRT (Cardiovascular Revascularization Therapies/Ron Waksman), SCAI (Society for Cardiovascular Interventions), CCI (Catheterization & Cardiovascular Interventions Journal), IAGS (International Andreas Gruentizig Society), and CBS (Left Main & Bifurcation Summitt). All of them will be present for the very first time in our SOLACI/CACI Congress held from Argentina.

The sessions will include conferences, live cases, case reports, and long discussions with speakers, panelists, and audience members through a website that will allow the fluid interaction of all participants.

This time we are glad to announce that we'll be presenting a record number of original studies in different modalities: original articles, case reports, pediatric cases, advancements, and reports from technicians, and nurses.

We have had a significantly higher number of submissions compared to other congresses held in our country. A total of 345 papers were submitted of which 298 were accepted in the oral presentation and poster modalities.

The top 5 papers will be selected by 3 truly blind independent evaluators who will be holding a CCI special meeting for paper assessment and possible publication in this journal. All abstracts will be published on our next *RACI* journal (issue #3, 2021).

In conclusion, despite of the huge difficulties sustained we are finally and safely coming through thanks to the support and contribution from all those involved including secretaries, technicians, and the invaluable support from our industry despite the limitations brought to our setting by this pandemic.

We'll be glad to welcome you next August 2nd in the SOLACI/CACI 2021 Congress official website

Alfredo E. Rodríguez MD, PhD, FACC, FSCAI, IAGS
Editor-in-chief of Revista Argentina de Cardioangiología Intervencionista (RACI)
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Repetitive and outpatient infusions of levosimendan to treat advanced heart failure.Clinical case review and presentation

Ciclos ambulatorios y repetitivos de levosimendán en insuficiencia cardíaca avanzada. Revisión y presentación de casos clínicos

Florencia Noutary[1], Sandra Swieszkowski[2]

ABSTRACT

Advanced heart failure is defined as a clinical condition characterized by persistent symptoms (NYHA FC III-IV) despite the optimal medical therapy including cardiac resynchronization therapy, when indicated, in patients with severe ventricular dysfunction. The prognosis of these patients is poor, and the mortality rate and the rate of rehospitalizations are both high.
Recently, a new drug has been proposed for this stage of the disease: levosimendan. The intermittent infusions of levosimendan brought different clinical benefits to these patients including improved cardiac biomarkers, symptoms, quality of life, lower hospitalization rates, and lower heart failure-induced mortality rates.

Keywords: *heart failure, advanced heart failure, levosimendan.*

RESUMEN

Se define como insuficiencia cardíaca avanzada al cuadro clínico caracterizado por la persistencia de síntomas en CF III-IV (NYHA) a pesar del tratamiento médico óptimo, incluida la terapia de resincronización cardíaca, cuando está indicada, en un paciente con deterioro grave de la función ventricular. Son pacientes con elevada mortalidad y alta tasa de reinternaciones1.
En el último tiempo se ha propuesto una nueva droga para este estadio de la enfermedad: el levosimendán. Las infusiones intermitentes de levosimendán demostraron varios beneficios clínicos en estos pacientes, como la mejora de los biomarcadores cardíacos, los síntomas, la calidad de vida, las tasas de rehospitalización y la reducción de la mortalidad relacionada con la insuficiencia cardíaca.

Palabras clave: *insuficiencia cardíaca avanzada, levosimendán.*

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INTRODUCTION

Advanced heart failure is an interesting topic of discussion today because its incidence rate just does not stop growing, in part, due to the aging of the population, the higher survival regarding the patients' comorbidities, and the advances made over the last few years in new therapies. Also, it has become a common reason for consultation in the coronary units of our country and abroad[1]. As a matter of fact, it has become a huge problem for the public healthcare systems because of the high budget required. But, also a problem for the patients because of the numerous and prolonged hospital stays required to treat the symptoms, and because it deteriorates the quality of life of terminally ill patients significantly[2,3].
Over the last few years, a new and promising drug to treat advanced heart failure has come up: levosimendan. This drug has had promising results for the management of acute decompensations. Currently, the intermittent and outpatient administration of this inotropic drug has been proposed to treat patients with advanced heart failure because it reduces the number of rehospitalizations and improves the quality of life of patients with these characteristics. Also, it is a safe and cost-effective drug for the healthcare system[4].The objective of this review article is to answer the following questions based on the data already published to this date:
Is levosimendan a safe drug for an intermittent use in these patients? Is it effective and efficient? Is it economically feasible? How often should the cycles be administered? What adverse events does it cause? What is its mechanism of action? What clinical trials have tested its utility in this type of patients?

MATERIAL AND METHODS

Randomized clinical trials, medical bibliographic databases, original articles, and consensus documents published in international journals were consulted. The searches were conducted in PubMed (the United States National Library of Medicine database). Also, a non-indexed citation was included [like the consensus documents published by the Argentine Society of Cardiology (SAC)] as the experience gained in our field was deemed necessary.
The following terms, whether isolated or in combination, were used to limit the searches: "advanced heart failure", "intermittent use of levosimendan", "treatment of chronic heart failure", "levosimendan", and "outpatient inotrope infusions".
After choosing the bibliographic material that would be used, it was classified by date and relevance. All those articles published in journals with the highest impact factor, and reports published in both Spanish and English were included. Low-impact journals with insu-

1. Servicio de Cardiología Clínica. Sanatorio Otamendi. CABA.
2. Subjefe de unidad coronaria Hospital de Clínicas José de San Martín UBA. CABA

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The authors declared no conflicts of interest whatsoever.

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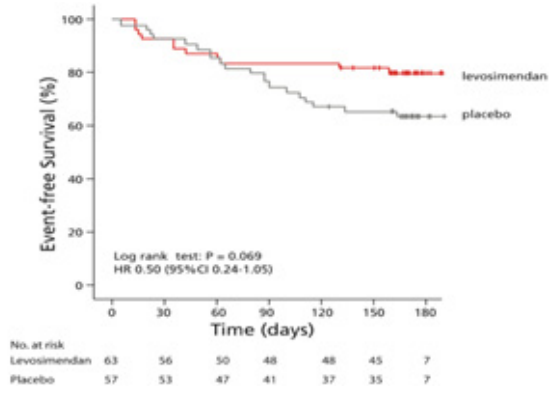

Figure 1. *Event-free survival rate at the 24-week follow-up. It shows the Kaplan-Meier curves for a secondary composite endpoint of absence of death, heart transplant or acute heart failure within the first 180 days after randomization (according to the intention-to-treat analysis) HR: hazard ratio. 95%CI: 95% confidence interval.*

fficient numbers of patients recruited (case report) were excluded. Articles published in languages different that the ones already mentioned were excluded too.

LEVOSIMENDAN

Mechanism of action

Levosimendan is an active enantiomeric drug of simendan, a pyridazinone-dinitrile derivative. For it to actually work, the action of levosimendan and its active metabolite OR-1896 are both required. Its main 3 mechanisms of action are: positive inotropism (this agent sensitizes troponin C to calcium in a manner dependent on the calcium concentration in the contraction-relaxation mechanism); vasodilation, and cardioprotective effect against ischemia and myocardial damage induced by ischemia-reperfusion thanks to its contribution opening the mitochondrial membrane-dependent ATP-sensitive potassium channels.

Its half-life is one of its most significant features: 1 h to 1.5 h for levosimendan, and approximately 80 h for its active metabolite. This means that its effects can still be seen almost 1 week after withdrawing the IV infusion, making it an attractive drug for patients with advanced heart failure. Regarding the drug washout in cases of patients with severe kidney or liver failure, only the prolonged washout of the OR-1896 metabolite has been described, and no pharmacological or hemodynamic changes have been reported to this date[5].

Posology

The patients who are eligible to receive intermittent infusions of levosimendan are those with a diagnosis of advanced heart failure with NYHA functional class (FC) III-IV, and an ejection fraction (EF) < 35%. Also, patients with recurring hospitalizations due to heart failure within the last year. Also, all of the above should have happened despite the optimal medical therapy too. Ineligible patients are those with a past medical history of drug intolerance, a diagnosis of severe LVOT obstruction, severe uncorrected valvular heart disease with significant hemodynamic compromise or SAP < 90 mmHg.

Although the early bolus of a loading dose has proven useful in cases of acute decompensated heart failure, it was found that in patients with advanced heart failure this strategy predisposes to a higher rate of adverse events since, in general, these patients are less tolerant to this drug due to their baseline hemodynamic status. Therefore, it is thought that the bolus of levosimendan should only be administered if immediate effects are sought and systolic arterial pressure exceeds 100 mmHg.

Therefore, the early dose will depend on the characteristics and needs of each particular patient. An early low dose of 0.1 μg/kg/min is advised that could be gradually up titrated to 0.2 μg/kg/min if tolerated. If it not tolerated, it can be reduced to 0.05 μg/kg/min and see what happens next. If not tolerated either, then the infusion should be withdrawn. Each infusion consists of a continuous 24-h IV infusion that should be repeated every 2 to 4 weeks[6-8].

Intrainfusion monitoring

Prior to the infusion it is recommended to keep arterial hypertension, heart rate, body weight, and the serum levels of sodium and potassium, and creatinine under control.

The patient's volume status should be carefully assessed since in cases of hypovolemia, fluid replenish fluids may be required during the infusion of levosimendan. In the presence of hypotension (SAP < 90 mmHg), it may be necessary to reduce the dose of levosimendan and/or add a vasopressor temporarily (such as noradrenaline).

In some patients increased diuresis can be seen as a result of treatment with levosimendan. Therefore, eliminating or reducing the routine diuretic on the day of the treatment and administering additional fluids should be considered, when appropriate. The assessment of renal function is relevant in patients with known kidney failure as well as in those on diuretic therapy. Although secondary kidney dysfunction is not a contraindication to treatment with levosimendan, we need to be very cautious about it. Given the specific nature of the progression of chronic advanced HF no general recommendations have been made on the threshold of glomerular filtration rate (GFR) regarding the repeated use of levosimendan; however, GFRs = 30 mL/min could be regarded as a safety threshold. If furosemide is coadministered simultaneously, the doses of the diuretic should be adjusted on the same day of levosimendan infusion[9].

Adverse events

Although levosimendan is a drug well-tolerated by most patients with heart failure, adverse events like arterial hypotension, headache, and dizziness due to its vasodilator effect can occur. Also, a higher rate of atrial fibrillation and ventricular tachycardia has been reported in most studies. Although fewer arrhythmias have been reported in clinical trials that compared levosimendan and dobutamine to placebo, ventricular tachycardia (25% vs 17%) and atrial fibrillation (8% vs 2%) were more common in the levosimendan group compared to the standard therapy group in the REVIVE II and other clinical trials; in the SURVIVE trial, atrial fibrillation (9.1% vs 6.1%), and ventricular tachycardia (7.9% vs 7.3%) were more common in the levosimendan group compared to the dobutamine group.

Regarding the lab parameters, some studies have described a slight decrease of red blood cell counts, hematocrit, and hemoglobin levels (10%), and, especially in patients who were getting high doses, a slight decrease of the serum levels of potassium has been reported. Serum creatinine levels were reduced even in patients with baseline renal dysfunction[10].

In general, the studies have proven that levosimendan does not deteriorate or trigger myocardial ischemia. However, the excessive reductions of arterial blood pressure can reduce the coronary perfusion pressure and even cause ischemia in some cases[11,12].

Cost-effectiveness

Heart failure is the leading cause of hospitalization in patients > 65 in developed countries. It is a progressive fatal disorder despite the optimal medical therapy.

Over the last few decades, the prevalence and hospitalizations due to heart failure have increased significantly in developed countries. This is mainly due to the growing number of old people across the world, the arrival of new therapies, and much better control of mortality and morbidity. That is how the survival rate of patients with acute myocardial infarction has increased. In addition, this higher survival rate has also increased the possibilities of developing heart failure[13].

Also, there is evidence that the best therapies against heart failure (angiotensin-converting enzyme inhibitors [ACEI], beta-blockers, neprilysin inhibitors [sacubitril-valsartan], and the newly arrived gliflozins) are having an impact on the population by improving the survival rate of patients with heart failure. Therefore, the population increasing survival rate is associated with a higher prevalence of heart failure[14].

Heart failure, especially in advanced stages, is associated with numerous hospitalizations posing a tremendous problem for public healthcare regarding costs (whether direct or indirect).

Direct costs include hospital services, healthcare workers, medications, devices, as well as outpatient and home care, and the follow-up patients may need.

Indirect costs include the loss of productivity as a result of the patient's morbidity and mortality, sick pays, and social care. There are data available on the economic impact of heart failure in 197 countries. Back in 2012 the overall annual cost attributed to heart failure were $108 billion. Of these, 60% corresponded to direct costs, and the remaining 40% to indirect costs.

For all this, the outpatient cycles of levosimendan in this type of patients are very interesting because they would reduce the number of hospitalizations saving costs for the entire healthcare system[15].

Based on the results seen in the LION HEART trial, the patients randomized to the levosimendan group experienced a significant drop in the rate of hospitalization due to heart failure (hazard ratio [HR], 0.25; 95% confidence interval [95%CI], 0.11-0.56; P = .001) compared to those who received placebo. Also, this improved rate of heart failure-induced hospitalizations translated into significant reductions of cardiovascular hospitalizations, all-cause hospitalizations, and fewer combined assessment criteria between hospitalization (all-cause, cardiovascular etiology or heart failure) and death or other end-stage events.

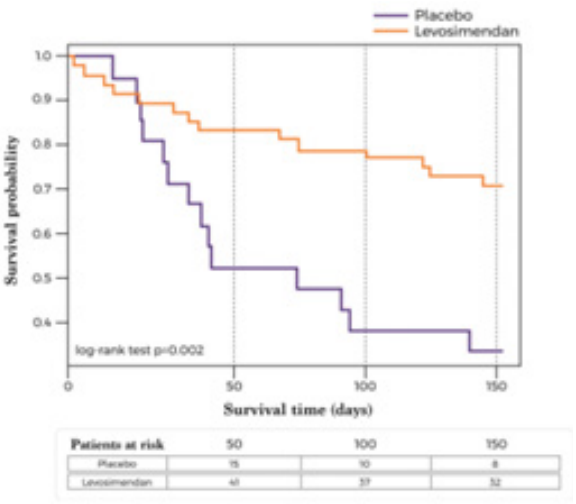

Figure 2. *Kaplan-Meier survival curves (time until the first event) for the composite endpoint of all-cause mortality or hospitalizations due to heart failure.*

Back in 2020, *Revista Española de Cardiología* published an article entitled "Economic analysis of intermittent intravenous outpatient treatment with levosimendan in advanced heart failure in Spain" (English translation from the Spanish original title "Análisis económico del tratamiento ambulatorio intermitente con levosimendán de la insuficiencia cardíaca avanzada en España". This article confirmed that nearly €700 per patient/month could be saved using outpatient cycles of levosimendan with the plan proposed in the LION HEART trial (6 cycles total) in patients with advanced heart failure. In conclusion, the chances that money would be saved with levosimendan compared to the option of not treating at all would be somewhere around 94.8%.[16]

Thus, the outpatient and repetitive cycles of levosimendan in patients with advanced heart failure not only improve the patients' quality of life but also reduce the number of rehospitalizations and the corresponding healthcare costs. Therefore, this plan is both effective as well as it is efficient[17].

OUTPATIENT CYCLES OF LEVOSIMENDAN TO TREAT ADVANCED HEART FAILURE: CURRENT EVIDENCE

Up until now, 3 studies have been published showing the benefits of this drug in patients with stage D heart failure. One of these studies is the LAICA trial. This Spanish, randomized, multicenter, double-blind, prospective, placebo controlled Spanish trial published in 2013 included patients with advanced heart failure of any etiology with, at least, 1 episode of decompensation requiring hospitalization over the last 6 months but still stable when entering the study. The study duration was 24 months total, 12 months of treatment, and 12 months of follow-up. All patients received the same standard therapy to treat their heart failure. The patients eligible to be treated with levosimendan received a dose of 0.1 µg/kg/min without loading dose for 24 hours once every 30 days.

The study primary endpoint was to determine the composite event rate of all-cause mortality and hospitaliza-

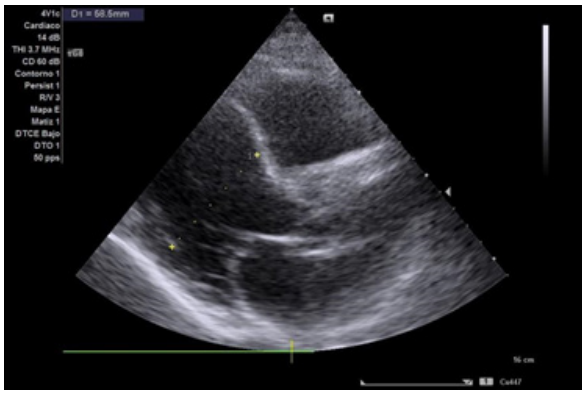

Figure 3. *Doppler echocardiography. Presence of left ventricular dilatation. Severe estimated EF <20%.*

tions or worsening of the heart failure symptoms. The study secondary endpoints were time from the administration of treatment until the next hospitalization, mortality at 1, 6, and 12 months, FC changes according to the NYHA, changes in the proBNP levels before and after treatment, and quality of life measured using the KCCQ at 1, 6, and 12 months.

Although the study had to be interrupted because it did not reach the 261 patient-mark required, which was the sample size needed to verify the hypothesis, 97 patients were eventually analyzed. The results obtained were encouraging. Regarding the rate of rehospitalizations due to acute decompensation in patients treated with levosimendan, it was found that the percentage of patients who were being rehospitalized was lower. However, we should mention that there was a statistically significant difference between the 2 groups within the 3 first months of treatment. Sometime later, although the difference in the rate of hospitalization due to acute decompensation still remained, this rate stopped being statistically significant. The same thing was seen in the analysis of the patients' mortality[18].

Another important study is the LevoRep trial. It was a randomized, multicenter, double-blind, prospective, placebo controlled trial published in 2014 that included a total of 120 patients randomized into 2 groups: 63 into the levosimendan group, and 57 into the placebo group. All patients had been diagnosed with advanced heart failure, at least, 3 months before entering the study (NYHA FC III-IV), had an EF ≤ 35%, and 6-minute walk test results < 350 m while on standard neurohormonal treatment. The exclusion criteria were SAP ≤ 100 mmHg, serum potassium levels < 3.5 mmol/L or > 5.5 mmol/L, and creatinine clearance levels < 30 mL/kg/m^2.

It was a 2-stage study. The first stage was the administration of a 6-month course of treatment where patients received a total of 4 cycles of levosimendan with doses of 0.2 μg/kg/min (without loading doses) for 6 hours every 2 weeks followed by an 18-month medical follow-up.

The study primary composite endpoint was a > 20% improvement in the 6-minute walking test and an increase of, at least, 15% in the KCCQ score at 24 weeks. The study secondary endpoint was the "event-free" state in the short and long-term (8 and 24 weeks, respectively). The percentage of patients who meet the study primary composite endpoint at the 24-week follow-up was not statistically significant between the levosimendan group (19%) and the placebo group (15.8%) (odds ratio [OR], 1.25; 95%CI, 0.44-3.59; P = .810). Similarly, no differences were seen between the groups after 8 weeks (OR, 1.17; 95%CI, 0.48-3.02; P = .823).

Regarding the study secondary endpoint, after 24 weeks, 11 patients from the levosimendan group (17.4%) and 20 patients from the placebo group (35.1%) were analyzed. One patient from the former group died (1.6%), another patient received a heart transplant (1.6%), and 9 experienced heart failure decompensations (14.2%) compared to the placebo group with 4 (7%), 2 (3.5%), 14 (24.5%) patients, respectively.

Therefore, although this study did not show significant differences in its primary endpoint, it actually did so in its secondary endpoint showing fewer cardiovascular deaths, decompensations due to CHF, and need for a heart transplant after 24 weeks[19].

Finally, we have the LION-HEART, a multicenter, double-blind, randomized, and placebo controlled trial published back in 2018 that included 69 patients. A total of 48 of these patients were randomized into the levosimendan group and 21 into the placebo group. The main inclusion criteria were age > 18 years, EF < 35%, and a clinical diagnosis of advanced heart failure.

Patients from the levosimendan group received a 6-hour IV infusion (0.2 μg/kg/min without bolus) every 2 weeks for 12 weeks (6 cycles) with a mean total cumulative dose of 31.5 mg. The study primary endpoint was the effect on the serum concentrations of the N-terminal pro B-type natriuretic peptide (NT-proBNP) during the entire period of treatment compared to placebo. The study secondary endpoint included the assessment of safety, clinical events, and health-related quality of life (HRQoL). The area under the curve of the NT-proBNP levels throughout the course of treatment for patients who received levosimendan was significantly smaller compared to the placebo group (P = .003). Also, compared to the placebo group, patients treated with levosimendan experienced fewer heart failure-related hospitalizations (P = .001). Also, patients on levosimendan had fewer chances of seeing their quality of life deteriorated significantly across time (P = .02). The rate of levosimendan-related adverse events was similar in both groups of treatment.

Therefore, this small study (69 patients total) proved that the intermittent outpatient administration of levosimendan is safe and improves the levels of NT-proBNP significantly after 12 weeks of treatment. Also, the number of rehospitalizations due to heart failure dropped[20].

The RELEVANT-HF is a multicenter trial published in 2018 designed to obtain information on the efficacy and safety profile of repeated and scheduled 24-hour infusions of levosimendan infusions in patients with advanced heart failure. A total of 185 patients with NYHA functional class III-IV were included, with ≥ 2 hospitalizations due to heart failure over the last 6 months and left ventricular systolic dysfunction. These patients were treated with levosimendan in doses somewhere between 0.05 μg/kg/min and 0.2 μg/kg/min, without a previous bolus, every 3 to 4 weeks.

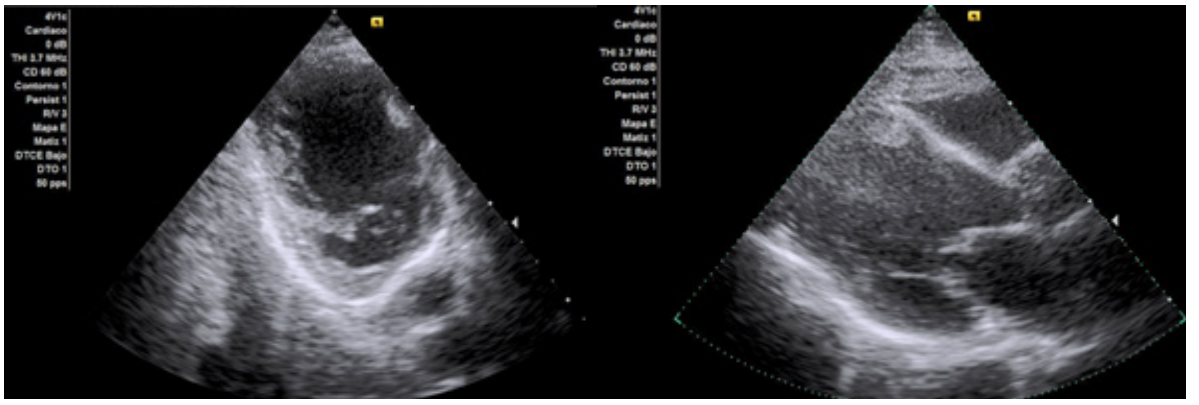

Figure 4. *Doppler echocardiography. Short axis and longitudinal axis. Presence of left ventricular dilatation with severe systolic dysfunction.*

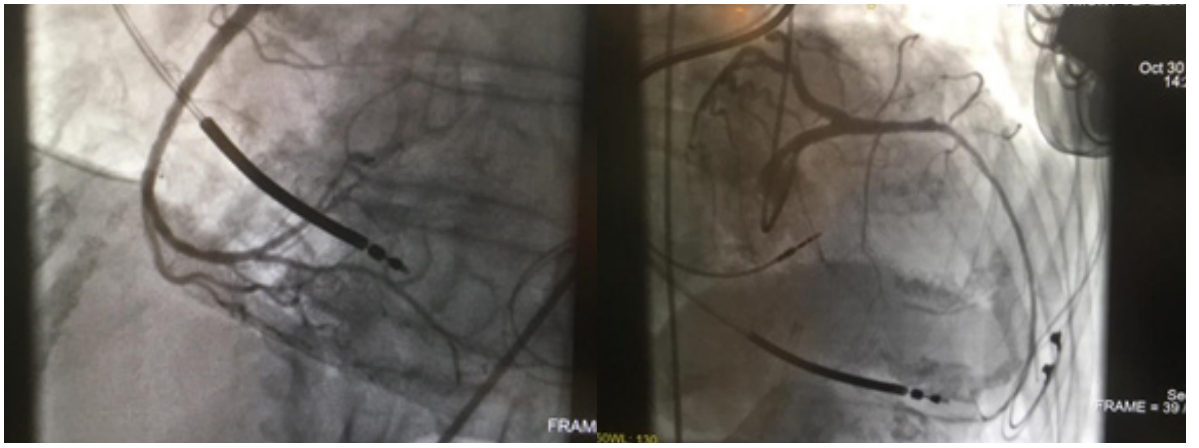

Figure 5. *Cine coronary arteriography. The image on the left shows the dominant right coronary artery with previous stent implantation at patent proximal level with collateral circulation towards the territory of the left circumflex artery. The image on the right shows a narrow-caliber left anterior descending coronary artery with stent implantation in its patent proximal third with a 30% restenosis, and a left circumflex artery occluded at 100%.*

The data on the hospitalizations due to heart failure at the 6-month follow-up before and after starting therapy were compared.

The results obtained were infusion-related adverse events occurred in 23 patients (12.4%) being the most common of all ventricular arrhythmias (16, [8.6%]). At the follow-up, 37 patients (20%) required treatment adjustments due to clinical instability (reductions in the infusion dose, infusion rate or infusion interval). The rate of hospitalization days dropped 6 months before and 6 months after treatment (9.4 [8.2%] vs 2.8 [6.6%]; $P < .0001$) as well as the duration of heart failure-related hospital stays (17.4 [15.6%] vs 21.6 [13.4%] days; $P = .0001$). Overall, the annual survival rate was 86% while 78% of the patients remained free from death, ventricular assist device or emergency heart transplant.

Nonetheless, this study is observational, meaning that the results need to be validated in randomized, double-blind, controlled clinical trials that are more accurate and reliable to assess the efficacy of drugs[21].

Currently, different studies are ongoing like the multicenter, international, double-blind, placebo controlled LeoDOR trial that will be studying the efficacy and safety profile of an intermittent therapy of levosimendan added to the optimal standard therapy in patients recently hospitalized due to heart failure decompensation. The inclusion criteria are: patients > 18 years with a diagnosis of heart failure, at least, 6 months prior to starting the study; patients on optimal medical therapy and devices implanted; LVEF ≤ 30% assessed on the echocardiography, ventriculography or contrast angiography during hospitalization; patients currently hospitalized or hospitalized within the previous 12 months due to decompensated heart failure and requiring diuretics, vasodilators or IV inotropic agents; patients with NT-proBNP levels after compensation ≥ 2500 ng/L and/or NYHA FC III-IV at the time of entering the study. The exclusion criteria are: heart surgery or coronary angioplasty within the 30 days prior to starting the study drug; acute coronary syndrome within the 30 days prior to starting the study; past medical history of torsades de pointes; systolic arterial pressure < 90 mmHg at the beginning of the study; heart rate ≥ 120 beats/min at the beginning of the study, serum potassium levels < 3.5 mmol/L; glomerular filtration rate ≤ 30 mL/min/1.73 m^2; administration of levosimendan within the 14 days prior to starting the study drug, and hypersensitivity to levosimendan, among others.

It is well-known that patients randomized to the levosimendan group can receive the drug through two different ways: as a 6-hour continuous infusion at an infusion rate of 0.2 μg/kg/min every 2 weeks (receiving the drug on days 0, 14, 28, 42, 56, 70, and 84) or as a 24-hour continuous infusion at an infusion rate of 0.1 μg/kg/min every 3 weeks (on days 0, 21, 42, and 84) with follow-ups 14 and 180 days after the first infusion.

The study primary endpoint is to compare the effects of intermittent pulses of levosimendan versus placebo in

patients with advanced chronic heart disease during a vulnerable period of 14 weeks after a recent hospitalization in a criterion of global assessment where all participants will be categorized into 3 hierarchical groups (in ascending order): time until death or emergency heart transplant or VAD implantation; time until the occurrence of a nonfatal heart failure event requiring vasoactive treatment; and time-averaged proportional change in the NT-proBNP since the beginning of treatment until the 14 week-mark.

The study secondary endpoints are the effects derived from intermittent pulses of levosimendan on each individual component of the primary assessment criterion after 14 and 26 weeks (the time-averaged proportional change in the NT-proBNP will be determined from baseline until week 14 only), the changes seen in the symptoms and functional status at the 14 week-mark, the cumulative number of episodes of acute heart failure, and the cumulative days of life out of the hospital setting after 14 and 26 weeks.

Additional study endpoints are to determine the effects that the intermittent administration of levosimendan has on the changes made to the baseline medication and the biomarkers as well as the cost-effectiveness ratio.

Estimating that a total of 264 patients will be included (6-hour infusion group: N = 88, levosimendan and N = 44, placebo; 24-hour infusion group: N = 88, levosimendan and N = 44, placebo) this study will have a simulated statistical power of ≈ 90% to detect differences between the groups of levosimendan and placebo. The Wilcoxon-Mann-Whitney test will be run at the two-sided 5% level of significance.

Although this study was intended to be completed in February 2020, it is still going, and its results are still pending publication[22].

CLINICAL CASE PRESENTATION

Clinical case #1

This is the case of a 67-year-old woman with a past medical history of dilated cardiomyopathy due to viral myocarditis during childhood, severe left ventricular systolic dysfunction (< 20%) with an ICD for primary prevention, and multiple hospitalizations due to decompensated heart failure. She was on complete medical therapy for that underlying condition and now presents with decompensated heart failure. The patient showed progressive dyspnea (FC II/III) at admission, and an increased weight of approximately 4 kg. On the physical examination, the patient showed clear signs of fluid overload. The lab results were positive: urea levels, 65 mg/dL; creatinine levels, 1.45 mg/dL; BNP levels, 2000 pg/mL, and lactate levels, 3.5 mmol/L.

Added to the symptomatic treatment started with IV loop diuretics for negative fluid balance due to signs of volume overload, the patient was administered a 24-hour cycle of levosimendan without loading dose while keeping an IV infusion of 0.2 µg/kg/min. She tolerated the cycle well and the dose was not reduced due to hypotension or other drug-related adverse events. Twenty-four hours after completing the infusion, the patient's symptoms improved significantly as well as the lab parameters of both the renal function, lactic acid, and the serum levels of BNP. The patient was discharged from the hospital 72 hours after the infusion of levosimendan.

Afterwards, it was decided to keep on administering outpatient cycles of levosimendan every 4 to 6 weeks as palliative treatment of advanced heart failure. The patient's heart failure improved after every cycle. Also, there was a significant reduction of hospitalizations due to decompensated heart failure, which eventually improved the patient's quality of life.

Clinical case #2

This is the case of a 74-year-old male patient with a past medical history of coronary artery disease (AMI at 40 years old: 3 bypass surgeries: LIMA to LAD, vein graft to CXI plus another vein graft to RCA). Severe deterioration of left ventricular systolic function (25%) of necrotic ischemic etiology treated with an ICD + resynchronization therapy in the year 2000 for primary prevention purposes. Also, chronic kidney disease (usual creatinine levels = 2.5 mg/dL to 3 mg/dL). The patient remains without the optimal medical therapy due to renal failure and intolerance. The patient presented to his GP with signs of asthenia, adynamia, a severely impaired renal function (creatinine levels = 4 mg/dL), and increased weight (5 kg) unresponsive to outpatient oral diuretics. It was decided to hospitalize the patient in the hospital coronary care unit. The physical examination showed signs of volume overload with RHY+, lower limb swelling 3/6, bilateral crakles, and no signs of low cardiac output. The only altered lab parameter was the acute exacerbation of chronic kidney disease, and BNP levels = 1890 pg/mL.

It was decided to administer IV diuretics and the continuous infusion of furosemide at 500 mg is started with good response; due to the patient's kidney disease and hemodynamic intolerance other drugs are contraindicated. The patient's dyspnea improved as well as his signs of congestion and returned to his normal creatinine levels with negative fluid balance.

Before being admitted to the hospital, it was decided to administer a 48-hour cycle of levosimendan without loading dose while keeping an infusion rate of 0.05 µg/kg/min (maximum dose tolerated). Finally, the patient was discharged with further outpatient follow-ups with his cardiologist who decided to continue with the same plan of outpatient and repeated infusions of levosimendan approximately every 8 weeks. The patient's quality of life improved although his heart failure was still in an advanced stage.

Clinical case #3

This is the case of a 79-year-old woman with a past medical history of coronary artery disease (AMI at 60; treated with primary angioplasty with 4-stent implantation (2 BMS in the LAD + 2 BMS in the RCA), ischemic-necrotic dilated cardiomyopathy, severe left ventricular systolic dysfunction (< 20%), ICD + resynchronization therapy for primary prevention, and chronic kidney disease (usual creatinine levels = 2.5 mg/dL to 3 mg/dL–on dialysis 3 times/week). The patient had been hospitalized multiple times due to heart failure. Her cardiologist had prescribed loop diuretics (80 mg/8 hours), spironolactone (12.5 mg/day), and sacubitril-valsartan (50 mg/12 hours).

The patient presented with progressive dyspnea from FC III to FC IV and an increased weight of 5 kg. The patient presented these values at admission: BP, 90/60 mmHg; HR, 60 bpm; O_2Sat, 94%, clear signs of volume overload, no clinical signs of low cardiac output, and the following lab parameters: creatinine levels of 2.7 mg/dL, BNP levels > 5000 pg/mL, and lactate levels of 3 mmol/L. Negative fluid balance is started through the continuous infusion of 500 mg of furosemide. Medication is withdrawn (sacubitril-valsartan, and aldosterone antagonists due to contraindications). The patient's hemodynamic status improved after adjusting the medication. Afterwards, a course of levosimendan was indicated at the maximum dose tolerated (0.05 μg/kg/min). The patient's symptoms improved, and she was discharged from the hospital with outpatient follow-up by her cardiologist; to this date, she is still on a 3-week dialysis plan.

Afterwards, the patient was hospitalized multiple times (at the 3-year follow-up) to alleviate her symptoms and received repetitive cycles of levosimendan in the last stage of the disease.

DISCUSSION

Levosimendan is a valid inotrope agent that can be administered intermittent and outpatiently through 24-hour infusions every 2 or 4 weeks in patients with advanced heart failure to improve symptoms and reduce the number of hospitalizations.

Although the current evidence mentioned in this review confirmed these benefits, several studies like the LION HEART (n = 69), the LAICA (n = 97), and LevoRep (n = 120) clinical trials included a rather small number of patients.

For example, the LION HEART trial was not statistically powered to assess the different clinical events, symptoms, and results reported by the patient. Given the size of the sample estimated, all assessments were planned as "exploratory". However, the findings for these secondary endpoints were consistent with the results of the criterion of global assessment and also statistically significant despite the limited size of the sample. Or else, the LAICA trial had to be suspended because the necessary 261 patients to conduct the study could not be recruited, which was the sample size estimated to verify the hypothesis. Therefore, the efficacy and safety profile of levosimendan in patients with advanced heart failure still needs further study in randomized, double-blind, clinical trials with larger recruitments of patients.

Regarding the drug cost-effectiveness ratio for this type of patients, different studies proved that this ratio is cost-effective and profitable because it reduces costs to the healthcare system by minimizing the number of hospitalizations significantly. Nonetheless, the studies focused on this issue have been conducted in developed countries where the prevalence of this condition is higher, and the economic resources destined to healthcare are different from our setting. Therefore, the cost-effectiveness ratio should be assessed in our country where two different parallel realities coexist: the public health and the private healthcare system.

CONCLUSION

The intermittent infusions of levosimendan brought several clinical benefits to patients with advanced heart failure. These infusions improved the patients' cardiac biomarkers, symptoms, quality of life, rates of re-hospitalization, and also reduced the mortality rate due to heart failure.

Levosimendan is different from any other inotrope agents (catecholaminergic drugs) thanks to its 3 mechanisms of action: positive inotropism, vasodilation, and cardioprotection. Also, its pharmacokinetics allows a prolonged action of metabolite OR-1986, thus providing additional therapeutic cardiovascular effects for days after interrupting the drug infusion, which is a huge advantage compared to other inotrope agents.

The data that back the use of levosimendan confirm that, overall, this drug is well tolerated and has few adverse events, mostly reversible, like hypotension, headache, and dizziness.

Patients diagnosed with advanced heart failure are unstable *per se*, and their decompensation starts long before being hospitalized; for this reason, the intermittent and outpatient administration of levosimendan for symptom improvement was proposed here. Also, because it improves the patients' quality of life and reduces the number of re-hospitalizations. However, further studies with more patients are still needed to assess the efficacy and effectiveness profile of levosimendan in our setting to confirm or deny the hypothesis presented in this article review.

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Neutrophil-to-lymphocyte ratio to predict adverse events after percutaneous coronary intervention

Índice neutrófilo-linfocitario en la predicción de eventos adversos del intervencionismo coronario percutáneo

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ABSTRACT

Introduction. The neutrophil-to-lymphocyte ratio is an inflammatory marker associated with cardiovascular risk. Objective: To determine the value of the neutrophil-to-lymphocyte ratio (NLR) to predict major adverse cardiovascular events (MACE) in patients treated with percutaneous coronary intervention. Methodological design. prospective study including 101 patients. A binary logistic regression model was applied (P values = .05 were considered statistically significant and a 95% confidence interval). Results. a total of 29.7% developed adverse events,and the need for new target lesion revascularization (16.8%) was the most common finding. MACE kept a statistically significant association with: reduced left ventricular ejection fraction (P = .021), multivessel coronary artery disease (P = .030), SYNTAX score (P< .001), multivessel procedure (P = .024), thrombus in the lesion (P = .004), true bifurcation lesion (P = .001), complex bifurcation technique (P = .044), number of implanted stents (P = .016), non-type A lesion treated (P = .011), absolute number neutrophils (P = < .001), and NLR 6 hours after the procedure (P = < .001). In the multivariate analysis, this ratio (P = .010, OR, 2.254; 95%CI, 1.217-4.178) was an independent predictor of major adverse cardiovascular events. Conclusions. In percutaneous coronary interventions, the neutrophil-to-lymphocyte ratio is an independent predictor of major adverse cardiovascular events.

Keywords: *neutrophil-lymphocyte ratio, major adverse cardiovascular events, percutaneous coronary intervention.*

RESUMEN

Introducción. El índice neutrófilo-linfocitario es un marcador inflamatorio, relacionado con el riesgo cardiovascular. Objetivo: Determinar el valor del índice neutrófilo-linfocitario (INL) en la predicción de eventos cardiovasculares adversos mayores (ECAM) en pacientes tratados con intervencionismo coronario percutáneo. Material y métodos. Estudio prospectivo en 101 pacientes. Se aplicó un modelo de regresión logística binaria (nivel de significación de 0,05 y confiabilidad del 95 %). Resultados. El 29,7 % desarrolló eventos adversos y la necesidad de nueva revascularización de la lesión diana (16,8 %) fue el más frecuente. Los ECAM mostraron asociación estadística con: disminución de la fracción de eyección del ventrículo izquierdo (p=0,021), enfermedad arterial multivaso (p=0,030), puntaje SYNTAX (p<0,001), intervención multiarterial (p=0,024), trombo en la lesión (p=0,004), lesión en bifurcación verdadera (p=0,001), técnica en bifurcación compleja (p=0,044), número de stent implantados (p=0,016), lesión tratada no tipo A (p=0,011) y número absoluto de neutrófilos (p≤0,001) e INL a las seis horas del proceder (p≤0,001). En el análisis multivariado este índice (p=0,010, OR 2,254; IC95%: 1,217-4,178) fue predictor independiente de eventos cardiovasculares adversos mayores. Conclusiones. En el intervencionismo coronario percutáneo el índice neutrófilo-linfocitario es un predictor independiente de eventos cardiovasculares adversos mayores.

Palabras clave: *índice neutrófilo-linfocitario, eventos cardiovasculares adversos mayores, intervencionismo coronario percutáneo.*

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INTRODUCTION

Major adverse cardiovascular events (MACE) associated with percutaneous coronary intervention (PCI) minimize procedural and clinical success alike. Percutaneous coronary intervention triggers myocardial inflammation whose size and magnitude depends on the duration of the ischemia produced and is divided into 3 phases: *1)* phase of alarm (release of protein molecules), *2)* phase of leukocyte migration (neutrophil recruitment into the blood flow and tissue infiltrating lymphocytes with a corresponding decrease in blood), and *3)* resolution phase.[1,2]

Elevated cardiac biomarkers are the clinical expression of the aforementioned cardiac inflammatory status. Consistent with this, the neutrophil-to-lymphocyte ratio (NLR) marker is easy to establish, easy-to-use, cost-effective, reproducible, and often available. The NLR is associated with a greater atherosclerotic load[3], more chances of stent thrombosis,[4] and type 4a myocardial infarction.[5]

The PCI reduces the symptoms of myocardial ischemia, the risk of infarction, and mortality rate when it is successful.[6] The risk stratification of complications at the follow-up is essential for secondary prevention purposes and imposes the search for markers associated with the results.[7]

The objective of this study was to determine the value of the NLR to predict MACE in patients treated with PCI.

METHODOLOGICAL DESIGN

This was a descriptive, correlational, and prospective study conducted between November 2018 and October 2019. Patients over 18 treated with PCI were included. The following patients were excluded: those with left ventricular ejection fraction (LVEF) < 30%, those treated with PCI on chronic total coronary occlusions, with myocardial revascularization surgery the previous 3 months, patients with severe pulmonary disease, neoplasm, on chemotherapy, with chronic blood disorders, on corticosteroid therapy over the last year, with chronic inflammatory disease, active infections, and patients who refused to participate in the study. The sample eventually included 101 patients.

The follow-up variable: MACE, as a composite endpoint, was defined based on the presence of some of the following

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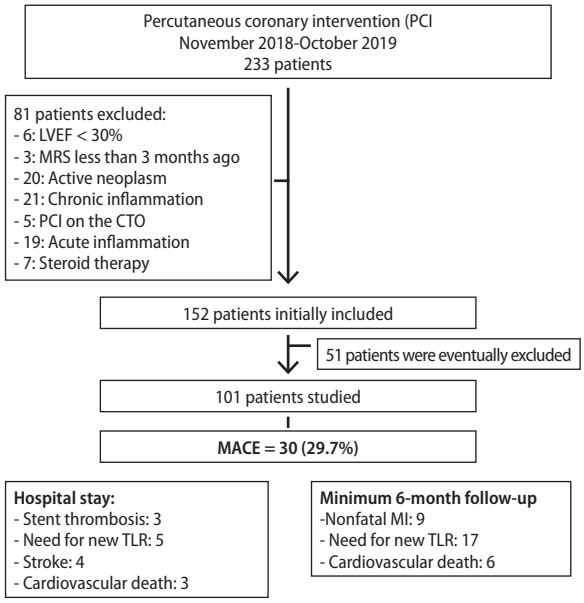

Figure 1. *Study flowchart. MI: myocardial infarction. MACE: mayor adverse cardiovascular events. TLR: target lesion revascularization.*

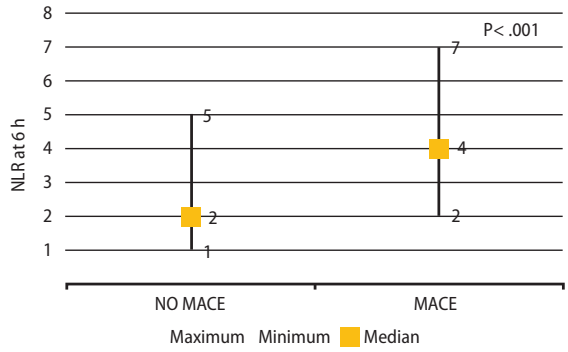

Figure 2. *Values of the NLR 6 hours after the PCI based on the presence of MACE.*

events during the hospital stay or at the follow-up: stent thrombosis, need for new target vessel revascularization, stroke, nonfatal myocardial infarction, need for new target lesion revascularization or cardiovascular death. All these events were studied separately. Cardiovascular death was defined as deaths associated with cardiovascular complications such as myocardial infarction, stent thrombosis, stroke, malignant ventricular arrhythmias, and heart failure.

Ethical considerations

This study was approved by the scientific research and technical review ethics committee. The patients' informed written consent was obtained prior to their participation in the study.

Techniques and procedures

leukogram conducted using the Pentra-DX NEXUS Hematology analyzer. Parameters analyzed: neutrophils and lymphocytes were expressed as absolute values (#). The differential WBC count was performed based on the packed cell volume, shape of the nucleus, granules, chromatic appearance of the nucleus, and intensity of the stain. It was conducted up to 1 week prior to the PCI and repeated 6 hours after the PCI.

Follow-up

A minimum follow-up of 6 months and a maximum follow-up of 17 months were conducted (median follow-up, 11-5 months).

Techniques of information processing and analysis

Qualitative variables were expressed as absolute numbers and percentages. Quantitative variables were expressed as mean and standard deviation (SD) when data had a normal distribution. For the lack of normal distribution, the median and interquartile range (IQR) [minimum and maximum] were used. In the univariate analysis performed for qualitative variables the chi-square test was used. The Student *t* test was used when data had a normal distribution; on the contrary, the Mann-Whitney *U* test was used. A binary logistics regression model was used for the multivariate analysis. Adjusted odds ratios (OR) and 95% confidence intervals were estimated for each variable. In all hypothesis testing, *P* values = .05 and 95% confidence intervals were considered statistically significant.

RESULTS

Out of the 152 patients initially included, 51 had incomplete data in their medical records or were lost to the follow-up. In 30 (29.7%) of the 101 patients studied, at least, 1 MACE occurred. The most common adverse event was the need for new target lesion revascularization (17 patients/16.8%). **Figure 1**.

The mean age was 60.6 ± 12.8 years, and the main clinical characteristics were diabetes mellitus (38.6%), previous myocardial infarction (49.5%), and PCIs performed in the acute coronary syndrome setting (56.4%). A total of 53.5% of the patients had multivessel coronary artery disease with a median/IQR in the SYNTAX score of 11.0/15 points. A total of 31 patients (30.7%) were treated with multivessel PCI, 46.5% with the simple bifurcation technique. The use of drug-eluting stents (DES) was predominant (76.2%). The angiographic success rate was 92.1%. **Table 1.**

The absolute number of neutrophils prior to the PCI, according to the median/IQR was 5.0/1 (a minimum of 2, and a maximum of 8), and 6.0/1 (4-10) after 6 hours; the NLR prior to the procedure was 3.0/1 (2-5), and 2.0/2 (6 hours later), although with a wider range (1-7). **Table 2**.

The variables associated with the presence of MACE were: LVEF (*P* = .021); 18 patients with left ventricular systolic dysfunction, multivessel coronary artery disease (21 cases, 20.8% vs 33 cases, 32.7%; *P* = .030), SYNTAX score (*P* < .001), multivessel PCI (14/13.9% vs 17/16.8%; *P* = .024), bifurcation lesions (21/20.8% vs 30%/29.7%; *P* = .011), true bifurcation lesions (17/16.8% vs 16/15.8%; *P* = .001), complex bifurcation techniques, and number of stents implanted, among others.

Table 2 and **figure 2** show that the absolute number of neutrophils 6 hours after the PCI was 7.0/2 vs 6.0/1; *P* < .001) and the NLR 6 hours after the PCI was 4.0/3 vs 2.0/1; *P* < .001) were associated with the presence of MACE. The absolute number of lymphocytes 6 hour after the PCI showed a trend towards statistical significance (2.0/0 vs 2.0/1; *P* = .006).

In the multivariate analysis, the SYNTAX score (*P* = .002; OR, 1.201; 95%CI, 1.067- 1.352), and the NLR after the

TABLE 1. Association between clinical and procedural variables and the presence of MACE at the in-hospitalmid- and long-term follow-up

Clinical variables (n = 101)		Total n (%)	MACE		P
			Yes (n=30)	No (n=71)	
			(#/%)	(#/%)	
Edad (media ± DE)		60,6±12,8	(61,3±12,6)	(60,2±13,0)	0,695 a
Sex	Male	71 (70)	(23/22,8%)	(48/47,5%)	0,362 b
	Female	30 (29,7)	(7/6,9%)	(23/22,8%)	
Past medical history	AHT	73 (72,3)	(23/22,8%)	(50/49,5%)	0,522 b
	DM	39 (38,6)	(9/8,9%)	(30/29,7%)	0,248 b
	CKD	13 (12,9)	(3/3,0%)	(10/9,9%)	0,575 b
	Previous MI	50 (49,5)	(14/13,9%)	(36/35,6%)	0,711 b
	CKD (mean ± SD)	28,4±4,3	(27,1 ± 3,7)	(28,9 ± 4,5)	0,047 a
Previous revascularization	No	76 (75,2)	(23/22,8%)	(53/52,5%)	0,893 b
	PCI	22 (21,8)	(6/5,9%)	(16/15,8%)	
	MRS	3 (3)	(1/1,0%)	(2/2,0%)	
Smoking habit	Non-smoker	38 (37,6)	(11/10,9%)	(27/26,7%	0,391 b
	Active smoker	42 (41,6)	(15/14,9%)	(27/26,7%)	
	Former smoker	21 (20,8)	(4/4,0%)	(17/16,8%)	
LVEF	30% - 50%	43 (42,6)	(18/17,8%)	(25/24,8%)	0,021 b
	> 50%	58 (57,4)	(12/11,9%)	(46/45,5%)	
Diagnosis	SCAD	44 (43,6)	(14/13,9%)	(30/29,7%)	0,857 b
	NSTEACS	48 (47,5)	(13/12,9%)	(35/34,7%)	
	STEACS	9 (8,9)	(3/3,0%)	(6/5,9%)	
Procedural variables					
Multivessel CAD		54 (53,5)	(21/20,8%)	(33/32,7%)	0,030 b
SYNTAX score (median/IQR)		11,0/15	(25/18)	(9/11)	< 0,001 c
Multivessel PCI		31 (30,7)	(14/13,9%)	(17/16,8%)	0,024 b
Type of target lesion	Type A	62 (61,4)	(13/12,9%)	(49/48,5%)	0,011 b
	Type B1	13 (12,9)	(5/5,0%)	(8/7,9%)	
	Type B2	25 (24,8)	(11/10,9%)	(14/13,9%)	
	Type C	1 (1)	(1/1,0%)	(0/0,0%)	
Thrombus at the lesion		8 (7,9)	(6/5,9%)	(2/2,0%)	0,004b
Heavy calcification		22 (21,8)	(10/9,9%)	(12/11,9%)	0,068b
Bifurcation lesion		51 (50,5)	(21/20,8%)	(30/29,7%)	0,011b
True bifurcation lesion		33 (32,7)	(17/16,8%)	(16/15,8%)	0,001b
Simple bifurcation technique		47 (46,5)	(18/17,8%)	(29/28,7%)	0,078b
Complex bifurcation technique		4 (4)	(3/3,0%)	(1/1,0%)	0,044b
Type of stent	Drug-eluting	77 (76,2)	(27/26,7%)	(50/49,5%)	0,035b
	Conventional	24 (23,8)	(3/3,0%)	(21/20,8%)	
no. of stents (median/IQR)		2,0/2	(2,0/2)	(1,0/1)	0,016c
Target SL (median/IQR)		23/15	(27,0/18)	(23,0/10)	0,056c
stent Ø (median/IQR)		3,0/1	(3,0/1)	(3,0/0)	0,257c
Angiographic success		93 (92,1)	(4/4,0%)	(4/4,0%)	0,193b
Ther. post-PCI	DAPTd	101 (100)	(30/29,7%)	(71/70,3%)	-
	Statins	88 (87,1)	(28/27,7%)	(60/59,4%)	0,228b
	BB	65 (64,4)	(23/22,8%)	(42/41,6%)	0,093b

EAHT, arterial hypertension; BB, beta-blockers; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; DM: diabetes mellitus; IQR, interquartile range; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular event; MI, myocardial infarction; MRS, myocardial revascularization surgery; no., number; NSTEACS, non-ST-segment elevation acute coronary syndrome; Ø, diameter; PCI, percutaneous coronary intervention; SCAD, stable coronary artery disease, SD, standard deviation; SL, segment length; STEACS, ST-segment elevation acute coronary syndrome; Ther, therapy.
a: Studentt test, P value. b: Pearson's chi-square test. c: Mann-Whitney U test. d: no statistics estimated because DAPT is a constant.

procedure (P = .010, OR, 2.254; 95%CI, 1.217-4.178) are independent variable predictors of events. A high NLR increases the chances of MACE by 2.254 times. **Table 3.**

DISCUSSION

This study assessed the value of the NLR in 101 patients treated with PCI to predict MACE with a median follow-up of 11.5 months.

The patients' baseline characteristics are consistent with those of other studies where having a medical history of male sex, age > 60, diabetes mellitus, and previous myocardial infarction is associated with higher chances of being treated with PCI.[7]

Over half of the study patients showed multivessel disease associated with a median SYNTAX score of 11.0; this estimate was made only in lesions with > 70% stenosis in vessels ≥ 2 mm in diameter. This strategy has been recommended by the ERACI IV trial to facilitate a more reasonable assessment of the coronary anatomy and more conservative percutaneous coronary interventions.[8]

The incidence rate of bifurcation lesions is between 15% and 20%.[9] The definition of a true bifurcation is the presence of a significant plaque in the secondary branch ostium. The stepped approach has yielded the best results proving superior to the complex or scheduled technique with 2 stents;[10] consistent with this, the present series (46.5%) used the stepped approach. The use of the PCI is not that

TABLE 2. Association between laboratory variables and the presence of MACE at the follow-up.

Laboratory variables (n=101)	Total Median/IQR (mín - máx)	MACE		p a
		Yes (n=30) (median/IQR)	No (n=71) (median/IQR)	
Absolute number of neutrophils before the PCI	5,0/1 (2-8)	(5,0/1)	(5,0/2)	0,142
Absolute number of lymphocytes before the PCI	2,0/0 (1-3)	(2,0/2)	(2,0/0)	0,215
Absolute number of neutrophils 6 hours after the PCI	6,0/1 (4-10)	(7,0/2)	(6,0/1)	**< 0,001**
Absolute number of lymphocytes 6 hours after the PCI	2,0/1 (1-3)	(2,0/0)	(2,0/1)	0,006
NLR before the PCI	3,0/1 (2-5)	(3,0/1)	(3,0/1)	0,564
NLR 6 hours after the PCI	2,0/2 (1-7)	(4,0/3)	(2,0/1)	**< 0,001**

IQR, interquartile range; MACE, mayor adverse cardiovascular event; NLR, neutrophil-to-lymphocyte rate; PCI, percutaneous coronary intervention. a: Mann-Whitney U test.

TABLE 3. Predictors of MACE. Multivariate analysis. Logistic regression model.

Variables	Exp (β)*	95%CI for Exp (β)		p
		Lower	Upper	
Diabetes mellitus	0,225	0,049	1,036	0,056
Previous revascularization	1,479	0,411	5,321	0,549
Previous MI	0,792	0,200	3,144	0,741
Age	1,025	0,969	1,085	0,388
LVEF between 30% and 50%	1,930	0,521	7,147	0,325
SYNTAX score	1,201	1,067	1,352	**0,002**
Multivessel PCI	0,516	0,061	4,361	0,543
True bifurcation	0,485	0,042	5,560	0,561
Complex bifurcation technique	2,975	0,138	64,016	0,486
Angiographic success	0,277	,018	4,267	0,358
NLR 6 hours after the PCI	2,254	1,217	4,178	**0,010**

MI, myocardial infarction; NLR, neutrophil-to-lymphocyte ratio; PCI, percutaneous coronary intervention

common in complex bifurcations (secondary branch with lesions ≥ 10 mm, stenosis diameter ≥ 70% in the left main coronary artery or ≥ 90% in the remaining bifurcations, < 45 or > 70-degree angles, among other) whereas the 2-stent technique systematically yields the best clinical results of all.[11]

Drug-eluting stents have been more widely used with more complex anatomies, multivessel PCI, for the management of bifurcation lesions, and in the clinical context of unstable patients. In all these clinical settings, the use of drug-eluting stents has proven undoubtedly favorable.[12]

During the PCI the blood flow towards the myocardium is reduced and microembolizations can occur causing specific metabolic changes and acute inflammatory activity in the myocardium and the damaged coronary artery. The most severe condition is myocardial necrosis that induces the production and activation of free radicals, the start of a cytokine storm, and the release of the tumor necrosis factor alpha.[13] This postoperative inflammation is obvious in the elevated levels of neutrophils reported and, consequently, in the NLR.

This study shows increased median absolute neutrophil counts, wider neutrophil absolute values (baseline levels: 5.0/1 between 2 and 8; after 6 hours: 6.0/1 between 4 and 10), and an elevated NLR (baseline levels: 3.0/1 between 2 and 5; after 6 hours: 2.0/2 between 1 and 7). Similar results were published by Rodríguez S et al.[14] who showed a significantly higher postoperative NLR (baseline levels: 3.316 [2.999 – 4.001] and 3.878 [3.214 – 4.491 after 6 hours] *P* = .003) in patients with acute coronary syndrome.

Major adverse cardiovascular events (MACE) are a group of complications associated with procedural failure, an impaired quality of life, and the patient's death. A total of 9 cases were reported during the hospital stay and 26 at the clinical follow-up for an incidence rate of 29.7% that is consistent with that reported by other authors.[15] The most common MACE was the need for new target lesion revascularization. Although the technological advances made with coronary stent grafts facilitate PCIs, they have proven insufficient to reduce significantly the incidence rate of restenosis reported in the United States (around 10%).[16] Of multifactorial causes, local inflammation is at the basis of the pathophysiology of restenosis of biological causes that eventually results in early aggressive neointimal proliferation or late neoatherosclerosis.[17]

Consistent with other studies that reported high incidence rates of new target lesion revascularization: 24.8%,[18] 19.1%,[19] and 10%,[16] this study incidence rate with first-generation conventional and drug-eluting stents is 16.8% in a sample with a high rate of diabetes mellitus, bifurcation lesions, and patients with acute coronary syndrome.

In this study, the rate of cardiovascular mortality is 8.9% (9 patients dead: 3 myocardial infarctions, 2 strokes, 2 stent thrombosis, and 1 malignant ventricular arrhythmia.1) The author believes that this is a high rate for a median follow-up of 11.5 months that could be associated with the clinical and anatomical complexity of the cases involved (acute coronary syndrome, 56.4%; multivessel disease, 53.5%; bifurcation lesions, 50,5%) compared to 30.7% of multivessel PCIs performed. A total of 70% of the patients with MACE (30 cases) had multivessel disease, 56,7% had true bifurcation lesions, and median SYNTAX scores of 25 compared to 46.6% of multivessel PCIs performed, an association that produces a high residual SYNXTAX score, which is an independent predictor of mortality.[20]

The number of neutrophils, lymphocytes, and NLR before the procedure showed no correlation with adverse events, a result that is not consistent with the study published by Verdoia M. et al.[21] where a NLR > 3 is a predictor of a common in-hospital complication after the PCI: type 4a myocardial infarction.

The NLR keeps a positive and significant correlation with ultrasensitive cardiac troponin, the creatine kinase-MB fraction, and the C-reactive protein, which is indicative of how suitable this NLR is to assess the intensity of myocardial damage. [22]

This study confirms the significant correlation that exists between the absolute value of neutrophils and the NLR measured 6 hours of the PCI and the presence of MACE, which is consistent with what other studies have already reported on this regard. After the primary PCI, a NLR > 3.31 increases the risk of adverse events and deaths during the in-hospital stay (12.7% vs 2.8%, P = .010), and (12.7% vs 1.9%, P = .003), respectively.[13] A higher postoperative NLR is associated with the presence of type a4 myocardial infarction, more immediate complications,[23],[14] with all the causes of in-hospital deaths (OR, 2.04, P = .013) and at the 6-month follow-up (OR, 3.88, P < .001),[24] with the presence of clinical restenosis (OR, 1.85, P < .001),[25] and with the prediction of early stent thrombosis (0.712; 95%CI, 0.610-0.988; P = .012).[4]

The multivariate analysis found that the NLR measured 6 hours after the PCI became an independent predictor of the risk of major adverse events at the follow-up, which increases the chances of MACE by 2.254 times, which by the way is consistent with a previous report of an OR = 2.45 of a NLR > 3 for the prediction of fatal coronary events.[26]

CONCLUSIONS:

In patients treated with percutaneous coronary intervention, the neutrophil-to-lymphocyte ratio measured 6 hours after the PCI is an independent predictor of major adverse cardiovascular events at the follow-up with a potential value in risk stratification.

KEY POINTS:

What is known about the topic?

- Inflammation plays a significant role in acute ischemia by rising the levels of neutrophils and reducing the number of lymphocytes in the bloodstream.
- The NLR is an inflammatory marker. When high it is associated with a greater load, severity, and spread of the coronary artery disease, and with worse prognoses for the patients.
- The NLR is a predictor of myocardial damage in patients with acute coronary events treated with percutaneous coronary intervention.

What does this study add?

- A cost-effective and fully available new marker for risk stratification in these patients.
- A higher NLR after a PCI has become an independent predictor of adverse events at the follow-up.

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Angioplasty in heavily calcified coronary lesions. Early experience with coronary intravascular lithotripsy

Angioplastia en lesiones coronarias severamente calcificadas. Experiencia inicial con litotricia intravascular coronaria en la Argentina

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ABSTRACT

The presence of heavily calcified coronary lesions has been our main public enemy for some time now because it affects the results of the angioplasty by initially preventing balloon crossing, complicating the proper passage of the drug from the surface of the stent to the vascular wall, and reducing stent expansion and apposition. These effects keep a direct correlation with the short and long-term progression of these patients. Different devices have been created like noncompliant balloons, cutting balloons, rotational and orbital atherectomy, and intracoronary laser with different crossover profiles and results. A new alternative is coronary lithotripsy, capable of achieving the circumferential fracture of calcified plaques without changing the flow after the procedure. The early outcomes of cases performed with the Shockwave 2 C IVL system are presented here.

Keywords: *coronary stenosis, lithotripsy, vascular calcification.*

RESUMEN

La presencia de lesiones coronarias severamente calcificadas ha sido nuestro principal enemigo porque afecta los resultados de la angioplastia al impedir el cruce inicial de los balones, no permite el adecuado paso del fármaco de la superficie del *stent* a la pared vascular, reduce la expansión y la aposición del *stent*. Estos efectos tienen una directa relación con la evolucion a corto y largo plazo de estos pacientes. Se han ideado diferentes dispositivos como balones no complacientes, balones con corte, aterectomía rotacional (AR) y orbitaria, láser intracoronario con diferentes perfiles de cruce y resultados. Una nueva alternativa es la litotricia coronaria, que logra la fractura circunferencial de las placas calcificadas, sin modificar el flujo luego del procedimiento. Se presentan los resultados iniciales de casos realizados con Shockwave 2 C IVL (*Shockwave Medical, Fremont, California*).

Palabras clave: *estenosis coronaria, litotricia, calcificación vascular.*

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INTRODUCTION

Heavily calcified coronary lesions complicate the advancement of balloons and a proper stent expansion and apposition. Different devices have come up today for the management of this type of lesions. High-pressure noncompliant balloons are initially used to dilate areas with fewer calcification with the possibility of generating dissections but without ever changing the plaque calcification. Special balloons like the scoring balloon and the cutting balloon have the same drawbacks regarding crossing difficulties due to the high profile of these devices. In moderate calcifications, another device that still remains unavailable in our country has been used: the intracoronary laser. It can be useful in unexpanded coronary stents. Other devices like rotational and orbital atherectomy are highly effective facilitating the crossing of the lesion. Still, there are instances that their mechanism of action can cause slow-flow or no reflow in the thrombotic lesion setting. Intravascular lithotripsy (IVL) is a new technique based on an already established therapeutic strategy for the management of kidney stones where multiple lithotripsy emitters mounted over a catheter deliver localized pulsatile sonic pressure waves to circumferentiallt modify vascular calcium and break down the calcium deposits of the tunica intima and tunica media. We present an early series of patients treated successfully in different centers with the Shockwave IVL system.

CLINICAL CASE #1

This is the case of a 71-year-old male patient with cardiovascular risk factors: arterial hypertension, non-insulin-dependent diabetes mellitus type 2, smoker of 60 packs/year, and overweight. Past cardiovascular medical history: acute myocardial infarction in 2005. Patient on medical therapy.
Triple vessel disease: myocardial revascularization surgery (2011 – LIMA to LAD; RADIAL graft to the LV side of the CXI, and VG to posterior descending branch of RCA). Functional class (FC) II stable chronic angina of 6-month evolution. Past medical history: appendectomy (at 16), vesical polypectomy of benign pathology, tear of the Achilles tendon repaired surgically back in 2010. Usual medication: acetylsalicylic acid, 100 mg/day; bisoprolol, 5 mg/12 hours. Rosuvastatin 10 mg/day; enalapril, 10 mg/12 hours; omeprazole, 20 mg/day; metformin, 850/12 hours, Lantus insulin 20 IU for subcutaneous use. On December 30, 2020, the patient was hospitalized with signs of left upper extremity arterial ischemia, probable paroxysmal atrial fibrillation, and FC IV angina pectoris. On January 1, 2021, a cine coronary arteriography and an arteriogram of the left upper extremity revealed: left main coronary artery without significant findings; left anterior descending coronary artery occluded in its proximal portion (70%) and middle third (100%); a heavily calcified left circumflex artery occluded in its proximal third (90%); right co-

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ronary artery occluded in its middle third; patent left internal mammary artery graft to left anterior descending coronary artery; radial graft to the LV side of patent left circumflex artery. Venous graft to posterior descending branch of patent right coronary artery. Unsuccessful percutaneous coronary intervention (PCI) approach to left circumflex artery. Occluded humeral artery treated with a Fogarty catheter. The echocardiogram shows an EF = 44%. Exercise-rest same-day SPECT protocol (February 2021): Inferior and inferior-lateral necrosis. Lateroapical and apical ischemia. Severely depressed ejection fraction (EF) after exercise. February 23, 2021.
Scheduled PCI: calcified lesion with Rotablator and then coronary lithotripsy (RotaTripsy) followed by the implantation of 1 DES into the left circumflex artery. The patient remains asymptomatic at the 3-month follow-up.

CLINICAL CASE #2

This is the case of a 60-year-old male patient with cardiovascular risk factors: arterial hypertension, and type II diabetes. Angina of 2-month evolution. Current medication: aspirin, 100 mg; clopidogrel, 75 mg; rosuvastatin, 20 mg; valsartan, 160 mg; bisoprolol, 5 mg, and omeprazole, 20 mg. The myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) revealed signs of ischemia of the anterior wall at 7 METs, 18 000/double product (ITT). The PCI was performed on the heavily calcified left anterior descending coronary artery via right radial approach. A XBU 3.5 6-Fr guide catheter was inserted with IVUS Philips Refinity guidance. Dilatation with the Shockwave device was performed followed by DES implantation and the corresponding follow-up (**Figure 1**). The patient remained asymptomatic at the 3-month follow-up.

CLINICAL CASE #3

This is the case of an 80-year-old male patient with cardiovascular risk factors: former smoker who quit smoking quite a few years ago. Past medical history of complete left bundle branch block. Current disease: FC I-II dyspnea of 1-year evolution. No signs of angina. The outpatient physical examination with SPECT revealed an impaired ejection fraction. A cine coronary arteriography was performed. Back in March 2020 the CCG had already been scheduled but never got to be performed. Mild ventricular dysfunction described in 2020. Transthoracic echocardiogram findings: severe left ventricular dysfunction, septal dyskinesia, moderate aortic regurgitation, moderate mitral regurgitation, aortic root diameter, 3.9 as seen on the CCG. Atherosclerotic coronary artery disease with compromise of left anterior descending coronary artery with significant ostial/proximal stenosis with heavily calcified plaque spreading from the distal third of the left main coronary artery (**Figure 2A**). Dominant left circumflex artery with irregularities. Right coronary artery: irregularities. It is decided to perform a PCI with IVL (Shockwave). Procedure: right radial puncture with a 7-Fr catheter is performed followed by the infusion of 7500 IU of heparin. 1) The intravascular ultrasound (IVUS) performed reveals a heavily calcified atherosclerotic plaque (180°) causing significant luminal stenosis. 2) Predilatation with intravascular lithotripsy (Shockwave) is attempted with good angiographic outcomes (40 pulses). The correct predilatation and fracture of the calcium deposit is confirmed on the IVUS (**Figure 2B**).

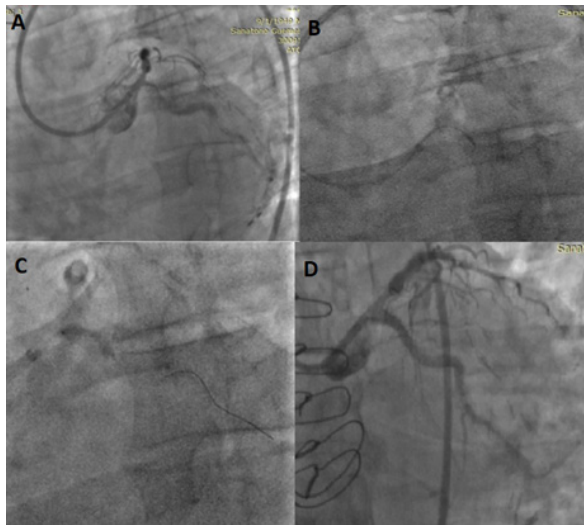

Figure 1. *A. Ostial and proximal circumflex artery. Cruce con microcatéter tipo Finecross y cuerda Runthrough.* ***B.*** *Rotational aterectomy with 1.25 burr. Dilatation with balloon NC 2,0 y 2,5.* ***C.*** *Shockwave 3,0x12 balloon.* ***D.*** *Outcome after DES 3,0x15 implantation.*

3) Afterwards, a PCI is performed on the ostial/proximal region of the left anterior descending coronary artery and one 4.0 mm x 18 mm drug-eluting stent is implanted. Postdilatation with a 5.0 mm noncompliant balloon is attempted. The correct stent expansion and apposition is confirmed on the IVUS (**Figure 2C**). NOTE: a total of 120 mL of low osmolar iodinated contrast were used. The patient remained asymptomatic at the follow-up.

CLINICAL CASE #4

This is the case of an 83-year-old female patient who presents with oppressive precordial pain (9/10 intensity) radiating to her left arm of 2-hour evolution with accompanying symptoms of profuse sweating, nausea, and vomiting. Cardiovascular risk factors: age, arterial hypertension, dyslipidemia. Past medical history: depression, lumbar spinal fusion, and bilateral total hip arthroplasty. Current medication: irbesartan, 12.5 mg; paroxetine, 20 mg, and simvastatin, 20 mg. The patient had no fever at admission, and 90 bpm. Blood pressure levels: 140/85. Systolic heart murmurs in mitral area radiating to the armpit with pulmonary middle crackles. ECG findings: atrial fibrillation, negative T waves in the anterior wall. Lab parameters: elevated troponin levels. Early diagnosis of non-ST-segment elevation acute coronary syndrome, Grace risk score 138, and TIMI grade-2 flow. The patient is administered clopidogrel, NTG, furosemide, and atorvastatin, and pain intensity goes down to 4/10. Echocardiogram findings: severe anterior hypokinesis at the anteroapical and apical segments, severe lateral hypokinesis. Moderate eccentric mitral regurgitation jet. EF = 48%. The cine coronary arteriography performed confirmed the presence of a calcified moderate ostial lesion of the right coronary artery, ostium, and left main coronary artery without lesions. Proximal severe lesion at left circumflex artery level. Heavily calcified left anterior descending coronary artery in its middle third with a 95% lesion compromising the origin of the diagonal artery with proximal severe lesion and occlusion receiving collateral circulation from the left anterior descending coronary artery. SYNTAX score = 40, and ERACI score = 32. A balloon angioplasty is performed with 1.25

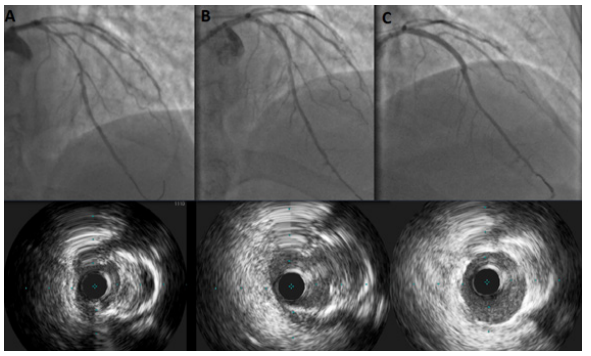

Figure 2. *A. Heavily calcified lesion in proximal and middle portions of the left anterior descending coronary artery. IVUS confirms a 180º calcification. B. Angiographic imaging after the dilatation of a 3.5 mm x12 mm IVL balloon. A total of 20 pulses were administed in each lesion. C.Post-implantationimaging of two3.5 mm x 13 mm, and 3.0 mm x 33 mm DESs. Correct stent expansion and apposition.*

mm, 1.5 mm, 2.0 mm, and 2.5 mm high-pressure balloons that fail to achieve plaque dilatation (**Figure 3**). Therefore, an IVL is performed with new gradual dilatations emitting a total of 80 pulses with a 2.5 mm x 12 mm Shockwave c2 IVL device (Shockwave Medical, Fremont, CA, United States) achieving a good diameter of dilatation without dissection images and a proper blood flow. Afterwards, 2 overlapping BMSs were implanted at high atmospheres of pressure (**Figure 4**). Finally, a PCI is performed on the left circumflex artery with 1 BMS implantation using the ORCA Colchicine 0.5 mg protocol. The patient remained asymptomatic for angor pectoris and dyspnea at the 2-month follow-up.

DISCUSSION

The use of imaging modalities in calcified lesions is crucial to determine the type of device that should be used for treatment purposes. Fluoroscopy underestimates the presence of endoluminal calcium. Also, the calcium detected on the fluoroscopy is sometimes found at the adventitia-tunica media interface (Mönckeberg's arteriosclerosis). IVUS is the most reliable diagnostic imaging modality for the detection of endoluminal and deep calcium. However, the border of endoluminal calcium hides in its shadow the actual mass of calcium in the vessel wall. Optical coherence tomography (OCT) has a limited capacity of penetration but high sensitivity and specificity rates to see images of superficial calcium and assess the posterior region of the calcified plaque being able to measure the entire actual calcified mass. Unfortunately, the last 2 imaging modalities described are not very much used due to their cost and the fact that they are not covered by most patients' health insurances. Maybe in the coming future, the multislice computed tomography (MTSC) will be used to define de load and show the interventional cardiology the plan he should follow for the management of these calcified plaques (rotational atherectomy, orbital atherectomy, lithotripsy).[5,6]

After experimental in vitro studies, in December 2015 the DISRUPT CAD I trial was started[1] including 60 patients from 7 hospitals from 5 different countries. The median stenosis rate was 72.5% and the average lesion length, 18.2 mm, and severe calcification was present in all the patients. The IVL was feasible and facilitated stent implantation in all the patients, brought the rate of stenosis down to 12.2% with an acute gain of 1.7 mm, a 95% rate of clinical success, and no MACE at the 30-day follow-up (rate of 95%). No dissections,

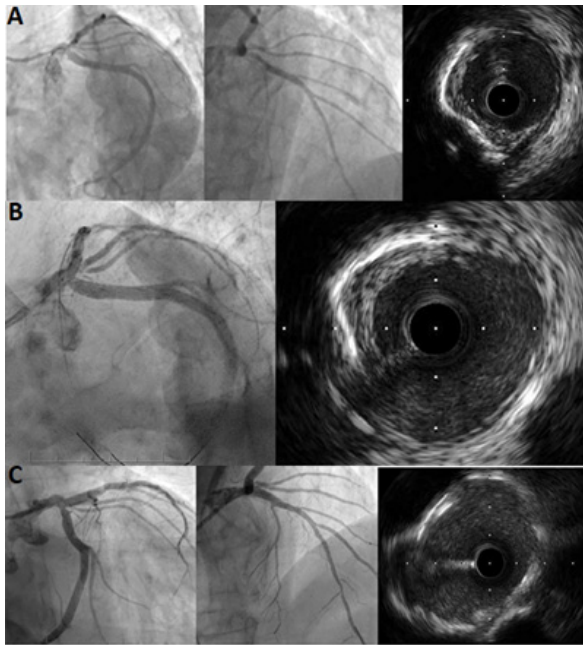

Figure 3. *A. Left anterior descending coronary artery with significant ostial/proximal stenosis, heavily calcified plaque, and a 180° calcification. B. Predilatation and fracture of the calcium deposit. C. Correct stent expansion and apposition.*

slow flow/no reflow, embolization or perforations were reported. The rate of MACE at the 6-month follow-up was 8.3%.

This first study describes the effect mechanism as seen on the optical coherence tomography (OCT) in heavily calcified lesions that would later be implanted with a stent,[2] with localized disruption as a way to prepare the vessel. It is an early sub-analysis of 31 patients from the DISRUPT CAD I trial. The lithotripsy broke calcium down in 43% of the lesions. The rate of calcium breaking increased in the most heavily calcified plaques. The mean gain of the acute area was 2.1 mm^2, but it went up even more with stent implantation achieving minimal stent areas of 5.94 mm^2 +- 1.98 mm^2. Deep dissections as part of the effect of the angioplasty occurred in 13% of the cases that were successfully treated with stent implantation without acute occlusions, slow flow/no-reflow or perforations ever occurring.

In order to confirm the safety and efficacy profile of IVL, the DISRUPT CAD II was conducted.[4] It is a prospective, multicenter, single-arm study conducted in 15 hospitals from 9 different countries. An OCT substudy was conducted to assess the mechanism of action of IVL. Independent central imaging core labs adjudicated the angiography and the optical coherence tomography, and an independent clinical events committee adjudicated the major adverse cardiovascular events. A total of 120 patients were recruited. IVL catheter implantation was successful in all the patients. The post-IVL angiographic acute luminal gain was 0.83 mm ± 0.47 mm, and residual stenosis, 32.7% ± 10.4% (that went down even more to 7.8% ± 7.1% after drug-eluting stent implantation). The main assessment endpoint consisting of 7 non-Q wave myocardial infarctions was met by 5.8% of the patients. No acute occlusions, slow flow, no-reflow or perforations were reported. The breaking of calcium deposits was identified in 78.7% of the lesions with 3.4 ± 2.6 fractures per lesion of an average 5.5 mm ± 5.0 mm in length.

These studies allowed us to start gaining experience in cases from numerous centers[10, 11, 12,13,14] thanks to their numerous case reports and editorials,[5,8,21,22] which extended the

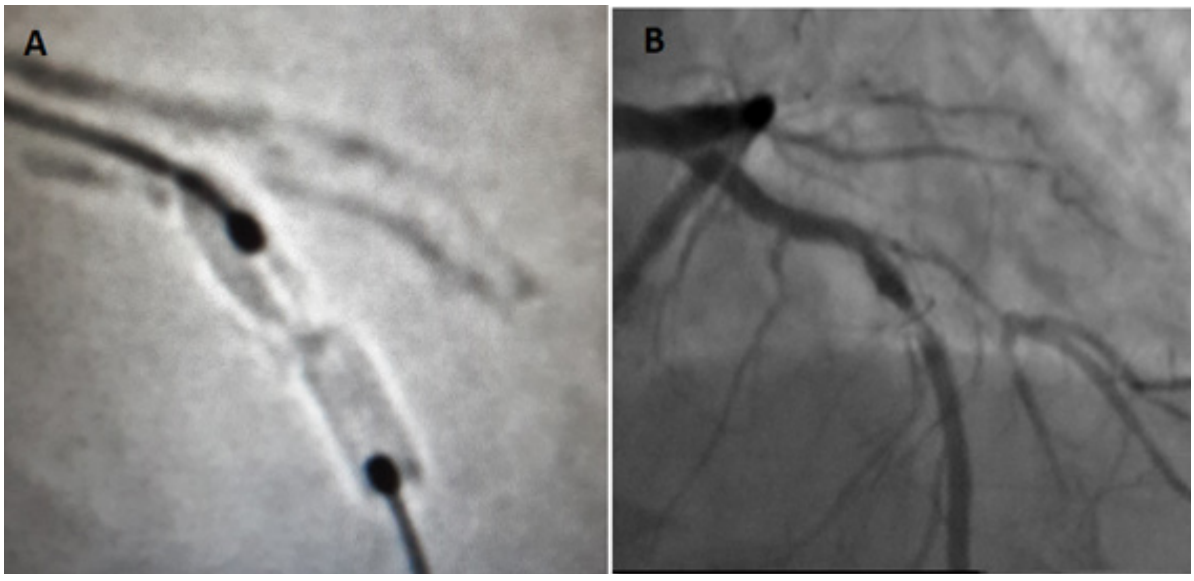

Figure 4. *A. Non compliant balloon (NCB) inflated at high atmospheres using the "dog bone" technique with the Stent Viz imaging system. Heavy calcification. B. Final angiographic result after early angioplasty.*

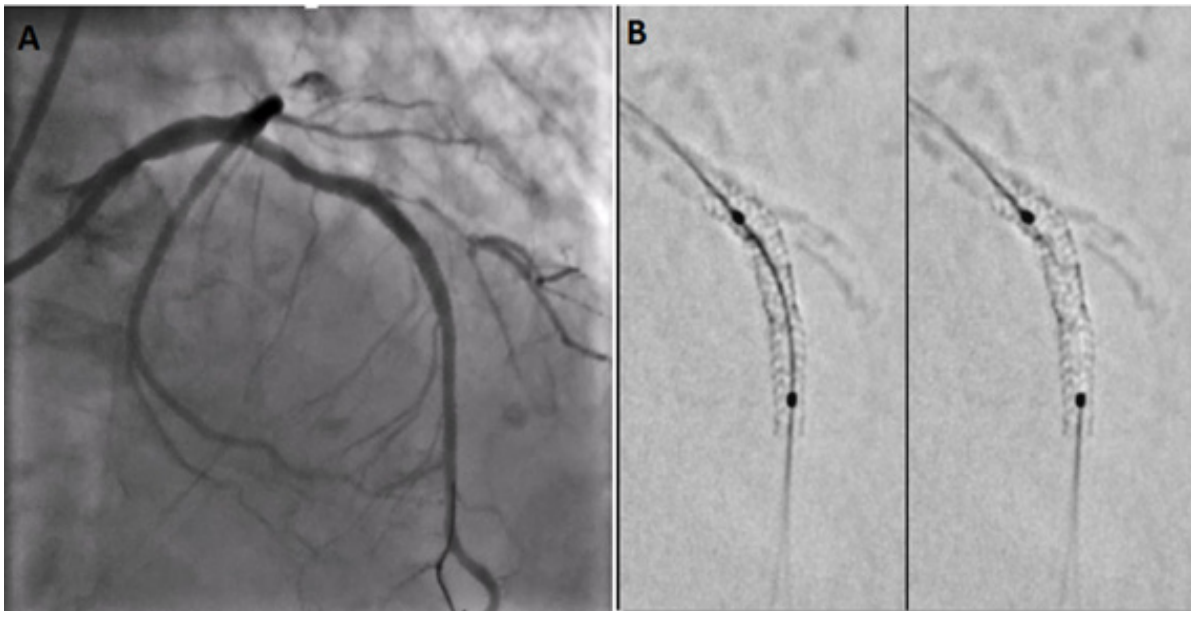

Figure 5. *A. Final angiographic results after the implantation of 2 overlapping stents. B. Properly expanded stents as seen on the Stent Viz imaging system.*

indications not only to de novo lesions, but also to the use of 5-Fr introducer sheaths via radial approach.[15] This added to the indications for underexpansions of previously implanted stents and to the recanalization procedure suggested to treat chronic total coronary occlusions[16] with large amounts of calcium.

An unexpanded stent in a heavily calcified coronary lesion is a common complication that can go on for years. It is associated with long-term failure and a poor evolution. Treatment with intracoronary lithotripsy may be an option here. In a case of an unexpanded coronary stent implanted 11 years ago, the optical coherence tomography revealed the mechanism of stent underexpansion by showing the presence of calcium deposits underneath the old struts.[27] The IVL breaks down the calcium underneath the stent struts changing its geometry from an elliptical to a round shape. Consequently, this transmits the old stent radial strength even better with the corresponding balloon dilatation.[28,29]

Another strategy that has joined the therapeutic armamentarium for the management of calcified lesions is combining rotational atherectomy (RA) and IVL. RA and IVL techniques can complement each other.[20, 25] The RA allows us to treat the calcium deposits of the tunica intima and cross balloons or stents through heavily calcified lesions; however, it may not be enough to achieve the proper expansion of these devices in the presence of deep circumferential calcium deposits. The IVL is a useful tool for the management of deep nondilatable calcium plaques. Nonetheless, it is very difficult to access severe and diffuse lesions due to their crossing profile. The combination of both techniques (called RotaTripsy) can be useful for the percutaneous management of heavily calcified lesions.

Thanks to the crossing profile of the IVL balloon, different accessories can be used to reach the target plaque. An early case of intracoronary lithotripsy used an extension catheter[7] to treat a heavily calcified and angulated left circumflex ar-

tery. Although the lithotripsy balloon available today is relatively large, the exchange extension catheter adapted it quite easily facilitating its placement. This case showed the utility of this combination of devices for patients with complex coronary anatomies.

We should mention that the IVL is a new technique that is still associated with some unwanted effects.[9] As a matter of fact, the IVL can cause ventricular ectopy.[17, 18, 24] Also, asynchronous cardiac pacing was described in a retrospective review of cases of coronary IVL performed in Belfast, Northern Ireland[3] with an incidence rate of ventricular capture of 77.8%. Heart rate > 65 bpm was identified as the only independent predictor of a higher risk of IVL-induced ventricular capture. However, no major adverse clinical events associated with this phenomenon in this series were reported. Another possible unwanted side effect on the conduction system that may occur during IVL is atrial fibrillation.[23] In the case reported reversion to sinus rhythm occurred a few hours after the procedure allowing an early hospital discharge. Another unwanted effect due to calcified plaques is the rupture of the IVL balloon.[19] This phenomenon is similar to other balloons that also rupture due to calcium deposits.

The most recent study on IVLis the DISRUPT CAD III trial.[30] It is a prospective, multicenter, single-arm study designed to approve coronary IVL. The main safety endpoint was the lack of MACE (a composite of death, myocardial infarction or target vessel revascularization at the 30-day follow-up). The main efficacy endpoint was procedural success. Both assessment endpoints were compared using a pre-established performance goal (PG). The mechanism of calcium modification was assessed on an optical coherence tomography (OCT) substudy. A total of 431 patients from 47 centers from 4 different countries were included. The primary safety endpoint at 30 days was the lack of MACE in 92.2% of the cases; The primary efficacy endpoint was procedural success in 92.4% of the cases. The mean length of the calcified segment was 47.9 mm + -18.8 mm, the calcium angle was 292.5º ± 76.5º, and calcium thickness was 0.96 mm + -0.25 mm at the most heavily calcified site. The OCT revealed the presence of fractures of multiplane and longitudinal calcium after the IVL in 67.4% of the lesions. The minimal stent area went from 6.5 mm^2 to 2.1 mm^2 and was similar whether fractures were seen on the OCT or not.

The IVL is a promising technique to overcome the problems associated with heavily calcified non-dilatable de novo lesions. Also, it helps in cases of inadequate stent expansion by eventually modifying the plaque and achieving successful stent implantations too as intravascular imaging confirm.[26]

CONCLUSIONS

In this early series of patients with heavily calcified lesions, the coronary intravascular lithotripsy facilitated a proper dilatation prior to stent implantation without any adverse events reported during the procedure or at the follow-up

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Traumatic arteriovenous fistula. Endovascular resolution

Fístula arteriovenosa de origen traumático. Resolución endovascular

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ABSTRACT

Vascular trauma is present in approximately 10% of all lesions affecting the extremities. The inadequate management of these lesions causes serious consequences such as death or loss of limb functionality. Vascular lesions due to firearms are one of the leading causes of the appearance of arteriovenous fistulas. This is the case of a 76-year-old male patient with a past medical history of gunshot wound to his right calf. The patientpresented to his GP 6 months after sustaining the trauma due to claudication at 100 m, pain, and coldness at rest. Additional methods were used to finally achievea diagnosis of arteriovenous fistula that was resolved via endovascular approach. The medical literature was reviewed to update the information on this regard.

Keywords: *gun wound, vascular trauma, arteriovenous fistula.*

RESUMEN

Los traumatismos vasculares se encuentran presentes en aproximadamente el 10% de todos los traumatismos que afectan a las extremidades. El manejo inadecuado de estos ocasiona consecuencias funestas como la pérdida de la vida o de la función de la extremidad. Las lesiones vasculares por arma de fuego constituyen una de las principales causas de la aparición de fístulas arteriovenosas. Se presenta el caso de un paciente de sexo masculino de 76 años, con antecedentes de herida por arma de fuego en pantorrilla de miembro inferior derecho, que consultó a los 4 meses del traumatismo a su médico de cabecera por presentar claudicación a 100 m, dolor y frialdad en reposo. Mediante métodos complementarios se realizó el diagnóstico de fístula arteriovenosa, resolviendo dicha comunicación de manera endovascular. Se revisa la literatura con el objetivo de actualizar la información al respecto.

Palabras clave: *fístula arteriovenosa, herida de arma de fuego, stent forrado.*

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CLINICAL CASE

This is the case of a 76-year-old male patient with hypertension, dyslipidemia, and diabetes type II. The patient is a heavy smoker (2 cigarette packs/month for the last 60 years), with asymptomatic severe aortic stenosis at the follow-up, and with unmonitored use of medication (vidagliptin, metformin, atorvastatin, valsartan) who presented to his general practitioner with right lower limb claudication at 100 m, pain, and coldness at rest. The patient complains of right calf trauma due to gunshot wound of 4-month evolution. The clinical examination revealed coldness at palpation and lack of popliteal and tibial pulses, presence of murmur and fremitus in the popliteal region. The Doppler echocardiography of the limb revealed these findings: presence of high-velocity continuous blood flow in the right popliteal artery middle third draining into the homolateral popliteal vein compatible with arteriovenous fistula (AVF), distal to it, and low-velocity blood flow in the tibial/peroneal territory.

The selective arteriography performed on the right lower limb revealed patent internal and external common iliac arteries without lesions, and patent deep and common femoral arteries without significant lesions. Patent superficial femoral artery with presence of severe diffuse atheromatous disease predominantly in its distal middle third (**Figure 1**). Patent popliteal artery with communication towards the popliteal vein, presence of gunshot and splinter wound, and slow ectatic flow in the tibial/peroneal territory (**Figure 2**).

The heart team decided to perform endovascular treatment through the revascularization of the superficial femoral artery using a 6.0 mm x 100 mm self-expandable stent (**Figure 3**) and seal of the AVF with a 5.0 mm x 30 mm covered stent. Before the covered stent implantation, the fistulous path was found by inflating a coronary balloon that confirmed the transient closure of the AVF (**Figure 4**). The procedure was performed successfully and eventless, and the patient was discharged 48 hours later on vidagliptin, metformin, atorvastatin, valsartan, aspirin, and clopidogrel.

In the serial follow-up performed 3, 6, and 9 months after hospital discharge, the patient confirmed he was feeling good and with no symptoms. Also, he required no hospitalization and was never admitted to the ER with any associated symptoms. Currently, he performs daily aerobic physical exercise without limitations. The control Doppler echocardiography performed at the 6-month follow-up confirmed the closure of the AVF, and normal velocities were reported in the tibial/peroneal territory.

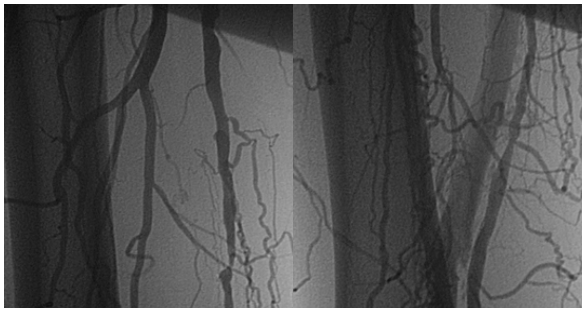

Figure 1. *Patent superficial femoral artery with presence of severe diffuse atheromatous disease predominantly in its distal middle third. Patent popliteal artery with communication towards the popliteal vein and superficial femoral vein.*

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DISCUSSION

Currently, vascular trauma is a problem of public health worldwide.[1,2] The growing violence, increasing use of firearms by civilians in the cities, rising speed limits, and labor accidents have all increased the incidence rate of vascular trauma.[3,4] Eighty per cent of the cases occur in arteries of the extremities, basically lower limb arteries; seventy per cent of the cases correspond to males between 15 and 42 years old in reproductive age. The rate of major amputations is between 10% and 15% and the rate of permanent sequelae due to bone or soft-tissue injuries is somewhere between 20% and 30%.[3,4]

It is common knowledge that in some types of penetrating trauma, even in the presence of early bleeding, if the trauma is not major, it can be said that the blunt or sharp object causing the trauma «has not touched» the blood vessels; that is why in injured patients, internal injuries can go unnoticed. Therefore, although a hypovolemic hemodynamic change may have not occurred, the possibility of vascular laceration «contained» by underlying tissues should always be ruled out. Or else, that the double vascular lesion has produced a communication called «arteriovenous fistula» (AVF).[5,6]

AVFs cause local and general effects in the physiology of cardiovascular apparatus that are directly associated with the size and location of the communication. Ischemia is among the local effects reported and it is directly correlated with the location and diameter of the fistula; cardiac mass effect is due to non-functional or dysfunctional vascular proliferation in the region affected while hyperemia—also associated with the size of communication—triggers distal venous hypertension and venous insufficiency. An increased cardiac output and an increased cardiac function with secondary hypertrophy are among the central or systemic effects reported depending on the diameter of the fistula and its proximity to heart. There are times that AVFs do not present as such, but are accompanied by aneurysmatic or pseudo-aneurysmatic dilatations.[7]

Overall, AVFs are described depending on their location in the superficial femoral territory (mainly) followed by the popliteal territory, the tibial/posterior territory, and the brachial region.[8]

The color Doppler ultrasound can be used to show the characteristics of the arterial and venous flow, the location of the fistula, and the size of the arteriovenous communication. The helical computed tomography scan can provide us with very useful images of the size and magnitude of the FAV. The arteriography should be selective in the artery damaged, and super-selective in the presence of fistula paths; in addition to being diagnostic, the arteriography can be the early treatment and, in some cases, the definitive treatment with the current endovascular methods.

Surgical treatment requires trained surgeons to control acute bleeding, perform wide incisions for the vessel proximal and distal control, for artery dissection with sufficient

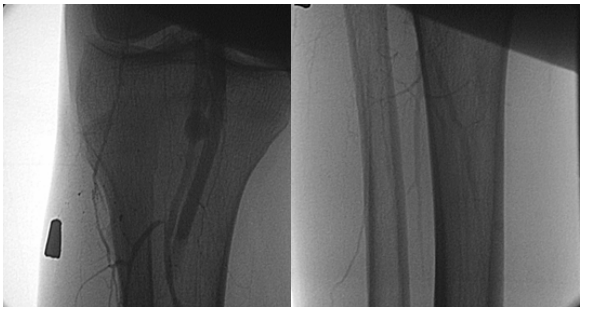

Figure 2. *Patent popliteal artery with communication towards the popliteal vein, presence of gunshot and splinter wound, and slow ectatic flow in the tibial/peroneal territory.*

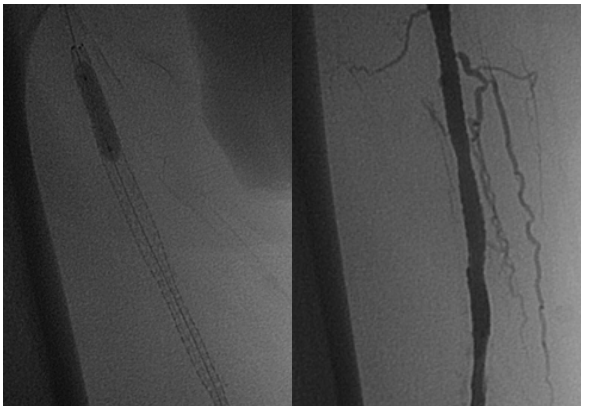

Figure 3. *Revascularization of the superficial femoral artery using a 6.0 mm x 100 mm self-expandable stent.*

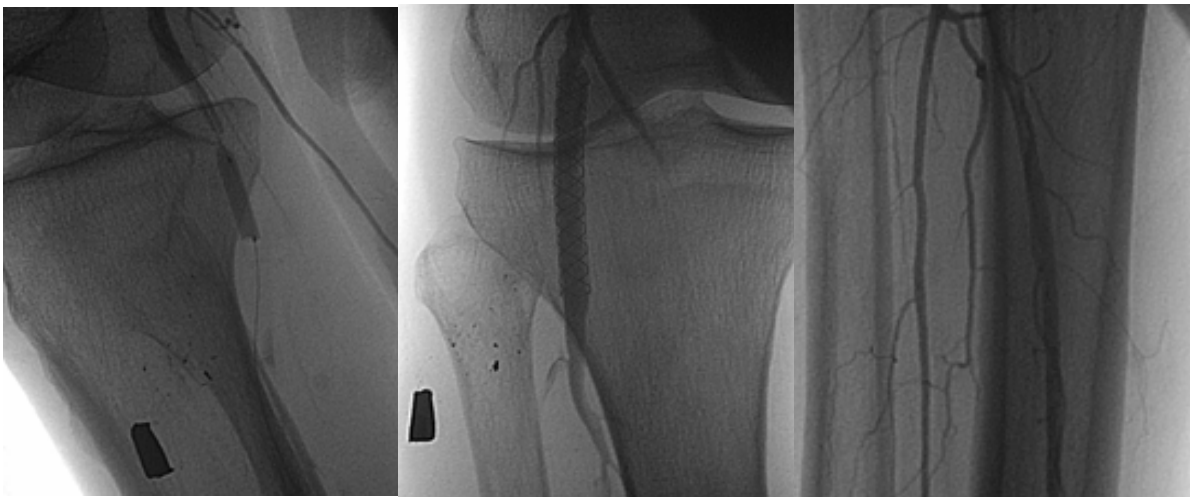

Figure 4. *Before the covered stent implantation, the fistulous path was found by inflating a coronary balloon that confirmed the transient closure. Afterwards, a 5.0 mm x 30 mm covered stent was implanted that closed the fistula and restored distal flow into the tibial/peroneal territory..*

amplitude, and for non-viable tissue extraction. The endovascular approach will vary, in each particular case, especially in hemodynamically stable patients with no signs of bleeding at that time. In post-acute phase AVFs, prognosis changes dramatically after the implantation of covered stents or endoprostheses.

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Cardiac hamartoma: role of endomyocardial biopsy in the diagnosis of cardiac neoplasm

Hamartoma cardíaco: rol de la biopsia endomiocárdica en el diagnóstico de neoplasias cardíacas

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ABSTRACT

Cardiac neoplasms are a rare entity. Due to the low specificity of imaging modalities in thisclinical setting, the surgical resection of tumors with subsequent microscopic evaluation is the technique of choice in most of the cases to achieve a definitive diagnosis. However, in selected cases, diagnosis can be achievedthrough an endomyocardial biopsy. We present a case of a cardiac neoplasm on which an endomyocardial biopsy was performed that resulted in a diagnosis of hamartoma of mature cardiac myocytes.

Keywords: *heart neoplasms, hamartoma, biopsy.*

RESUMEN

Las neoplasias cardíacas son lesiones poco frecuentes. Debido a la baja especificidad de los métodos de imágenes en estos escenarios, la resección quirúrgica del tumor con posterior evaluación microscópica es la técnica seleccionada en la mayoría de los casos para establecer un diagnóstico definitivo. Sin embargo, en casos seleccionados, el diagnóstico puede lograrse mediante biopsia endomiocárdica. Presentamos un caso de neoplasia cardíaca al que se le realiza biopsia endomiocárdica y se diagnostica hamartoma de miocitos cardíacos maduros.

Palabras clave: *neoplasias cardíacas, hamartoma, biopsia.*

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INTRODUCTION

Cardiac neoplasms are rare lesions mostly found in autopsies or during cardiac imaging studies.[1] The hamartoma of mature cardiac myocytes (HMCM) is a rare cardiac neoplasm that was first described by Tanimura et al. back in 1988.[2] We present the case of a patient diagnosed of HMCM through a transthoracic echocardiography (TTE)-guided-endomyocardial biopsy (EMB).

CLINICAL CASE

This is the case of a 32-year-old male patient without cardiovascular risk factors and a past medical history of pulmonary tuberculosis that required complete tuberculostatic treatment. The patient had been showing signs of congestive heart failure [NYAH functional class (FC) I] for 3 months now with progression into FC III. No heart murmurs were found on the physical examination. The ECG showed signs of biatrial dilatation and complete right bundle branch block. The TTE performed revealed the presence of preserved right ventricular (RV) systolic function, moderate tricuspid failure, and mild-moderate pulmonary hypertension. Also, a mass occupying the RV was found, but its thrombotic origin could not be ruled out.

For better characterization purposes, a cardiac computed tomography scan was performed that confirmed a RV hypodense image of a similar density to that of the cardiac muscle both in the arterial and late phases that was consistent with a primary and/or secondary organ process of the right ventricle. Afterwards, the cardiac magnetic resonance imaging performed revealed in the RV—at midventricular level and in close relation with the interventricular septum—the presence of a fixed endocavitary image of a similar intensity to that of the myocardium in the cine, T1, and T2 sequences, and in the fat-suppression sequences (on T1 and T2). The administration of gadolinium triggered the contrast enhancement of all the phases and the possibility of an image compatible with a thrombus was eventually ruled out. A whole-body positron emission tomography was performed to assess the origin of the tumor and eventually rule out the possibility of a secondary origin.

Together with the hospital Interventional Cardiology and Cardiovascular Surgery Unit the heart team decided to perform a TTE-guided EMB due to the patient's poor general health status to eventually perform heart surgery with tumor resection. The EMB was performed via right anterior transjugular access through an 8-Fr Avanti+ introducer sheath (Cordis, California, United States) with a 50 cm 8-Fr Novatome bioptome (Scholten Surgical Instruments Inc, California, United States). A total of 8 samples were taken, 3 for a TB culture test that ended up testing negative, and 5 for the histopathological analysis that confirmed the presence of cardiac tissue with disorganized and hypertrophic mature cardiomyocytes with cytoplasmic vacuolization, interstitial fibrotic foci, and presence of adipocytes consistent with HMCM.

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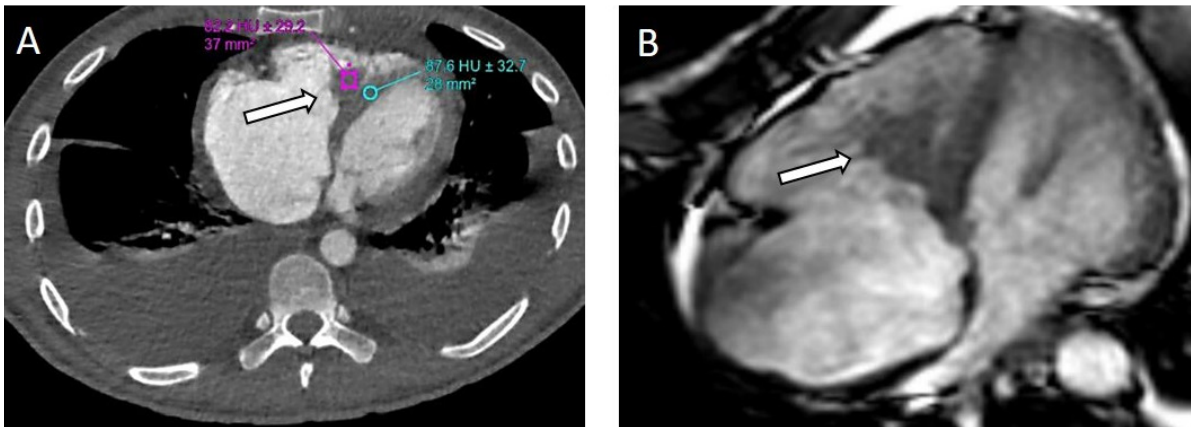

Figure 1. *Axial cardiac computed tomography (A) of right ventricle as seen on the cardiac magnetic resonance imaging [long-axis view] (B). Hypo- and hypointense imaging of the right ventricle (arrow) with similar density and intensity to that of the cardiac muscle.*

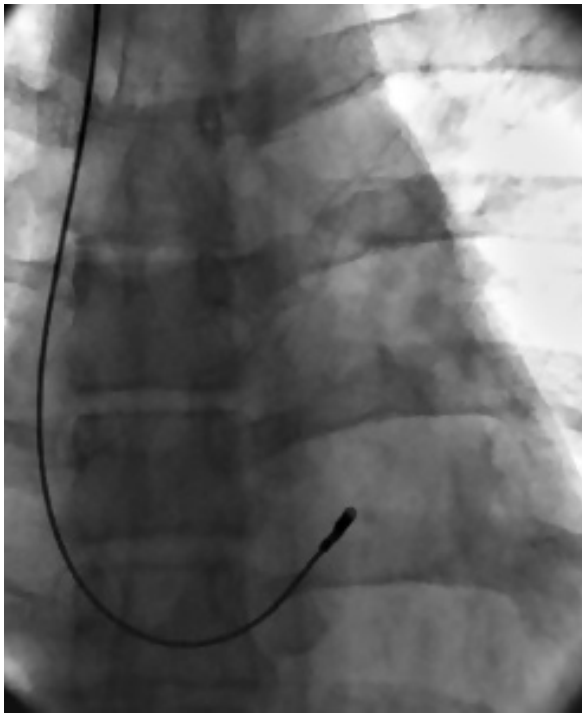

Figure 2. *Fluoroscopic imaging in the anteroposterior projection showing the bioptome in the RV while the endomyocardial biopsy was being performed.*

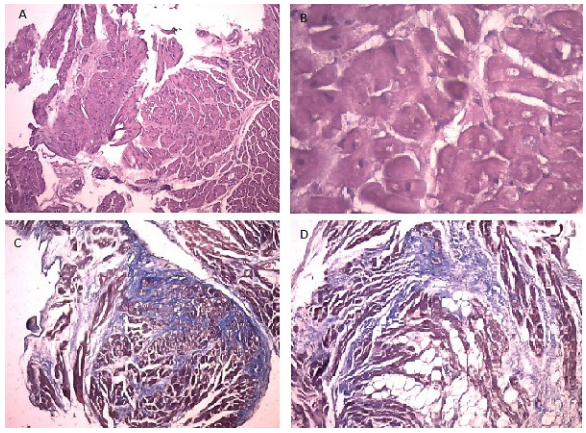

Figure 3. *Biopsy of right ventricular mass. The histological cuts were analyzed using hematoxylin and eosin (A andB), andthe Gomoritrichrome stain (C and D). The cardiac tissue revealed the presence of disorganized and hypertrophic mature cardiomyocytes (A) with cytoplasmic vacuolization (B), interstitial fibrotic foci (C), and presence of adipocytes (D). Also, presence of a superficial focal fibrin-leukocytic deposition was confirmed too. Histopathological findings consistent with hamartoma of mature cardiac myocytes.*

The patient progression was good with medical therapy, and he was eventually discharged from the hospital. Currently, he is waiting for the surgical resolution of his case.

DISCUSSION

Primary cardiac neoplasms are a rare entity with an incidence rate of 0.001% to 0.3%. Of these, 75% are benign.[1] Differentiating the different tumors is challenging. The echocardiography, the cardiac computed tomography scan, and the cardiac magnetic resonance imaging often reveal the location and precise size of cardiac tumors. Still, achieving a definite diagnosis is difficult because the appearance of the image is not pathognomonic.[3] Due to the low sensitivity of imaging modalities achieving definitive diagnoses, the tumor microscopic assessment has become the gold standard.[1,3] EMB, described by Sakakibara and Konno in 1962[4] is a safe method with a rate of serious complications < 1%.[5,6] Currently, its main indication is for heart transplant rejection monitoring and in patients with early-onset heart failure associated with dilated cardiomyopathy and ventricular arrhythmias.[5] According to the different studies published to this date EMB is not very much used to diagnose cardiac masses because it can provide inconclusive tissue samples.[3,5] Heart surgery with tumor resection is the treatment of choice because it provides a more detailed histopathological analysis. However, in selected cases, diagnosis can be achieved through an EMB, thus sparing surgery (eg, lymphomas or infiltrative masses where surgical resection may not be feasible).[6]

The current ACC/AHA/ESC clinical practice guidelines establish that the EMB is a reasonable procedure to diagnose cardiac tumors (Class IIa recommendation) if 4 specific criteria are met: diagnosis cannot be achieved otherwise; the diagnosis achieved through the EMB will change treatment; the EMB success rate is reasonably high; the EMB should be performed by an experienced operator.[7]

Different reports have described the diagnostic utility of TTE-guided EMB or transesophageal echocardiography (TEE)-guided EMB.[8,9] The TEE is the most suitable imaging modality here, although it is also the most invasive of the two. Regarding TTE and TEE-guidance, another option to acquire more information, avoid general sedation,

and minimize the radiologist's exposure to radiation is to use intracardiac echocardiography (ICE). It is a new imaging modality based on the use of a diagnostic ultrasound catheter.[10] Although it is a useful new imaging modality in this type of cases, the ICE is limited by its high cost associated with single-use catheters.

CONCLUSION

Cardiac tumors are rare entities. The TTE, TEE or ICE-guided EMB is a safe and reliable procedure to achieve a definitive diagnosis of cardiac tumor. However, surgical resection followed by microscopic assessment is still the gold standard.

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Coronary stenting in the right ventricular outflow tract

Stent coronario en el tracto de salida de ventrículo derecho

Jorge Gómez[1], Andrea Hozbor[2], Andrés Lucas[3], Manuel Porto[4], Carlos Vázquez[5], Ramiro Pelliciari[6]

ABSTRACT

Three-month-old patient diagnosed with Down syndrome, tetralogy of Fallot with hypoplastic pulmonary branches, hypoxia, and a past medical history of prematurity, sepsis, infective endocarditis, protein-losing enteropathy, and respiratory distress syndrome. Stent implantation in the rightventricular outflow tract was decided as an alternative to surgical treatment. After the interventional procedure the properoxygen saturation was achieved. Technical details of the case and indications of this intervention are discussed in this clinical case.

Keywords: *cardiology, pediatric, interventionism.*

RESUMEN

Paciente de 3 meses de edad con diagnóstico de síndrome de Down, tetralogía de Fallot con ramas pulmonares hipoplásicas, crisis de hipoxia y antecedentes de prematurez, sepsis, endocarditis infecciosa, enteropatía perdedora de proteína y síndrome de distrés respiratorio. Como alternativa al tratamiento quirúrgico se decide colocar un stent en el tracto de ventrículo derecho. Después del procedimiento se loga mantener una saturación estable. Detalles técnicos del caso y las indicaciones de esta intervención son discutidas en este reporte.

Palabras clave: *cardiologia, pediatría, intervencionismo.*

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INTRODUCTION

We present the case of a male patient with prenatal diagnosis of tetralogy of Fallot, emergency cesarian section due to pathological Doppler findings; gestational age, 32 weeks; weight, 1460 grams.

No pulmonary growth. The prenatal diagnosis of tetralogy of Fallot is confirmed. The karyotype test performed confirms a result of trisomy of chromosome 21 (Down syndrome).

During the hospital stay, prostaglandins are infused due to hypoxemia with signs of small ductus.

Until the intervention the patient shows:

- Culture-positive sepsis and 2 suspicious presentations that were medicated. Presence of suspected 7 mm x 7 mm thrombus vs endocarditis on a hyperechoic image of the right atrium that disappears 28 days after continuous antibiotic and anticoagulation therapy.
- Protein-losing enteropathy due to chronic diarrhea.
- Respiratory distress syndrome. The patient required mechanical ventilation for 27 days and, eventually, oxygen through nasal canula.

To this point and considering the patient's general state of health including pulmonary low flow, hypoxemia due to infundibular spasm and also the long-term deleterious effects of prostaglandins, the presence of hypoplastic pulmonary branches, and the patient's low weight, a different alternative to palliative or corrective surgery is proposed.

Coronary stent implantation in the right ventricular outflow tract is suggested to secure pulmonary flow, allow the withdrawal of prostaglandin infusion, and the development of hypoplastic pulmonary branches.

PROCEDURE

A coronary stent was implanted into the right ventricular outflow tract of a 3-month-old-3260-gram newborn baby after consultation with the heart team of the Cardiology and Pediatric Heart Surgery Unit.

A 6-Fr introducer sheath was inserted under general anesthesia via femoral vein access. A series of coronary angiographies in 30° right anterior oblique projection with 20° cranial tilt and 90° left profile are performed. These angiographies revealed the presence of a 15 mm-long outflow tract with severe dynamic narrowing during systole 4 mm away from the pulmonary valve (**Figure 1**). A 5-Fr JR catheter was mounted over a 0.035 in hydrophilic guidewire and then advanced inside the right pulmonary branch. Afterwards, the guidewire was exchanged for another 0.035 extra support guidewire for the insertion of a 6-Fr catheter to achieve good support and reach the final destination with the stent. By changing the support guidewire to the left pulmonary branch, the tip of the catheter can be placed just underneath the right ventricular outflow tract. The 4-Fr guide catheter was exchanged for a 0.014 in guidewire. To advance the coronary stent (Rebel®, from Boston Scientifics, a 4 mm x 16 mm chrome-cobalt stent) a different 0.014 in guidewire was required to better position the guide catheter and facilitate the advancement of the balloon catheter with the stent in the position indicated. This last guidewire was removed, and the balloon was inflated at 10 atm to achieve a stable 4 mm-diameter at the infundibulum (**Figure 2**). The angiography confirmed good blood flow through the infundibulum with valve regurgitation for having run through it plus a 4 mm-hypoplastic annulus.

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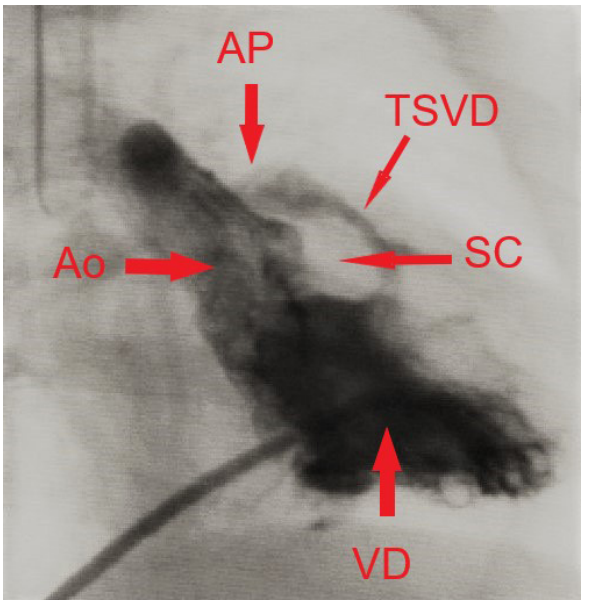

Figure 1. *Angiography in right anterior oblique projection showing the body of the right ventricle (VD), the right ventricular outflow tract (TSVD), the hypertrophied conal septum (SC) causing the stenosis of the TSVD, the pulmonary artery (AP), and the aorta (Ao)..*

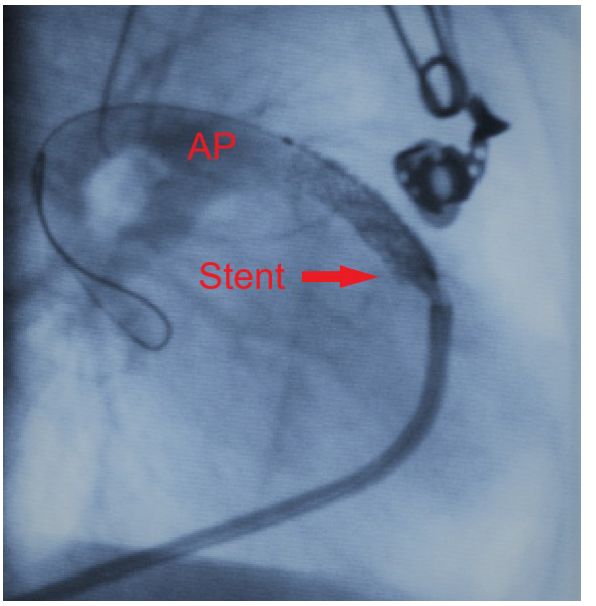

Figure 2. *Angiography performed underneath the stent inserted in the right ventricular outflow tract that achieved a stable diameter; the two branches of the pulmonary artery (AP) can be seen here.*

The patient was referred back to the Neonatology Unit. The next day, the patient progression was good with a more stable oxygen saturation between 90% and 93%. The follow-up echocardiogram revealed a 46 mmHg-gradient through the stent.

DISCUSSION

Surgical interventions in newborn babies with tetralogy of Fallot, whether corrective or palliative, as it is the case with Blalock Taussig shunt, are a huge challenge, particularly in the presence of hypoplastic pulmonary branches or other comorbidities like prematurity, respiratory distress, post-sepsis syndrome, etc.[1] No treatment in the presence of cyanotic events increases the risk of complications.[2] The latest protocols published on stent implantation in the right ventricular outflow tract for the palliative management of these patients have given excellent results, effective lower-risk treatments, high clinical improvement, better oxygen saturation, and good development of pulmonary branches when they are hypoplastic.[3] As an option to the subclavian-pulmonary artery shunt, this procedure allows us to postpone corrective surgical procedures ideally between 3 and 4 months after stenting and after crossing the threshold that increases the chances of a torpid postoperative period and/or reduces the rate of success.[4,5] This case was presented to back up the results obtained in the aforementioned publications and keep this option alive as an alternative to surgical palliative therapy.

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Endovascular therapeutic options for vascular liver lesions. Case report

Opciones de tratamiento endovascular para lesiones vasculares hepáticas. Reporte de un caso

Daniela Battisti[1], Julián Dalurzo[2], Rubén Retamar[2], Oscar Birollo[2]

ABSTRACT

Benign vascular lesions of the liver are being observed more frequency; in many cases the resolution is complex given the vital importance of the organ and the possibility of failure of the different therapeutic approaches classically described. We present a case where endovascular treatment offers different possibilities for the management of trauma-induced vascular liverlesions.

Key words: *blunt hepatic injury, angioembolization, hepatic vein embolization.*

RESUMEN

Las lesiones vasculares del hígado de etiología benigna se observan con frecuencia progresivamente creciente, siendo en muchos casos de resolución compleja dadas la importancia vital del órgano y la posibilidad de fracaso de los diferentes abordajes terapéuticos clásicamente descriptos. Presentamos un caso donde el tratamiento endovascular por cateterismo ofrece diferentes posibilidades para lesiones vasculares hepáticas de etiología traumática.

Palabras claves: *trauma cerrado hepático, angioembolización, embolización hepática venosa.*

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INTRODUCTION

Over the last few years, nonsurgical management of trauma-induced vascular lesions of solid abdominal viscera through angioembolization (AE) has been gaining more ground.[1] This is the case of a patient with late bleeding after surgery and transarterial embolization of the liver.

CLINICAL CASE

We present the case of a 15-year-old male patient admitted with polytrauma in the traffic accident setting (motorcyclist). The patient presents with close abdominal trauma with grade III liver laceration as seen on the computed tomography (CT) scan.[2] **(Figure 1A)**

He immediately underwent surgery due to his compromised hemodynamic status and the presence of hemoperitoneum. The surgical team performed liver packing with an early good clinical response. The patient progressed into a postoperative low hematocrit associated with clinical and tomographic signs of re-bleeding **(Figure 1B)**.

The abdominal arteriography performed via right femoral access revealed signs of active bleeding in branches of the right hepatic artery **(Figure 2A)**. Superselective embolization with gelatin sponge followed (Spongostan™; Ferrosan Medical Devices A/S, Søborg, Denmark) through a 5-Fr Cobra hydrophilic catheter (Radiofocus™ Glidecath™; Terumo Medical Corporation, Tokyo, Japan), and a 2.8-Fr microcatheter (Progreat™; Terumo Medical Corporation, Tokyo, Japan) with satisfactory results **(Figure 2B)**.

Sometime later (25 days later), the patient shows new signs of anemia and bleeding on the CT scan **(Figure 4A)**. The new arteriography performed reveals no signs of bleeding **(Figure 3A)**. However, the hepatic venography performed via right jugular access reveals signs of minor tissue bleeding coming from the right supra-hepatic vein **(Figure 3B)**. The heart team decided a new percutaneous endovascular strategy.

The right supra-hepatic vein was selectively catheterized via right jugular access with a 5-Fr catheter for visceral angiography (Imager™ II; Boston Scientific Corporation; Massachusetts, United States). Another 10 mm x 40 cm fiber coil was successfully released through the catheter in a controlled way (Interlock™; Boston Scientific Corporation; Massachusetts, United States) with good results **(Figure 3C)**.

The patient's favorable progression has been confirmed both in-hospital and at the long-term follow-up with a good correlation of clinical signs and imaging modality findings as **Figure 4B** shows.

DISCUSSION

AE is seen as part of the nonsurgical management of trauma-induced vascular lesions of solid abdominal viscera such as the liver. It is indicated in hemodynamically stable patients without peritoneal signs.[3]

In the case of unstable patients, as in our clinical case, the early surgical management is advised. However, the-

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The authors declared no conflicts of interest whatsoever.

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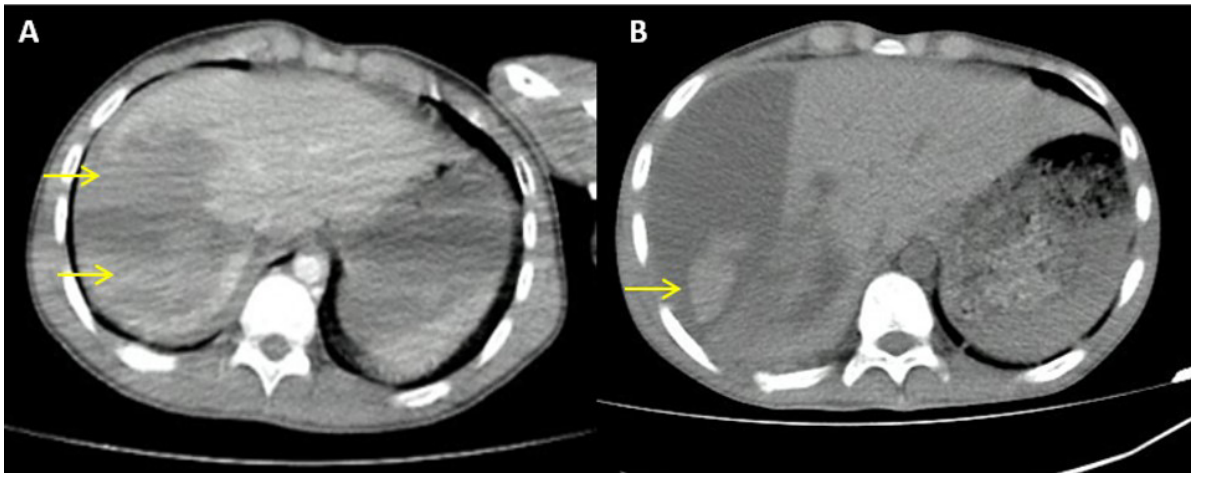

Figure 1. *Abdominal computed tomography.* ***A.*** *Preoperative. Arrows mark the area of liver laceration and subcapsular hematomar.* ***B.*** *Postoperative. Arrows marks area of re-bleeding*

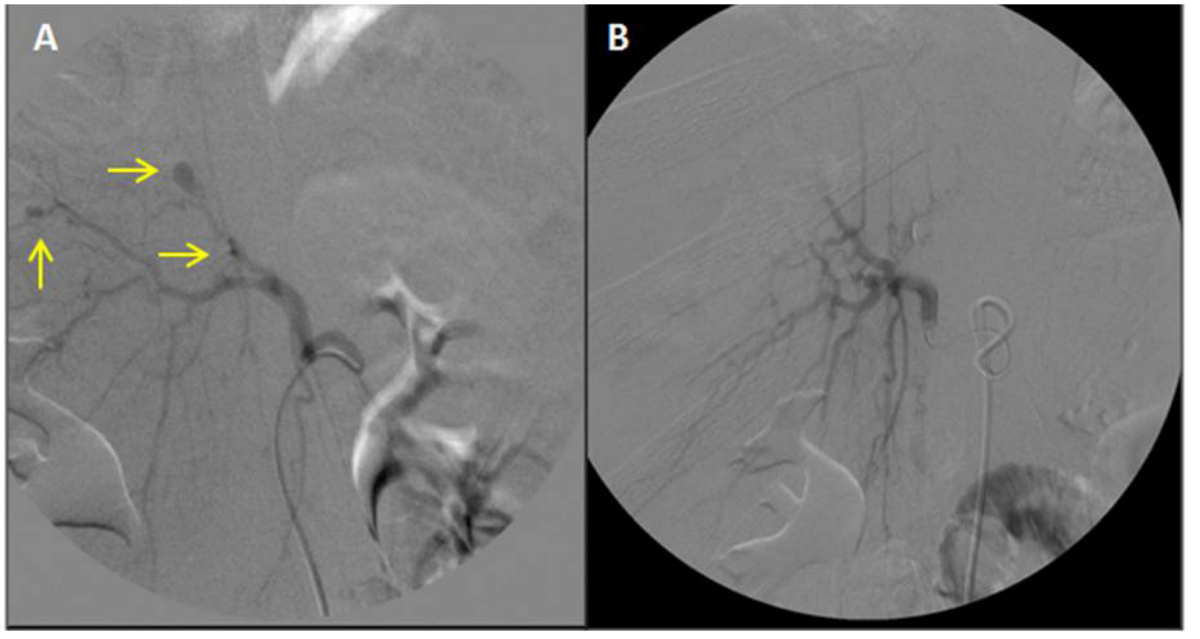

Figure 2. ***A.*** *Selective hepatic arteriography. Arrows indicate sites of active bleeding in the right hepatic artery.* ***B.*** *Post-embolization transarterial outcome.*

re is no consensus in the medical literature on how to act when this procedure fails. Much less in situations where both techniques fail.

When indicated, AE has a 93% success rate stopping arterial bleeding, which proves it is an effective approach. The possible complications described in the medical literature are hepatic necrosis, 14.9%; hepatic abscess, 7.5%; bilioma/biliary leak, 15.2%, and vesicular infarction, 7.4%.

Procedural failure, defined by immediate bleeding (6.9%), is associated with several problems that may lead to incomplete target vessel embolizations such as celiac trunk stenosis, impossible selective catheterization due to numerous anatomical curves, and persisting myocardial blush without an identifiable vessel or due to numerous nonembolizable collateral branches. Also, the presence of severe vascular lesions is associated with procedural failure in such a way that the predictors of failure are intraperitoneal contrast extravasation and hemoperitoneum in multiple abdominal compartments. On the other hand, the predictors of success are low-grade hepatic or intraparenchymal lesions with capsular retraction.

These patients' survival depends on the degree of tissue lesion, damage to the biliary tract, and additional compromise of other viscera and systems due to polytrauma and complications.

Hepatic event-related mortality in embolized patients is somewhere around 5.6% (range between 0% and 12%) according to different series published to this date.

Also, there are scenarios where failure of the nonsurgical management is reported despite successful arterial AE, as it was our case. This makes us think of juxtahepatic venous injuries whose clinical sign is late bleeding, which is also the leading cause of death.[4]

The presence of clinical factors like abdominal pain, low hematocrit, elevated transaminase levels, peritoneal signs, persistent systemic inflammatory response, and jaundice are all markers of suspected re-bleeding—which although rare (2.8% to 3.5%)—is of vital impor-

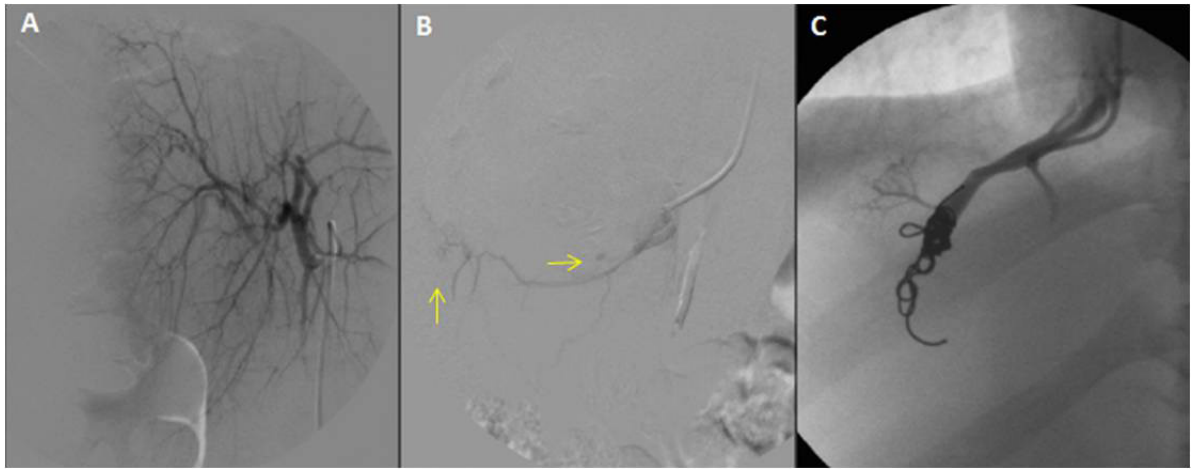

Figure 3. *A. Hepatic arteriography. Control. B. Hepatic venography. Late phase. Arrows indicate tissue bleeding sites (suprahepatic vein). C. Venous embolization. Outcome.*

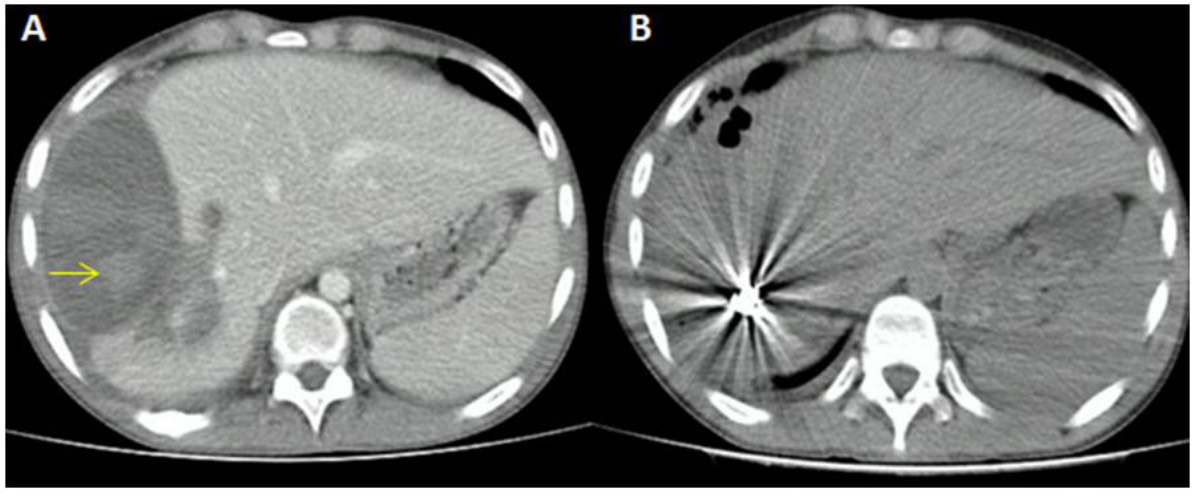

Figure 4. *Abdominal computed tomography. A. Venous liver pre-embolization. B. Post-embolization follow-up.*

tance; performing a computed tomography scan here is mandatory.[1]

A hybrid approach has been proposed in the medical literature: AE to treat arterial bleeding plus laparotomy with packing to treat juxtahepatic venous injuries.[3]

However, in our case, our suspect was intrahepatic venous injury and here surgical treatment is limited considering that hepatectomy, although partial, would be adding significant morbidity and mortality.[5]

And this is how the concept of hepatic vein embolization (HVE) was born. However, up until now, there are only two classic indications for this therapy: scheduled pre-hepatectomy to facilitate the formation of interlobar venous collateral branches and combined with portal embolization (sequentially) to increase the volume of the future hepatic remnant. Both indications have been described for the management of liver cancer.[6]

The physiological bases of this technique rest on hepatic hemodynamic changes where two mechanisms of tolerance are produced: retrograde portal venous drainage in an early stage, and the development of intrahepatic venous collateral branches that become established within the first two weeks after the procedure[4].

These means of compensation contribute to tolerate venous occlusion as long as it is segmental and selective.

CONCLUSIONS

The HVE is a rare procedure that should be performed in the liver cancer setting only.[4]

This is the first case ever reported in the trauma setting with satisfactory results and no complications, which proves it is a safe and decisive procedure in cases of failed surgeries.

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The importance of cardiovascular innovation and development

La importancia de la innovación y desarrollo cardiovascular

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The arrival of new medical technologies in prevention, diagnosis, and recovery of the patient is directly associated with the result indicators of the health status and with the increased hope, quality of life, and safety of the healthcare processes.

Medical innovation touches everybody on this planet. This innovation promises new ways to prevent, diagnose, and monitor health issues while the new drugs and devices available are intended to treat and eventually cure diseases. Medical innovation also enriches knowledge while transforming the entire healthcare process.

The ongoing search for better, safer, more effective, less invasive, and less painful diagnostic tools and therapies has encouraged doctors to become true innovators.

Innovation is a true reality in the routine clinical practice. That is precisely how medicine has evolved and advanced together with the scientific and technological development of other disciplines, always in the search for a better care for the patient.

For all these reasons, the Argentine College of Interventional Cardioangiologists (CACI) created an area for innovation called Innova CACI. Actually, this year the first course on innovation focused on the development of technologies to treat cardiovascular disease (mainly) and other medical conditions has come to life. We are proud to announce we have the invaluable collaboration of Dr. Alberto Hendler, and support from the ICI meeting (Innovation in Cardiovascular Intervention), the annual single most important cardiovascular innovation event worldwide.

The history and significance of cardiovascular innovation started in Argentina with Dr. Favaloro (and the development of coronary artery bypass surgery), Dr. Julio Palmas (and his coronary stent), Dr. Juan Carlos Parodi (and his aortic endoprosthesis and carotid shunt, among other important medical advances), and Dr. Luis de la Fuente (innovator and part of the interventional cardiology history of Argentina and Latin America), among other innovators and developers that our country has given to the world.

This first course that is already in in its final stage of development includes the excellent discussions and dissertations of Dr. Alberto Hendler who shared his experience showing us the different steps required for the developers of innovative and disruptive ideas to be successful in their innovative enterprise. Dr. Palmaz, Dr. Parodi, and Dr. de la Fuente have also collaborated with us sharing their life experiences and giving us recommendations and projections on the future of cardiovascular medicine as well as on the obstacles they had to overcome in their professional careers to become the excellent contributors to worldwide medicine they are today.

The first INNOVATION DAY with support from the ICI Meeting will be held at the SOLACI CACI Congress of 2021 in the city of Buenos Aires, Argentina. New ideas and innovations from LATAM innovators will be presented here. Also, they will be able to discuss their ideas with other groups or societies interested in their implementation

I wish to thank the teaching department that is always so involved with these important educational events. We simply could not have done it without it.

In 2022 CACI Innovation will be back with the same idea and commitment we have always had: bring scientific and administrative support to our members and partners to encourage their professional and personal achievements.

Diego Grinfeld
President of CACI 2020 – 2021

Publication Guidelines of the *Revista Argentina de Cardioangiología Intervencionista*

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

The *Revista Argentina de Cardioangiología Intervencionista (RACI)* is a quarterly journal published by the Argentinian College of Interventional Cardiologists (CACI). Its goal is to spread scientific and educational material on this medical specialty. Distribution is nation wide and open-access and is targeted at interventional cardiologists, clinical and pediatric cardiologists, radiologists, neurologists, operators, and other specialists. The publication is both digital (www.caci.org.ar) and in print.

The editorial principles of the journal are based on the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals and have been written by the International Committee of Medical Journal Editors - ICMJE in its most recent iteration available online at www.icmje.org.

For editorial reasons starting with issue #2, volume 9, year 2018 the graphic elements of the journal (figures, tables, and pictures) will be published in two colors only (blue and black). Readers who wish the full-color edition will need to pay an additional US$200.

The articles submitted to the journal shall be originals. The Editorial Committee will study the papers submitted and confirm whether they follow the Publication Guidelines established by the journal. The Director, and/or Associate Directors will be responsible for submitting these papers for the external blind peer review process. This means that the authors do not know the reviewers' name and the reviewers do not know the name of other reviewers. This policy established by RACI follows the same criteria implemented by the Review and Editorial Committee of the *Journal of the American College of Cardiology* (JACC), the highest impact factor cardiology journal. The Editorial Committee will make the final publication decision in accordance with the conclusions drawn by blind peer reviewers. Similarly, the Editorial Committee can introduce grammar related editorial changes according to the publication needs of the journal always after obtaining prior consent from the authors. Review articles and editorials will be subject to the same review process. Editorials are often required by the Editorial Committee as well.

After the first review, the articles can be accepted in the same form they were initially submitted; minor reviews are those pertaining to articles with significant contributions that still have some minor limitations that need to be corrected or proof read before its eventual publication; major reviews are those pertaining to articles that are unfit for publication as originally submitted to the journal. In any case, the Editorial Committee can consider new submissions called de novo submissions as long as the article is modified substantially; the rejection of the article occurs when both the reviewers and the Editorial Committee deem the article unfit for publication in the RACI journal.

In special cases of diagnostic and/or treatment consensus achieved by CACI and related scientific societies combined, such consensus will be supervised by the latter and being the Editorial Committee fully aware. Only then this consensus can be published exceptionally by the official journals of both societies simultaneously.

INSTRUCTIONS TO AUTHORS AND GUIDELINES FOR MANUSCRIPT SUBMISSION

All authors and members from the Editorial Committee shall declare any conflicts of interest associated with the publications

Each article shall be presented with a first page that should include: (a) title (both informative and precise); (b) the complete names of the authors and centers involved in the writing of the manuscript; (c) a short version of the title for the runner head; (d) the total amount of words contained in the paper excluding the references; (e) the name and full address, fax, and e-mail address of the corresponding author. The second page will include the abstract in Spanish and English with 3-6 keywords at the end of both abstracts with terms from the Index Medicus term list (Medical Subject Headings - MeSH). The third page will carry the content of the manuscript (see Preparation of the manuscript) including a new page per section. All pages will be numbered from the title page.

The paper (text, tables, and figures) will be submitted electronically to the following e-mail address *revista@caci.org.ar* with a note signed by all authors (see model in website)with the name of the section the manuscript belongs to, and a clear statement that the contents of the manuscript have never been published before.

Those appearing as authors of the article need to have contributed to the study or writing of the manuscript and will be liable for the content published.

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SECTIONS (See Preparation of the manuscript)

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These are scientific or educational papers of original basic or clinical studies. Requisites: a) general text, up to 5000 words

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These are articles on relevant issues on the specialty requested by the Editorial Committee to renown authors (whether foreign or domestic). They can be written by different types of doctors (no more than 3 different authors). Requisites: the same ones established for the publication of original articles.

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Under the title "How did I approach it?" the authors will be presenting a challenging case and a description of their management. The title needs to be included at the beginning of the text, for instance, "How did I treat an aneurysm in the left anterior descending coronary artery?" Then the authors' names, last names, specialties, and working centers should be included as well. Corresponding author, address, and e-mailwill be included as well. All authors need to declare their conflicts of interest. If they do not have any they need to say so. Text, figures, and references will follow the same criteria established for the clinical case.

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They are analyses and/or comments on relevant issues on the specialty or general cardiology field in relation with our specialty and always upon request by the Editorial Committee to a subject matter expert. Similarly, comments on issues unrelated to an article in particular can be requested by the Editorial Committee. Requisites: a) general text, up to 2000 words; b) references, up to 40.

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This is an opinion on an article published in the last issue of the journal that requires the arbitrage of the members of the Editorial Committee. Requisites: a) text, up to 250 words; b) one table and/or figure can be published; c) references, up to 5. Only letters submitted within a month following the print edition of the issue of the journal where the original article was published will be accepted.

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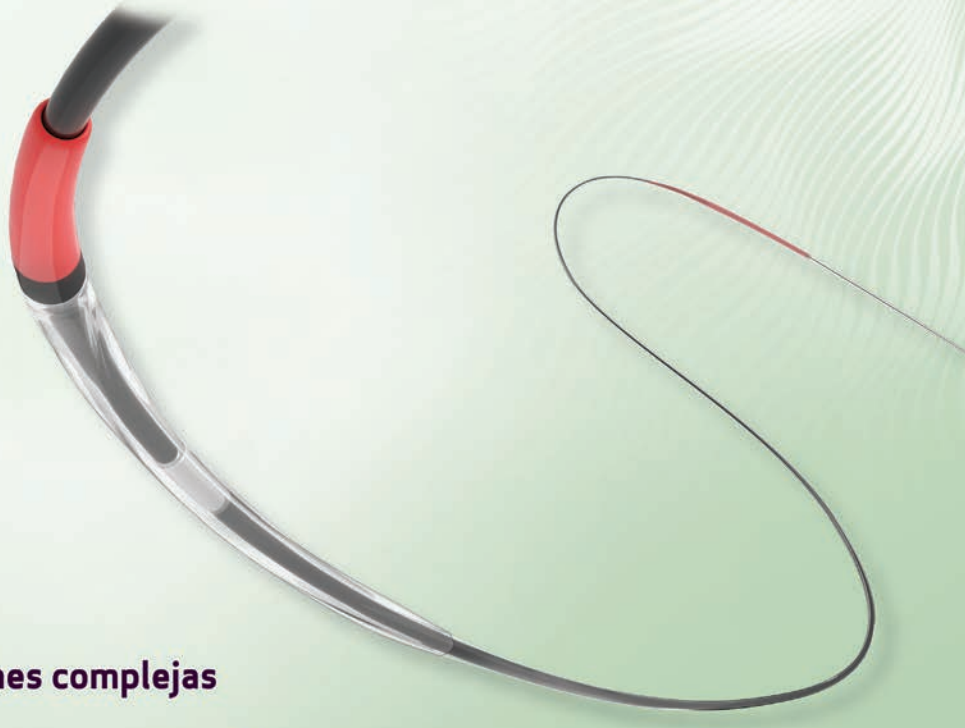

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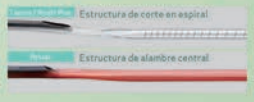

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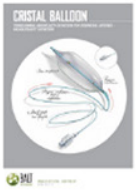

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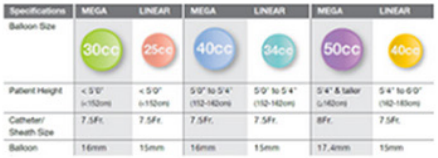

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