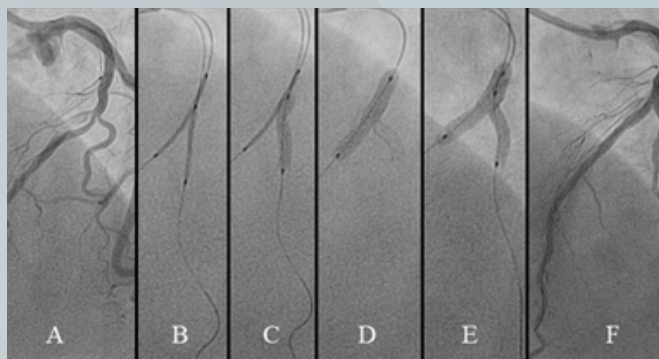




# ARGENTINIAN JOURNAL OF INTERVENTIONAL CARDIOLOGY

July - September 2020 | Year 11 | Issue 3



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Lessons learned from the SARS COVID-19 pandemic

*Rodríguez AE*

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*Saaby N et al.*

Indexado en



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## Sumario Analítico

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### EDITORIAL / EDITORIAL

#### LESSONS LEARNED FROM THE SARS COVID-19 PANDEMIC

Rodríguez AE

Six months after the World Health Organization (WHO) declared the COVID-19 pandemic that probably started at the city of Wuhan, China, several personal reflections that can be made to this point. In the first place, this viral disease is causing an unprecedented health and economic crisis around the world. Most RACI readers and CACI members have never seen anything like this in their lifetime before and the only reference we have on global crises like this comes from history books such as the Second World War.

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### REVIEW ARTICLES / ARTÍCULOS DE REVISIÓN

#### SAME-DAY HOSPITAL DISCHARGE PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY: CAN WE CONSIDER IT THE STRATEGY OF CHOICE DURING THE COVID-19 PANDEMIC?

Dionísio G

The better understanding of ischemic heart disease, associated with the progress of endovascular techniques, has positioned percutaneous coronary intervention (PCI) as a safe and effective therapeutic method. Currently, scheduled PCI is a procedure with a very low probability of presenting a serious complication in the first 24 hours. Various protocols have successfully applied the same-day discharge PCI strategy in selected patients, with good results. This initially very restricted strategy is impressive to represent a viable alternative. This review attempts to address the issue, its relevance in routine practice, and in this particular moment of healthcare medicine during the COVID-19 pandemic.

#### SEARCHING FOR MYOCARDIAL VIABILITY: WHAT METHOD SHOULD WE CHOOSE IN PATIENTS WITH SEVERE VENTRICULAR DYSFUNCTION?

Fontana L et al.

One of the main causes of left ventricular dysfunction is coronary artery disease. A transient ischemic event generates an imbalance between oxygen supply and demand with reversible damage to myocardial tissue. If persistent in time, this event evolves from progressive ventricular dysfunction into heart failure. The management of this condition is based on the optimal medical therapy including drugs and, in some cases, combined with myocardial revascularization as an option to improve both quality and quantity of life.

The correct identification of a viable myocardium is essential to know what treatment strategy should be followed. The cardiac magnetic resonance imaging is considered the best imaging modality for the study of myocardial viability, its size, function, valves, and even the aorta. The positron emission tomography imaging modality is also a viable option for a complete study of myocardial viability. Revascularization in patients with severe ventricular dysfunction and myocardial viability reduces mortality, cardiovascular mortality, and hospital stays.

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### ORIGINAL ARTICLES / ARTÍCULOS ORIGINALES

#### CORONARY TRANSLUMINAL ANGIOPLASTY IN BIFURCATION OF THE ANTERIOR DESCENDING CORONARY ARTERY, USING THE CRUSH STENTING TECHNIQUE

Ittig A et al.

**Introduction.** Coronary angioplasty for the management of obstructive bifurcation lesions is associated with a high degree of cardiovascular complications. This article shows the immediate and mid-term results of patients with unstable angina and obstructive bifurcation lesions of the left anterior descending and first diagonal coronary arteries treated using the crush stenting technique. **Material and methods.** Twelve consecutive patients were treated between January 2018 and July 2019. For the crush stenting technique, two Promus PREMIERTM everolimus-eluting platinum chromium stents were used.

**Results.** The mean age was  $60 \pm 7$  years. One third of the patients ( $n=4$ ; 33.3%) showed 3-coronary vessel disease and 2 of the bifurcations treated ( $n=2$ ; 16.7%) revealed in-stent restenosis. All procedures ( $n=12$ ; 100%) were technically successful and the patients had no major complications during hospitalization. During the patient's mid-term disease progression, the death of a male patient ( $n=1$ ; 8.3%) was reported 3 months after hospital discharge due to heart failure. The actuarial survival free of major adverse cardiovascular events (myocardial infarction, target lesion revascularization, stroke and/or death) at the 24-month follow-up was 92%.

**Conclusions.** Coronary angioplasty in a very select group of patients with unstable angina, obstructive bifurcations of the left anterior descending and first diagonal coronary arteries using the crush stenting technique followed by the implantation of 2 Promus PREMIERTM everolimus-eluting stents was safe and showed a low rate of major cardiovascular adverse events in the mid-term.

#### NEUTROPHIL-LYMPHOCYTE RATIO FOR THE DIAGNOSIS OF TYPE 4A MYOCARDIAL INFARCTION

Rodríguez Blanco S et al.

**Introduction.** Periprocedural type 4a myocardial infarction is among the complications associated with percutaneous coronary interven-

tions. The important role played by inflammation in cardiovascular disease is well-known, and a better expression of this inflammatory state is the neutrophil-lymphocyte ratio.

**Objective.** To assess the association between the neutrophil-lymphocyte ratio and the appearance of type 4a myocardial infarction and the potential diagnostic value of this biological marker.

**Methodology.** Applied, descriptive-correlational, and prospective study. The neutrophil-lymphocyte ratio was obtained six hours after coronary intervention at the "Hermanos Ameijeiras" Hospital, Havana, Cuba, between November 2018 and January 2020.

**Results.** A total of 184 patients were studied, 25 of whom developed type 4a infarction. In patients with heart attack, the ratio increased after the procedure [ $4.26 \pm 0.95$ ; (3.87-4.65)] vs [ $3.19 \pm 0.86$ ; (2.83-3.54)]. Ratios  $>2.63$  were associated with the diagnosis of the complication, with an area under the ROC curve for diagnosis of 0.932 (95%CI: 0.868-0.995;  $p < .001$ ).

**Conclusions.** The neutrophil-lymphocyte ratio has high sensitivity, high specificity, and high positive and negative predictive values in the diagnosis of type 4a myocardial infarction.

### FIRST NATIONAL SURVEY ON TRAINING IN INTERVENTIONAL CARDIO-ANGIOLOGY IN THE ARGENTINE REPUBLIC (ENFOCIRA I)

*Seropian IM*

**Introduction.** Interventional cardiology is a medical specialty listed in the Argentine Ministry of Sanitation. In order to be licensed, a course including a theoretical and a practical part needs to be passed.

**Objective:** To evaluate the characteristics of practical training in interventional cardiology.

**Methods.** Retrospective, cross-sectional study of a voluntary anonymous survey on 3 characteristics of the doctors in training: demographics, training, and working conditions.

**Results.** The survey included 65 participants aged 34 years old (33-37), mostly males (94%), 80% from Argentina and most of them practicing in the City of Buenos Aires (55%) and the Province of Buenos Aires (20%). The trainees performed different endovascular interventions including coronary interventions (96%), arterial peripheral procedures (92%), and structural heart disease procedures (82%). Differences were seen in the learning curve and in the degree to independence among the trainees. Working conditions were not the right ones and 21% of the trainees never got paid. Eighty-five percent of them needed a second or third job to make it through the month. Only 34% had health insurance (only 39% had an occupational accident insurance and only 19% malpractice insurance).

**Conclusion.** In Argentina, interventional cardiology trainees undergo extensive training, have different learning curves, and lack proper working conditions.

### CASE REPORT / CASO CLÍNICO

#### CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: UNEVENTFUL PREGNANCY AFTER PULMONARY BALLOON ANGIOPLASTY TREATMENT. CASE REPORT

*Saaby N et al.*

La hipertensión pulmonar durante el embarazo implica un riesgo significativo tanto para la madre como para el recién nacido. Mientras que la endarterectomía pulmonar es el tratamiento de elección en pacientes con hipertensión pulmonar tromboembólica crónica, la angioplastia pulmonar con balón se convirtió en una alternativa válida para los pacientes que no son candidatos a cirugía. Presentamos el caso de una mujer de 33 años con hipertensión pulmonar tromboembólica crónica, no candidata para resolución quirúrgica, que cursó su embarazo después de ser tratada con angioplastia pulmonar con balón, lográndose un parto sin complicaciones bajo un monitoreo estricto multidisciplinario.

### LETTER FROM THE PRESIDENT / CARTA DEL PRESIDENTE

#### WHAT ARE WE LEARNING DURING THE COVID-19 PANDEMIC

*Grinfeld D, Peralta S*

Summary of the webinar conducted with Drs. Juan Granada from New York City (USA), Miguel Montero Baker from Houston (USA) and Eduardo Aptekar from Paris (France). The importance of maintaining cardiovascular health care strategies in large metropolises and the management of acute coronary syndromes during the COVID-19 pandemic was discussed, with a very large attendance, both nationally and from Latin America. In this sense, the aforementioned specialists contributed their experiences in their respective cities.

# Lessons learned from the SARS COVID-19 pandemic

## Las enseñanzas que nos dejó la pandemia SARS COVID-19

Revista Argentina de Cardioangiología Intervencionista 2020;11(3):104-105. <https://doi.org/10.30567/RACI/202003/0104-0105>

Six months after the World Health Organization (WHO) declared the COVID-19 pandemic that probably started at the city of Wuhan, China, several personal reflections that can be madeto this point.

In the first place, this viral disease is causing an unprecedented health and economic crisis around the world. Most RACI readers and CACI members have never seen anything like this in their lifetime before and the only reference we have on global crises like this comes from history books such as the Second World War.

When one reads the daily reports on infections, mortality, and lethality (table 1, figure 1) we can see how the different countries of the world have been affected by the pandemic from the most economically viable onesto those still in their early stages of development.

It is surprising to read thecoronavirus in the world website and see how the world’s leading economies rank first in the number of contagions and mortality per 1 million population.

Among the 214 countries reporting their results—and arbitrarily excluding a few countries due toquestionable (in my personal opinion) data reporting—it is interesting to see that the world’s strongest economy with over 6,500,000 infections ranks first in the number of infections.This may be explained, in part, by the dynamics of this country’s economic policy based onconsumer economy. Nonetheless, the 589 deaths/million po-

#	Country, Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/ 1M pop	Deaths/ 1M pop	Total Tests	Tests/ 1M pop	Population
<b>World</b>		<b>29,536,091</b>	<b>99,544</b>	<b>934,41</b>	<b>1,963</b>	<b>21,356,017</b>	<b>7,245,665</b>	<b>60,828</b>	<b>3,789</b>	<b>119.9</b>			
1	USA	6,755,222	5,933	199,25	245	4,030,500	2,525,477	14,107	20,384	601	92,944,272	280,456	331,404,570
2	India	4,963,097	36,183	81,168	360	3,887,371	994,558	8,944	3,589	59	58,312,273	42,17	1,382,789,568
3	Brazil	4,349,544		132,12		3,613,184	604,243	8,318	20,433	621	14,505,652	68,143	212,871,450
4	Russia	1,073,849	5,529	18,785	150	884,305	170,759	2,3	7,358	129	41,122,307	281,761	145,947,569
5	Peru	733,86		30,812		573,364	129,684	1,46	22,194	932	3,552,710	107,445	33,065,274
6	Colombia	721,892		23,123		606,925	91,844	863	14,156	453	3,194,202	62,639	50,994,019
7	Mexico	671,716	3,335	71,049	228	475,795	124,872	2,747	5,199	550	1,520,463	11,767	129,210,414
8	South Africa	650,749		15,499		579,289	55,961	539	10,944	261	3,928,614	66,07	59,461,240
9	Spain	593,73		29,848		N/A	N/A	1,157	12,698	638	10,756,835	230,051	46,758,571
10	Argentina	565,446		11,71	43	438,883	114,853	2,992	12,487	259	1,602,403	35,388	45,281,033
11	Chile	437,983	1,536	12,04	27	409,944	15,999	905	22,871	629	2,887,903	150,804	19,149,979
12	Iran	407,353	2,705	23,453	140	349,984	33,916	3,811	4,837	278	3,613,891	42,914	84,212,176
13	France	387,252		30,95		89,507	266,795	712	5,93	474	10,000,000	153,131	65,303,652
14	UK	374,228	3,105	41,664	27	N/A	N/A	106	5,507	613	20,292,025	298,588	67,959,950
15	Bangladesh	341,056	1,724	4,802	43	245,594	90,66		2,067	29	1,756,746	10,645	165,026,102
16	Saudi Arabia	326,93	672	4,338	33	305,022	17,57	1,286	9,361	124	5,817,955	166,59	34,923,731
17	Pakistan	302,424	404	6,389	6	290,261	5,774	563	1,364	29	2,995,890	13,51	221,753,645
18	Iraq	298,702	4,224	8,166	80	233,346	57,19	570	7,393	202	1,948,531	48,228	40,402,436
19	Turkey	294,62	1,742	7,186	67	261,26	26,174	1,327	3,486	85	8,742,535	103,431	84,524,981
20	Italy	289,99	1,229	35,633	9	214,645	39,712	201	4,798	590	9,943,944	164,517	60,443,131
21	Philippines	269,407	3,544	4,663	34	207,352	57,392	1,048	2,452	42	3,164,465	28,8	109,878,149
22	Germany	263,954	733	9,437	1	237,55	16,967	237	3,148	113	13,436,301	160,262	83,839,732
23	Indonesia	225,03	3,507	8,965	124	161,065	55		821	33	2,715,346	9,906	274,116,377
24	Israel	162,273	1,905	1,141	5	120,443	40,689	533	17,643	124	2,771,732	301,354	9,197,590
25	Ukraine	159,702	2,905	3,264	53	70,81	85,628	177	3,656	75	1,870,790	42,831	43,678,008
26	Canada	138,01		9,179		121,224	7,607	53	3,65	243	6,235,465	164,915	37,810,245
27	Bolivia	127,619	828	7,394	50	85,198	35,027	71	10,903	632	275,394	23,527	11,705,429
28	Qatar	122,214	239	208	1	119,144	2,862	55	43,527	74	700,414	249,453	2,807,805
29	Ecuador	118,911		10,922		97,063	10,926	381	6,719	617	354,883	20,053	17,697,388
30	Kazakhstan	106,92	65	1,634		100,836	4,45	221	5,68	87	2,571,562	136,621	18,822,593
31	Romania	105,298	1,111	4,236	51	43,244	57,818	460	5,481	221	2,110,024	109,837	19,210,423
32	Dominican Republic	104,11		1,984		77,79	24,336	210	9,578	183	422,07	38,828	10,870,231
33	Panama	102,204		2,173		74,782	25,249	158	23,612	502	402,072	92,889	4,328,525
34	Egypt	101,177		5,661		84,969	10,547	41	985	55	135	1,314	102,722,504
35	Kuwait	96,301	829	568	5	86,219	9,514	84	22,482	133	684,204	159,734	4,283,392
36	Belgium	94,306	851	9,927	2	18,737	65,642	72	8,13	856	2,655,639	228,932	11,600,101
37	Oman	90,66	438	797	7	84,113	5,75	184	17,664	155	309,212	60,248	5,132,330
38	Morocco	88,203		1,614		68,97	17,619	275	2,384	44	2,251,763	60,859	36,999,965
39	Sweden	87,345		5,851	4	N/A	N/A	17	8,638	579	1,250,488	123,66	10,112,294
40	China	85,202	8	4,634		80,426	142	2	59	3	160,000,000	111,163	1,439,323,776
41	Netherlands	84,778	1,379	6,258	2	N/A	N/A	74	4,945	365	1,832,451	106,893	17,142,784
42	Guatemala	82,172		2,972		71,352	7,848	5	4,57	165	277,555	15,435	17,982,263
43	UAE	80,94	674	401	2	70,635	9,904		8,164	40	8,278,380	834,951	9,914,809
44	Japan	75,657		1,442		67,242	6,973	185	599	11	1,718,055	13,593	126,394,784
45	Poland	75,134	605	2,227	24	61,548	11,359	92	1,986	59	3,016,740	79,728	37,837,902
46	Belarus	74,552	192	761	5	72,661	1,13		7,89	81	1,666,468	176,371	9,448,671
47	Honduras	68,62	831	2,087	8	18,487	48,046	26	6,906	210	161,483	16,251	9,936,502
48	Portugal	65,021	425	1,875	4	44,362	18,784	59	6,381	184	2,280,220	223,761	10,190,439
49	Ethiopia	64,786		1,022		25,333	38,431	344	561	9	1,147,268	9,931	115,528,092
50	Venezuela	61,569		494		49,371	11,704	154	2,166	17	1,864,663	65,613	28,418,951

Figura 1. Cifras de la pandemia COVID-19 al 15/9/2020 de los 50 países más afectados.

pulation reported is surprising and maybe due to the well-known deficiencies of this country's public and private healthcare system.

A total of 15 countries (including Mexico, and Brazil) out of the 20 countries with the highest number of deaths per million population are developed economies.

In the opposite side of the spectrum we have the world's third and fourth economies—China, Germany, and Japan—with death rates/million population that rank #171 (3 deaths/million population), #57 (112 deaths/million population), and #138 (11 deaths/million population), respectively. Actually, the death rate per million population of Asian countries is extremely low: Vietnam 11 deaths/million population, Taiwan, 21 deaths/million population; New Zealand, 5 deaths/million population, and South Korea, 7 deaths/million population. In our region, Uruguay (13 deaths/million population) and Cuba (9 deaths/million) are among the lowest death rates reported per million population.

Considering that I arbitrarily excluded countries whose data I am hesitant about, I believe that the numbers presented above can be explained beyond the mere analysis of each country's GDP.

As I mentioned one of the reasons that may explain the number of infections reported may have to do with the characteristics of economy that happens to be heavily influenced by consumer economy driven by private initiative. The importance given by the governments of each of these countries to the management of the pandemic may have played a role too. Nonetheless, the social, cultural, rational, and even racial characteristics of the population and the interest shown by the leaders of each country in the management of this pandemic could explain why countries with a very low GDP have had such an effective sanitary response.

These sometimes conflicting result analysis in the number of infections, mortality and lethality reported by, on the one hand, the so-called leading countries, and on the other hand, Uruguay, Taiwan, Singapore, Cuba, and New Zealand, among others may have different explanations. However, the characteristics of each population, the decisions made at central government level, the citizens' observance of the protective measures implemented to avoid contagion, and solid public and private healthcare systems are the most plausible explanations to these findings.

In our repeated visits to China and Japan we saw that the use of face masks is mandatory in these countries.

By September 8th, Argentina had the sad privilege of being among the top 10 countries with the highest numbers of infections. However, it ranks #30 in the death rate/million population. Although this speaks of a civilized behavior as a nation that has been courageous for centuries, it actually shows that, while I am writing these lines, our public and private healthcare systems still hold to the highest standards of quality.

Finally, we should not forget that the approval of a vaccine will require the completion of three long stages as part of clinical research. So, until the necessary data on efficacy and safety become available by regulatory bodies, I strongly recommend to all of you that you take care of yourselves.

**Alfredo E. Rodríguez MD, PhD, FACC, FSCAI**

Editor-in-chief of Revista Argentina de Cardioangiología Intervencionista (RACI)

# Same-day hospital discharge percutaneous transluminal angioplasty: can we consider it the strategy of choice during the COVID-19 pandemic?

Angioplastia coronaria con alta hospitalaria en el día: ¿podemos considerarla como la estrategia de elección durante la pandemia COVID 19?

Gabriel Dionisio<sup>1</sup>

## ABSTRACT

The better understanding of ischemic heart disease, associated with the progress of endovascular techniques, has positioned percutaneous coronary intervention (PCI) as a safe and effective therapeutic method. Currently, scheduled PCI is a procedure with a very low probability of presenting a serious complication in the first 24 hours. Various protocols have successfully applied the same-day discharge PCI strategy in selected patients, with good results. This initially very restricted strategy is impressive to represent a viable alternative. This review attempts to address the issue, its relevance in routine practice, and in this particular moment of healthcare medicine during the COVID-19 pandemic.

**Keywords:** percutaneous coronary interventions, same day discharge PCI, COVID-19 pandemic.

## RESUMEN

El mejor entendimiento de la cardiopatía isquémica, asociado al progreso de las técnicas endovasculares, ha posicionado a la angioplastia transluminal coronaria (ATC) como un método terapéutico seguro y eficaz. Actualmente, la ATC programada constituye un procedimiento con una muy baja probabilidad de presentar una complicación grave en las primeras 24 horas. Diversos protocolos de trabajo han logrado aplicar la estrategia de ATC con alta en el mismo día, en pacientes seleccionados, con buenos resultados. Esta estrategia, inicialmente muy restringida, impresiona representar una alternativa viable. La presente revisión intenta abordar el tema, su relevancia en la práctica habitual y el lugar que ocuparía en este particular momento de la medicina asistencial durante la pandemia COVID-19.

**Palabras clave:** angioplastia coronaria, angioplastia coronaria con alta en el día, pandemia COVID-19.

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## INTRODUCTION

Cardiovascular disease is a major health issue in developed countries<sup>1</sup>. In this context, the better understanding of ischemic heart disease associated with the advance of endovascular techniques has turned the percutaneous transluminal angioplasty (PTA) into a safe and therapeutic procedure. Twenty-five years ago, a high percentage of patients who required myocardial revascularization surgery (MRS) with day-or-week long hospital stays and who had other associated comorbidities can now be treated with a PTA with regular follow-up 24 hours after the procedure<sup>2</sup>.

Currently, eligible PTAs are a procedure with very low chances of serious complications within the first 24 hours after the procedure<sup>3</sup>. Also, radial access facilitates very fast recoveries and avoids the risk of femoral artery bleeding that can lead to serious complications<sup>2</sup>. Over the past two decades, several proposals have been made to shorten the hospital stay of patients treated with PTA by using the same-day modality.

## CRITERIA PROPOSED BY THE SOCIETY FOR CARDIAC ANGIOGRAPHY AND INTERVENTIONS FOR THE SELECTION OF PATIENTS ELIGIBLE TO UNDERGO PTA WITH SAME-DAY HOSPITAL DISCHARGE

The criteria initially proposed by the *Society for Cardiac Angiography and Interventions* (SCAI) to include a patient in a same-day hospital discharge program are<sup>4,5</sup>:

- Stable angina or silent ischemia.
- Normal ejection fraction.
- Preload with thienopyridines.
- Lack of comorbidities.
- Single-vessel disease.
- Single-vessel PTA with only 1 stent <28 mm via radial, humeral or femoral access with an occluder device or safe manual compression.
- Lack of complications.
- A distance of less than 32 kilometers from the patient's home to the PCI-capable center.
- Proper home care at and access to the emergency system.

These recommendations limited access to PTA with same-day hospital discharge percutaneous transluminal angioplasty (SDHD-PTA) to a small group of patients despite the good results reported by several clinical trials, reviews, and meta-analyses with much wider criteria<sup>6-9</sup>. Back in 2018, SCAI published an expert consensus document update extending the indication to the following groups<sup>10</sup>:

- Preload with thienopyridines (not exclusive).

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- Presence of compensated comorbidities: diabetes, heart failure, COPD, chronic kidney disease, peripheral vascular disease.
- Multi-vessel PTA, chronic total coronary occlusions without limits to the number or length of the stents used.

## INTERNATIONAL EXPERIENCE

The first large scale clinical trials ever conducted were the EPOS and the EASY<sup>6,7</sup>. The first one published in 2007 included 800 patients randomized to undergo an elective angioplasty followed by 4-hour hospital discharges versus 24-hour hospital stays. Patients with previous PTA or myocardial revascularization surgery, left main coronary artery disease or multivessel disease were treated with an elective angioplasty. The presence of comorbidities or heart failure were not considered exclusion criteria. Femoral access was used with doses of 100 mg of aspirin followed by the intra-arterial administration of 5000 units of sodium heparin or 7500 units for procedures over 90 minutes. In cases of stent implantation an additional 100 mg of aspirin, 300 mg of IV clopidogrel, and 75 mg/day for a month were administered. Hemostasis was manual. Although the inter-group results did not show any significant differences, there was a non-negligible crossing rate towards the hospital stay group.

The EASY trial was published in 2018 included 1005 patients between 2003 and 2005 following an angioplasty performed via radial access in the NSTEMI (non-ST-segment elevation acute coronary syndrome) setting. Patients were randomized to a single bolus of abciximab and SDHD-PTA vs a 12-hour continuous infusion bolus without same-day hospital discharge. No differences were seen between the 2 groups.

The CathPCI registry included over 107,000 patients and showed that elderly patients (69 years to 78 years) with comorbidities, femoral access, ventricular dysfunction, and angioplasty of complex lesions had good results in selected cases<sup>8</sup>.

Successive reviews and meta-analyses showed no differences of mortality, myocardial infarction, and MACE between the SDHD-PTA strategy and conventional postprocedural management with hospital stays beyond 24-hour mark<sup>9-11</sup>.

## NATIONAL EXPERIENCE

Several observational national experiences have been developed with good results. Back in 2009 an observational protocol included 100 very low-risk patients treated with SDHD-PTA via radial access without complications. Other additional protocols have been designed including more complex patients in the NSTEMI (non-ST-segment elevation acute coronary syndrome) setting. The results of one of these protocols was reported at the annual Argentine Congress of Cardiology of 2016<sup>12</sup>.

An observational, retrospective clinical trial conducted in 2018 included over 600 patients treated via right radial access. The characteristics of patients treated with

SDHD-PTA were compared to those of patients who remained hospitalized. Many of the patients from the SDHD-PTA group were over 70 years and had ventricular dysfunction, some with left main coronary artery disease or previous revascularization surgery and other high-risk criteria. The results of this study did not vary between both groups<sup>13</sup>.

In 2019 we presented the AHORA 6 clinical trial (coronary angioplasty with fast hospital discharge in 6 hours)<sup>14</sup>. This trial was our very first randomized, prospective, and comparative approach on the management of selected patients to undergo a coronary angioplasty with fast hospital discharge in just 6 hours. We compared a group of patients <75 years with stable chronic angina, and an ejection fraction of 30% or higher, no previous MRS, left main coronary artery disease or a single patent vessel. Radial access was used, and patients were divided into 2 cohorts: the intervention group (G1) and the control group (G2). The G1 was closely monitored for 6 hours if the PTA results were optimal and after an independent core lab reviewed the operators performing the procedure. In the absence of symptoms or postprocedural electrocardiographic changes, the patients were discharged the same day with telephone follow-ups that night and the next day. The G2 was treated using the routine clinical practice and was discharged the next day.

After treating nearly 100 patients, we did not see a higher risk in the PTAs performed via radial access with hospital discharges at the 6-hour mark compared to the conventional strategy in selected patients.

## COMMENTS

The same-day hospital discharge percutaneous transluminal angioplasty has proven to be a safe alternative in selected patients. However, some health professionals and institutions are still reluctant to establish programs with this procedure in their therapeutic armamentarium.

The COVID-19 pandemic has impacted the care provided to cardiovascular patients. Recent publications confirm a significant reduction of outpatient practice<sup>15</sup>.

Actually, this is a multifactor phenomenon. Having to create spaces for confinement purposes has reduced the capacity of hospitals to have stay areas available for patients in the intensive care setting. Detecting a patient who tests positive for COVID-19 means even fewer hospital stay areas following the activation of confinement protocols. Finally, in many cases, patients say they do not want to seek medical attention because they fear they may get infected.

Offering an alternative with a short hospital stay in a "green" or "clean" intermediate care setting may be a viable and cost-effective option for the healthcare system. Another important aspect is the need to inform the population on the safety profile of this therapeutic approach.

The new challenge that the COVID-19 pandemic poses for all of us can be an opportunity to rethink our routine clinical practice.

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# Searching for myocardial viability: what method should we choose in patients with severe ventricular dysfunction?

En búsqueda de la viabilidad miocárdica: que metodo elegir en pacientes con deterioro ventricular severo

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## ABSTRACT

One of the main causes of left ventricular dysfunction is coronary artery disease. A transient ischemic event generates an imbalance between oxygen supply and demand with reversible damage to myocardial tissue. If persistent in time, this event evolves from progressive ventricular dysfunction into heart failure. The management of this condition is based on the optimal medical therapy including drugs and, in some cases, combined with myocardial revascularization as an option to improve both quality and quantity of life.

The correct identification of a viable myocardium is essential to know what treatment strategy should be followed. The cardiac magnetic resonance imaging is considered the best imaging modality for the study of myocardial viability, its size, function, valves, and even the aorta. The positron emission tomography imaging modality is also a viable option for a complete study of myocardial viability. Revascularization in patients with severe ventricular dysfunction and myocardial viability reduces mortality, cardiovascular mortality, and hospital stays.

**Keywords:** heart failure, myocardial viability, severe left ventricular dysfunction, coronary revascularization.

## RESUMEN

Una de las principales causas del deterioro de la función ventricular izquierda es la enfermedad coronaria. Un evento isquémico transitorio genera un desequilibrio entre el aporte y la demanda de oxígeno, con daño reversible del tejido miocárdico. Si dicho evento persiste, evoluciona con deterioro de la función ventricular de carácter progresivo hasta insuficiencia cardíaca. El tratamiento se basa en una terapéutica médica óptima que incluye fármacos y puede en algunos casos combinarse con la revascularización miocárdica como opción para mejorar calidad y cantidad de vida.

La correcta identificación del miocardio viable es fundamental para una estrategia de tratamiento. Se considera la resonancia nuclear magnética cardíaca como el mejor método para evaluar viabilidad miocárdica, tamaño, función, válvulas e inclusive la aorta. Las imágenes por tomografía por emisión de positrones también presentan una opción para la evaluación completa de la viabilidad miocárdica. La revascularización en pacientes con deterioro severo de la función ventricular y con miocardio viable disminuye mortalidad, mortalidad cardiovascular y reducción de hospitalizaciones.

**Palabras clave:** insuficiencia cardíaca, viabilidad miocárdica, deterioro ventricular severo, revascularización coronaria.

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## INTRODUCTION

Heart failure (HF) is a highly prevalent syndrome with high rates of hospitalization, disability, and mortality, and generates costs for the healthcare system. In the presence of mild HF-like symptoms, the annual risk of death is between 5% and 10%. However, it goes up to 30%-40% with severe symptoms and advanced stages of the disease<sup>1</sup>.

One of the main causes of left ventricular dysfunction is coronary artery disease. A transient ischemic event generates an imbalance between oxygen supply and demand with reversible damage to myocardial tissue<sup>12</sup>. If persistent in time, this event evolves into progressive ventricular dysfunction. Prolonged ischemia causes the rupture of cellular membranes and myocardial necrosis. The myocardium has mechanisms of acute and chronic adaptation to manage the transient or maintained reduction of coronary blood flow. Thanks to these mechanisms store enough energy to protect plasma membrane integrity and mitochondrial function at the expense of a lower force of contrac-

tion. This complex mechanism of adaptation has been described as hibernating myocardium.

The management of this HF is based on the optimal medical therapy (OMT) including drugs and angiotensin-converting enzyme inhibitors, beta-blockers, diuretics, sacubitril, and aldosterone antagonists. Also, myocardial revascularization combined with these drugs is another option to improve the patients' quantity and quality of life. The treatment strategy is based on the patient's clinical progression and functional state, degree of HF, spread of coronary artery disease, and identification of viable myocardium. The idea we have today of myocardial dysfunction due to transient ischemia is a viable myocardium that exhibits prolonged left ventricular dysfunction after the resolution of a discrete and transient episode of ischemia without evidence of necrosis. The revascularization of ischemic territories offers the possibility of improving the left ventricular (LV) function and, therefore, survival, although it is associated with a non-negligible mortality and morbidity rate. Therefore, the correct identification of this pathophysiological process and the right selection of patients who may benefit the most is of paramount importance<sup>19</sup>. A high-quality diagnostic methodology is essential here to be able to rule out the presence of hibernating myocardium, determine if the patient should be revascularized or not, receive a heart transplant or remain on medical therapy only.

The objective of this review was to assess the actual evidence on the pathophysiological processes of myocardial metabolism in the presence of ischemia and the adaptive

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responses of myocardial tissue, the role of detecting viability in patients with severe ventricular dysfunction, the different diagnostic methods available today to assess myocardial viability, the indicators, and the results of revascularization in selected patients.

## MATERIALS AND METHODS

An intense search of the different bibliographic sources was conducted between 2000 and 2019.

Randomized clinical trials, reviews, original articles, and medical consensus papers were looked into. The browser most often used for the searches was PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) that gives free open access to MEDLINE bibliographic database that includes references and abstracts on biomedical research and is run by the United States National Library of Medicine.

Also, non-indexed searches on consensus papers by the Argentine Society of Cardiology (SAC) were conducted since the knowledge accumulated in our field was considered necessary as well.

The following keywords were used in our queries both in isolation or combined with each other: "myocardial viability", "severe left ventricular dysfunction", "low ejection fraction", "myocardial stunning", "myocardial hibernation", "chronic heart failure", "ischemia", "revascularization", "PCI", "MRS."

When we had all the bibliographic material available, we proceeded to classify it by date and relevance. Articles published both in scientific journals with the highest impact factor and in Spanish or English were included. Low-impact journals or with a low number of patients recruited (such as brief communications and case reports) and papers published in languages different from the aforementioned were excluded.

## DEFINITIONS

Ischemic heart disease is defined as a myocardial dysfunction due to occlusive or obstructive coronary artery disease<sup>4</sup>.

There are different pathophysiological processes involved in Ischemic heart disease: stunned myocardium, hibernating myocardium or cellular death, and myocardial necrosis. Myocardial viability is defined as a tissue with enough blood flow to be able to preserve the integrity of cellular membranes and preserve metabolic activity with reversible dysfunction of the force of contraction.

Severe left ventricular dysfunction is defined as a left ventricular ejection fraction  $\leq 35\%$ . The complete optimal medical therapy (OMT) is the one recommended by clinical practice guidelines: diuretics, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II-receptor antagonists (ARAI) or angiotensin receptor-neprilysin inhibitors (ARNI), aldosterone antagonists (AA), and beta-blockers (BB) for the management of patients with severe ventricular dysfunction.

## PATHOPHYSIOLOGY: MYOCARDIAL CELLULAR METABOLISM

The main function of cardiac muscle cells (cardiomyocytes) is to perform the cardiac cycle of contraction and

relaxation. Under baseline conditions energy-rich sulfates like adenosine triphosphate (ATP) provide the energy needed to generate the contraction of cardiomyocytes. The ATP is produced through 2 different metabolic processes called oxidative phosphorylation and glycolysis<sup>5</sup>. When oxygen supply is normal, the metabolism of free fatty acids generates ATP and citrates that accumulate in the myocardial tissue suppressing the oxidation of glucose.

In the presence of sudden drops of coronary blood flow, the cardiac muscle starts producing energy from the anaerobic metabolism of glucose. This causes contractility disorders, a reduced action potential of the membranes, and changes in the conduction system. The production of high-energy phosphates through anaerobic glycolysis leads to the accumulation of glucose-1-phosphate, glucose-6-phosphate,  $\alpha$ -glycerophosphate, and lactate. As a result of this process, intracellular pH drops causing the accumulation of osmotically active particles (construct of glycolytic pathway) causing intracellular edema. The increased concentration of intracellular hydrogen ion ( $H^+$ ) induces the entry of sodium through the  $Na^+/H^+$  exchange. In turn, an excess of sodium induces the entry of calcium through the  $Na^+/Ca^{++}$  exchanger<sup>6</sup>. Calcium overload can change troponin levels contributing to a sensitivity loss to myofibrils inducing myocardial contractility alterations. In states of severe hypoperfusion, the rephosphorylation of ADP to ATP (draining the reserves of high-energy phosphates) and glycolytic enzymes are inhibited rupturing the cellular membrane and inducing cellular death.

Before cellular death arrives, the myocardium develops mechanisms of acute and chronic adaptation to the transient or maintained reduction of coronary blood flow: stunned myocardium and hibernating myocardium. Within the clinical setting both adaptive responses may coexist.

Stunned myocardium is due to the sudden reduction of coronary flow, which induces transient severe ischemia and reversible ventricular dysfunction if myocardial tissue perfusion can be recovered (depressed function at rest, preserved perfusion). Myocardial contractility often recovers within 1 to 2 weeks<sup>7</sup>.

Hibernating myocardium can be associated with reduced chronic contractility due to prolonged hypoperfusion at rest (reduced function and perfusion at rest) or to transient reduced coronary blood flow (repetitive stunning). Some studies have confirmed that tumor necrosis factor alpha (TNF- $\alpha$ ) and nitric oxide are overexpressed here promoting fibrosis and lack of myocardial contractile reserve<sup>8,9</sup>.

Unlike stunned myocardium, at histological level, hibernating myocardium presents changes both at the intra and extracellular levels. There are more glycogen deposits, loss of serial sarcomeres, myofibrils, and extracellular fibrosis. The severity of extracellular changes is associated with contractility recovery time after flow restoration.

Hibernating myocardium is a process of persistent exposure to coronary hypoflow with diffuse epicardial compromise that progresses to local and global ventricular systolic dysfunction. After revascularization, the hypokinetic myocardium can delay the recovery of contractile function between 6 to 12 months<sup>3</sup>. The reversibility of ventricular dysfunction will depend on the presence of viable myocardium. Therefore, if blood flow is restored, both the

stunned and the hibernating myocardia are potentially recoverable tissues.

For all these reasons, the prerequisites of cellular viability are:

1. the presence of enough myocardial blood flow to carry substrates to cardiac myocytes for metabolic processes and eliminate final products of metabolism;
2. the integrity of the cellular membrane; and
3. the preservation of intracellular metabolic activity.

We should mention how important it is to establish the presence of myocardial viability in patients with severe ventricular dysfunction because it is still possible to optimize treatment and restore the perfusion of myocardial tissue.

## VIABILITY ASSESSMENT. DIAGNOSTIC METHODS

In patients with HF, it is necessary to determine whether cardiac myocyte scan restore their contractile function if perfused properly. There are different diagnostic methods available to confirm the presence of viable myocardium:

1. Dobutamine stress echocardiography;
2. Single-photon emission computed tomography (SPECT);
3. Positron emission tomography (PET);
4. Cardiac magnetic resonance imaging (CMR).

### Dobutamine stress echocardiography

Stress echocardiography is an excellent imaging modality to assess and compare contractile reserve by measuring its motility, size, shape, and parietal thickness. Contractile reserve is the capacity of a myocardial segment to increase its performance after stimulation. The detection of contractile reserve with low doses of dobutamine is the distinctive seal of a viable myocardium.

The normal LV response to an increased workload represents a uniform increase of parietal motility, regional thickness, and a reduction of size of the end-systolic left ventricular cavity with minimum changes of diastolic size during exercise in vasodilatation. The motion and thickness of the wall during systole can be normal, reduced (hypokinetic), abnormal (dyskinetic) or absent (akinetic) in the dysfunctional left ventricle due to ischemia<sup>10</sup>. A reduced thickness of diastolic wall in the dysfunctional LV is indicative of scar tissue while a hypokinetic or dyskinetic segment with preserved systolic wall is probably indicative of a viable myocardium. A  $\geq 6$  mm myocardial thickening at the end of the diastole is considered viable while a thin, echogenic segment (fibrotic) is suggestive of scar.

The administration of dobutamine induces the contractility of viable segments both stunned and hibernating. The dobutamine-sensitive improved parietal motion predicts the later improvement of the regional thickening of the LV wall after revascularization<sup>5</sup>.

In the early phase, doses of 5-10  $\mu\text{g}/\text{kg}/\text{min}$  of dobutamine are used. Doses of up to 10-40  $\mu\text{g}/\text{kg}/\text{min}$  can be administered to detect ischemia. The viable myocardium has a biphasic pattern of response to dobutamine. During infusion at low doses, an improved parietal motion of the dysfunctional myocardium can be seen due to coronary flow and the recruitment of myocardial contractile reserve.

With higher doses, coronary flow will be reaching its limit. However, it will never go over the limit due to ischemia and the presence of coronary artery stenosis irrigating the region. A worse parietal motility will be seen too. The sensitivity and specificity of predicting the recovery of myocardial function using dobutamine stress echocardiography is 71% to 97% and 63% to 95% respectively, which is associated with a biphasic pattern of response that increases the degree of prediction.

This method has limitations regarding qualitative assessment with high interobserver variability and presence of poor acoustic window in some patients to be able to conduct the study.

We have the possibility of administering IV contrast that causes microbubbles that behave quite like red blood cells (due to their molecular weight) and cause myocardial opacification, which is indicative of the integrity of vascular microcirculation. In a viable myocardium there is normal or irregular segment perfusion. However, in a non-viable myocardium there is no perfusion. Contrast echocardiography can distinguish a stunned myocardium from necrosis. This imaging modality has higher sensitivity and similar specificity compared to dobutamine stress echocardiography.

### Single-photon emission computed tomography (SPECT)

It is a nuclear cardiology imaging modality where injected radiotracers are captured by the viable myocardium. The cardiomyocytes extract the isotope from the blood retaining it over a certain period of time. The myocardium emits photons based on the number of radiotracers captured which is associated with the perfusion of myocardial tissue. A gamma camera is used to capture these gamma-ray photons and turn them into visible light data. The final result of the SPECT is the creation of multiple slices that make up a digital image that represents the distribution of radiotracers in the heart. The 3D reconstruction is performed with images from the LV 3 myocardial axes: short axis, horizontal long axis, and vertical long axis.

The radiotracers used to perform a SPECT are thallium 201 and 3 classes of markers with technetium-99m: sestamibi, tetrafosmin, and teboroxim<sup>17</sup>. Thallium 201 is a monovalent cation with biological properties similar to potassium. It is captured by cardiomyocytes with integrity of their membranes through the  $\text{Na}^+/\text{K}^+/\text{ATPase}$  pump (active transport) and facilitated diffusion (approximately 85% of radiotracers). The maximum concentration of thallium occurs within the first 5 minutes depending on blood flow. Redistribution starts between 10 to 15 minutes after the injection of the tracers and depends on the intensity of the myocardial excretion of thallium. The kinetics of secretion is faster in normal myocardial tissues and slower in ischemic myocardia.

The uptake defect reversal since the initial overload until the acquisition of redistribution images (between 3 and 4 hours later) is indicative of viable myocardium with reversible ischemia. In the administration of thallium at rest, the reversibility of the initial uptake defect after late redistribution is indicative of viable myocardium with hypoperfusion at rest. The viable tissue can be identified when the late images show significant filling of the defects found on the early studies (absorption increase  $>10\%$ ) or in the pres-

ence of defect reversal while marker activity is  $>50\%$ <sup>15</sup>. On the other hand, necrotic myocardium shows an uptake defect both at rest and in redistribution images (a steady-state defect).

In some patients, uptake can be very much reduced after overload and not show the redistribution of images after 3 to 4 hours—even 24 hours later—due to coronary artery disease and presence of highly ischemic regions. The viable myocardium can be regulated by increasing the concentrations of thallium in blood through the reinjection of small doses at rest.

Sestamibi is the most studied liposoluble cationic compound 10 and the most widely used of these agents. The dispersion of Tc 99m in the myocardium is proportional to blood flow mainly through passive diffusion and gets trapped inside the mitochondria by the membrane electrochemical gradient. The absorption of these radioactive substances requires viable myocardial cells and an intact cellular membrane<sup>10</sup>. The studies conducted with Tc 99m require 2 separate injections: during maximum overload and at rest. That is how the reversibility of the uptake defect will present in the presence of viable myocardium, although it will not be possible to distinguish a stunned from a hibernating myocardium. Tc 99m-based tracers have a shorter half-life and exposure to radiation, and a greater preponderance of high-energy gamma emissions that reduce soft-tissue attenuation compared to thallium 201. The addition of nitrates improves both the uptake of the tracers and the accuracy of this imaging modality. Different studies were conducted comparing SPECT and PET (positron emission tomography) and SPECT underestimated the presence of myocardial viability. One of the setbacks of this imaging modality is its non-uniform soft-tissue attenuation (breast tissue, diaphragm or other extracardiac structures close to the heart) that degrades the quality of the images acquired or creates artifacts that mimic the actual anomalies of perfusion. Attenuation correction can improve the accuracy of viability tests using SPECT techniques. Attenuation correction should be patient-specific with an attenuation map created for image acquisition purposes.

### Positron emission tomography (PET)

This imaging modality uses nuclear technology to detect segments with reduced perfusion and/or myocardial metabolism in quantitative terms (which is an advance over the SPECT)<sup>20</sup>. Two different categories of positron-emitting radiotracers are used: 1) perfusion: rubidium-82 and [13N] ammonia; 2) metabolic tracers: [18F] fluoro-2-deoxy-D-glucose (FDG). The study protocol includes 2 parts: the initial study of myocardial perfusion and the study of myocardial metabolism. Traditionally, a study at rest is conducted that can also be used to study exertional ischemia if necessary.

Diagnoses are achieved by comparing the distribution of radiation activity to normal parameters or by measuring the rate of accumulation or disappearance of radioactivity in the long-term<sup>18</sup>. In normal conditions, the myocardium uses the oxidation of free fatty acids as energy source. However, in the presence of coronary flow alterations (presence of ischemia), oxidative metabolism is reduced, and the anaerobic metabolism of glucose is activated. The FDG uses the same transporter as glucose to enter the cell

which is why the FDG uptake is a marker of the glucose metabolism present in the viable myocardium. Four different uptake patterns during image acquisition can be distinguished: 1) mismatch between perfusion and metabolism: there is a reduced myocardial perfusion and contractile function with a normal FDG uptake suggestive of the presence of viable myocardium: hibernating; 2) regions of perfusion and normal metabolism with motility dysfunction in segments: it can be representative of a stunned myocardium and, in conditions of ventricular dilatation of the presence of remodeling; 3) segments with reduced perfusion and metabolism indicative of the presence of necrotic effects; and 4) reverse mismatch: normal perfusion with a reduced FDG uptake as seen in early revascularization after infarction, right branch bundle block, non-ischemic heart disease, and diabetes mellitus<sup>13</sup>.

Myocardial blood flow is a marker of viability because the viable tissue requires blood supply. Blood flow is often within normal or almost normal ranges in dysfunctional though viable myocardium suggestive that most of the reversible dysfunction is indicative of repetitive stunning, not hibernation. As described before, PET myocardial perfusion quantification is often used with the PET metabolic findings to identify viable myocardium that may benefit from revascularization.

### Cardiac magnetic resonance imaging (CMR)

CMR is a noninvasive imaging modality that does not use radiation. Instead, it uses a powerful magnetic field, radiofrequency impulses, and a computer to generate detailed images for the assessment of myocardial viability. Also, it provides information on the anatomy, global and regional left ventricular function, ischemia, and coronary flow. The phenomenon of magnetic resonance imaging occurs in the hydrogen nuclei (abundant in the human body and highly sensitive) that behave like magnets aligned with an external magnetic field. The excitement and relaxation of these nuclei transmits as a signal that can be used to generate images. Contrast among different tissues in the images depend on excitement delay, signal reading (TE or echo time), and the time elapsed between repeated excitations and radio waves (TR or repetition time). The different ways of contrast derive from 2 processes of main relaxation that affect net magnetization: the decay in the longitudinal axis (T1) and in the cross-sectional view (T2). The CMR draws a spatial map of radio signals<sup>5</sup>.

Two types of cardiac magnetic resonance imaging are often used to assess myocardial viability: dobutamine stress cardiac magnetic resonance imaging (DS-CMR) for the assessment of motility and parietal thickening, and delayed contrast-enhanced cardiac magnetic resonance imaging (CE-CMR) to distinguish ischemic from non-ischemic cardiomyopathies and be able to assess the presence of myocardial damage due to necrosis, fibrosis, inflammation or infiltration.

### Dobutamine stress cardiac magnetic resonance imaging

As it occurs with the echocardiography, it is used to measure the left ventricular dysfunction contractile reserve. The administration of dobutamine shows areas with contractile dysfunction and preserved parietal thickness ( $>5$  mm) indicative of preserved viability. The presence of transmural scar tissue between 50% and 75% of parietal

thickness is suggestive of a myocardial tissue that will not improve after revascularization. The improved contractile reserve seen after the administration of dobutamine, the parietal thickness seen at the end of diastole, and the quantification of necrotic tissue predict benefits for the myocardium if revascularized.

#### **Gadolinium-based magnetic resonance imaging (late enhancement).**

Several contrast agents can be used although for the management of cardiovascular system substances with gadolinium are used. This contrast agent is administered intravenously and remains at extracellular level. Therefore, under normal conditions, contrast never enters the cell. However, in the infarction or chronic fibrosis setting, the extracellular compartment expands at the expense of cellular disruption and the distribution of contrast is different. The kinetics of how gadolinium enters the myocardial infarction (MI) territory is delayed and after 10 to 15 minutes the distribution of gadolinium can be perfectly seen. The regions of necrotic tissue will show a high concentration of contrast (bright) compared to normal myocardium (black). Several patterns with gadolinium have been described: in the MI setting, there is late enhancement at subendocardial level with transmural spread depending on the size of infarction. Conversely, the presence of subepicardial late enhancement and at mid-wall level—whether diffused or in a patchy pattern—rules out the possibility of ischemic compromise. The spread of transmural enhancement is opposite to the prediction of functional recovery with revascularization, meaning that the presence of transmural late enhancement >50% of the wall has fewer chances of improving with treatment.

In the clinical practice, the visual estimate is the easiest method to quantify late enhancement with gadolinium by establishing a percentage of the infarcted myocardial thickness in relation to the global wall to be able to define transmural spread. A model established by the American Heart Association (AHA) is used. This model divides the ventricle into 17 segments with scores that go from 0 to 4 (0: no scar; 4:100% scar tissue). The segments final score divided by the total number of segments allows accurate assessments of the compromised ventricular mass<sup>7</sup>.

Late CMR imaging with gadolinium detects Q-wave MI and non-Q-wave MI accurately with such high sensitivity that it can show small MIs that cannot be seen on the SPECT<sup>5</sup>. Former studies have proven that the CMR can distinguish between the infarct core and the adjacent peri-infarction area that appears with a lower signal intensity due to the mixture of infarction and viable tissue. The larger the peri-infarction area the higher the chances of cardiac death and cardiovascular events in the future<sup>16</sup>. T1-mapping allows global and regional analyses of myocardial structure at microscopic level. Signal intensity at T1-weighted imaging is altered due to an increase of water or fibrosis in the tissue. The signal intensity at T1-weighted imaging intensifies in the presence of edema due to myocardial lesion, cellular edema, and necrosis and in cases of diffusion of extracellular space due to amyloidosis or focal or diffuse fibrosis<sup>7</sup>.

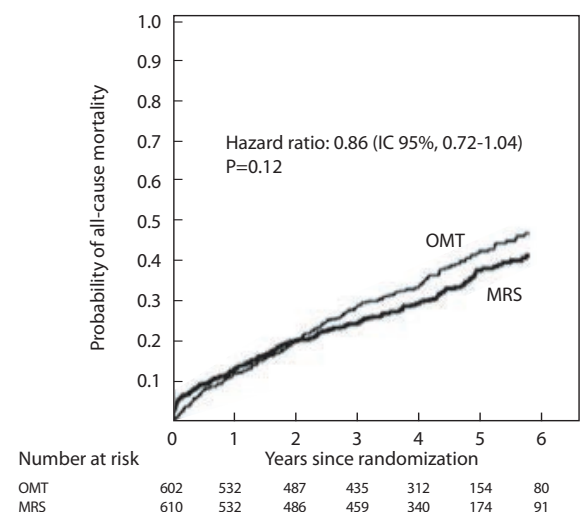
The advantages of CMR include the capacity to provide simultaneous information on anatomy, function, and perfusion with high-quality images.

## DISCUSSION

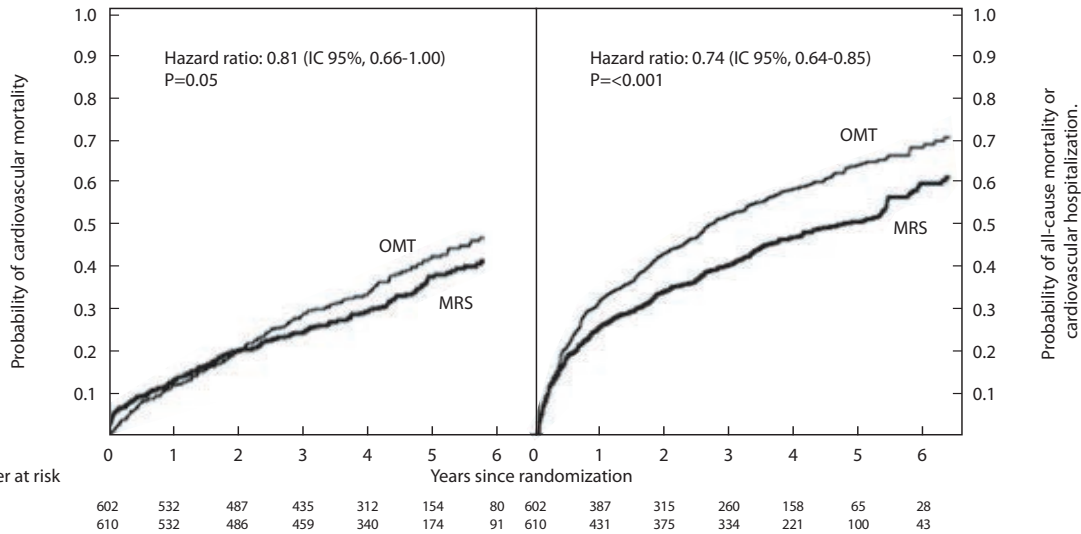
The detection of viable myocardium is essential to determine the optimal therapy of a subgroup of patients with HF due to atherosclerotic coronary artery disease.

Over the last few years several studies have been conducted on the recovery of cardiac contractility after revascularization in subjects with severely depressed ventricular function. These studies suggest that, currently, the CMR is the best option available to determine cardiac viability. However, since it is an expensive imaging modality that is not fully available everywhere, in our setting the remaining imaging modalities are valid options for the detection of viable myocardium.

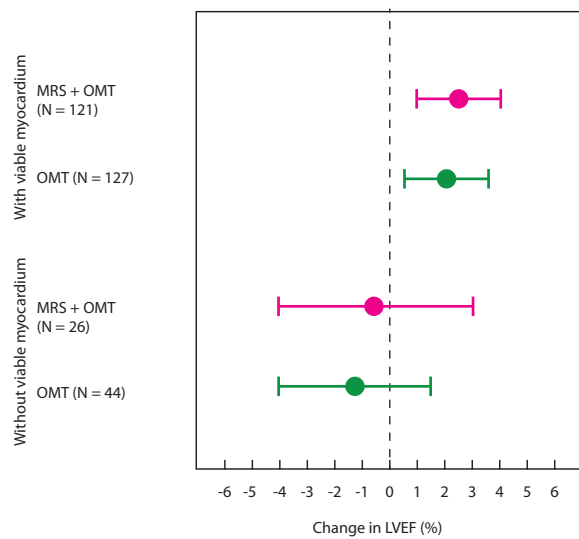
The STICH trial<sup>2</sup> is a randomized, multicenter study with 2 study hypotheses. The so-called Hypothesis #1 suggests that myocardial revascularization surgery (MRS) plus the optimal medical therapy (OMT) may reduce mortality compared to only the optimal medical therapy. From 2002 to 2007, a total of 1212 patients recruited were identified using SPECT or dobutamine stress echocardiography for the detection of myocardial viability and to assess all-cause mortality as the primary endpoint. The study secondary endpoints were cardiac death and hospitalizations. This study compared 602 patients who received OMT to 610 patients who received OMT plus conventional MRS. Nearly 17% of the patients from the OMT group were finally treated with revascularization therapy. Reasons were symptom progression (40%), acute decompensation (27%), family decision (28%), and the doctors' best clinical judgment since the study was not double-blind (5%). The median follow-up was 56 months until 2010. All-cause mortality rate (primary endpoint) was 41% in those who received OMT and 36% in those treated with MRS (hazard ratio of MRS=0.86, 95%CI [0.72-1.04], P=.12) (**Figure 1**). The cardiovascular mortality rate was 33% and 28% in patients treated with OMT and MRS, respectively (hazard ratio MRS=0.81, 95%CI [0.66-1], P=.05). Sixty-eight percent of patients treated with OMT and 58% of patients treated with MRS were hospitalized due to cardiovascu-



**Figure 1.** Adapted from Velazquez EJ et al. Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction. *New England Journal of Medicine* (2011).



**Figure 2.** Adapted from Velazquez EJ et al. Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction. *New England Journal of Medicine* (2011). The Kaplan-Meier curves of the STICH trial show a statistically significant benefit over OMT on the probabilities of cardiovascular mortality, all-cause mortality or cardiovascular hospitalization.



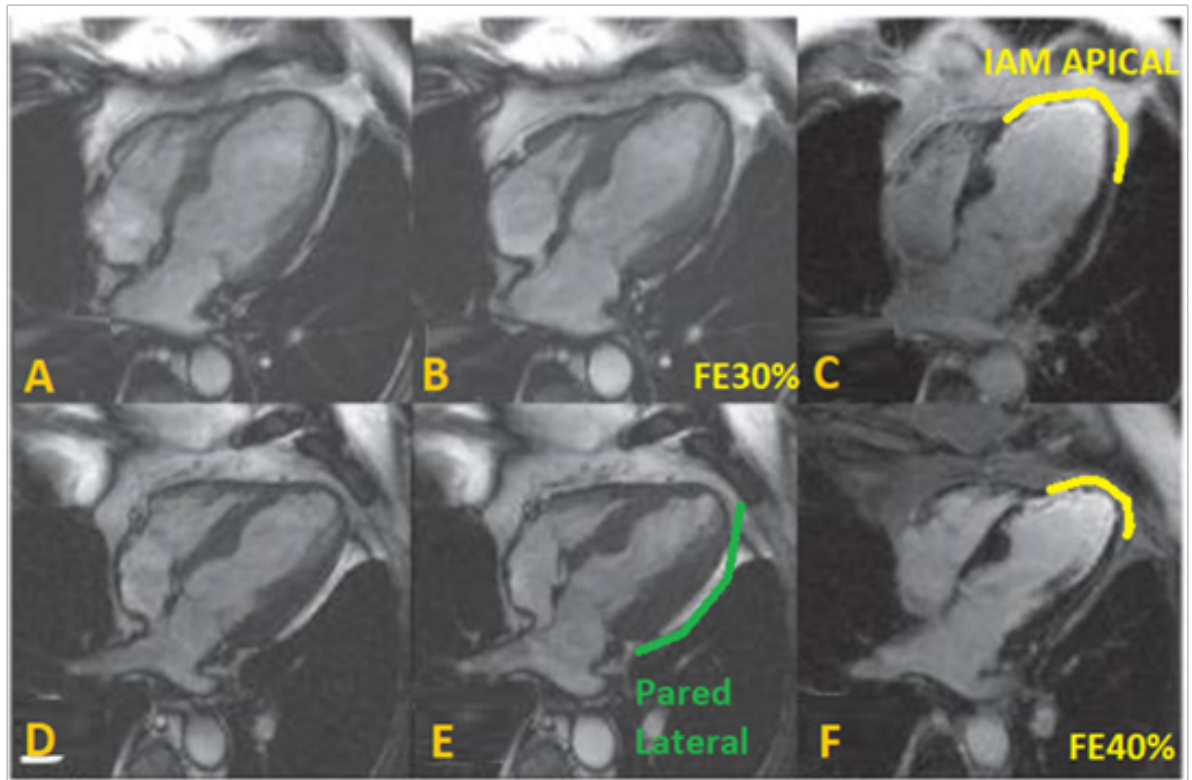
**Figure 3.** Adapted from Panza JA et al. Myocardial viability and long-term outcomes in ischemic cardiomyopathy, *New England Journal of Medicine* (2019). Left ventricular ejection fraction improved in patients with myocardial viability. Those who benefited the most were revascularized patients.

lar causes (hazard ratio of MRS=0.74, 95%CI [0.64-0.85], P <.001) (Figure 2). The intention-to-treat analysis showed a significant difference between both groups regarding the all-cause mortality rate. However, it was significantly favorable to patients treated with MRS regarding mortality and hospitalizations due to cardiovascular causes. However, the STICH trial was severely criticized<sup>11</sup>. In the first place, the detection of viability was determined by the doctors involved in the study based on availability with not much use of CMR, considered the best diagnostic imaging modality, or PET that also has high rates of sensitivity and specificity to assess myocardial viability. In the second place, this was not a double-blind study, meaning that the clinical knowledge of the patients by the doctors may have impacted the reasons that eventually led to hospital-

ization. Finally, no significant benefit was seen after years of follow-up.

In 2016 the STICHES trial was published<sup>14</sup>. The 10-year results showed a significant reduction of the main variable of all-cause mortality in patients randomized to MRS. This long-term follow-up study establishes that patients with ischemic heart disease and left ventricular dysfunction benefit from revascularization. In the presence of dilated ischemic-necrotic cardiomyopathy with evidence of myocardial viability, MRS seems beneficial as long as the conditions established in the STICH trial are observed (surgical centers experienced in the management of patients with moderate-to-severe ejection fraction dysfunction and low mortality rate). For the management of severe ventricular function dysfunction with a significantly viable myocardial mass (>20%), MRS seems like a good and valid treatment option if the coronary anatomy is technically eligible for bypass surgery.

Back in 2019, a subanalysis of the STICHES trial<sup>23</sup> was published. It assessed the correlation between the detection of myocardial viability and the benefit of revascularization and medical therapy. However, it did not provide enough statistical evidence on the presence of myocardial viability and lower mortality rate. However, the ejection fraction actually improved in patients with viable myocardium regardless of the treatment used (Figure 3). The authors mention the existence of a biological correlation between myocardial viability and the benefit of revascularization that could not be proven maybe because of the number of patients with non-viable myocardium (19%) compared to those with actually viable myocardium (81%). The clinical guidelines of the European Society of Cardiology (ESC)<sup>21</sup> establish the benefit of revascularizing patients with ischemic-necrotic chronic HF and severe ventricular dysfunction. This benefit may be actually seen in practice by performing a baseline CMR and after revascularization resulting in improved ejection fraction and regional motility (Figure 4). Although clinical practice guidelines recommend revascularizing these patients, the optimal strategy has not been established yet. Both MRS



**Figura 4.** Adapted from Thielmann M et al. Magnetic resonance imaging in coronary artery bypass surgery – improvement of global and segmental function in patients with severely compromised left ventricular function by M Thielmann. *Vasc Health Risk Manag* (2007). Cardiac magnetic resonance imaging of a 64-year-old male patient before (upper line) and after (lower line) coronary revascularization. The end-diastolic (A) and end-systolic images (B) reveal a severe left ventricular systolic dysfunction before surgery (EF of 30%) that is akinetic in the inferior septal wall, apical anterolateral wall, and apical wall, and hypokinetic in the lateral basal and mid wall. The image in (C) shows wide late subendocardial enhancement (bright signal) in the apical septum, thin in the lateral wall, and transmural in the apex indicative of chronic scar. The left ventricular function after surgery (D, E) does not show an improved apical septum or apex while the entire lateral wall actually improved and turned normokinetic. No changes were seen on the spread of the scar (F). The global left ventricular function improved with an EF of 40% while left ventricular volumes decreased.

and percutaneous coronary intervention (PCI) should be assessed and decided upon by the heart team while taking into consideration the patient's opinion, his coronary anatomy, comorbidities, and myocardial viability. The clinical trials that compared MRS and PCI often exclude patients with ventricular ejection fractions  $\leq 35\%$ .

The clinical practice guidelines (2016) of the Argentine Society of Cardiology (SAC) for the management of chronic heart failure establish that the coronary revascularization of ischemic territories may improve left ventricular function and survival and should be considered in all patients with HF. Therefore, it is of paramount importance to know what patients with myocardial viability may benefit from this intervention. Therefore, the SAC guidelines recommend MRS or PTA (percutaneous transluminal angioplasty) in patients with severely depressed left ventricular ejection fraction and a significant lesion in the left main coronary artery or its equivalent or multiple vessel disease with compromise to the proximal left anterior descending coronary artery with myocardial viability (Class I, level of evidence C). Also, the SAC guidelines recommend MRS in patients with ventricular dysfunction and a significant non-contractile myocardial mass without the coronary characteristics described above (Class IIa, level of evidence B)<sup>1</sup>.

At the same time, in its guidelines for the management of ST-segment elevation acute myocardial infarction published in 2015, the SAC recommends assessing myocardial viability (without establishing a specific method including echo-

cardiogram, SPECT, PET or CMR) in patients with multiple vessel disease or in cases where myocardial revascularization may be considered (Class I, level of evidence C)<sup>22</sup>.

## CONCLUSION

Myocardium develops different adaptive processes to manage transient or chronic ischemia. Both myocardial stunning and myocardial hibernation suggest viability states that can be reversed through revascularization by eliminating exposure to ischemia.

The correct identification of viable myocardium is essential to develop a therapeutic strategy based on OMT and revascularization. The cardiac magnetic resonance imaging is considered the best imaging modality of all due to its high resolution and quality of images regarding myocardial viability. Also, because it provides additional information on the size and function of the left ventricle and other structures (valves, aorta) that can contribute to the strategy to be followed. However, PET is also a valid option for the complete assessment of myocardial viability compared to the other imaging modalities. Hybrid imaging modalities are still in the pipeline for future use in clinical practice.

Revascularization plus the optimal medical therapy improved mortality, cardiovascular mortality, and shortened the hospital stay. The detection of these myocardial adaptive processes that have been known for decades has not been statistically confirmed yet. In this context, the pres-

ence of myocardial viability should be interpreted individually in each particular case to be able to choose the best possible treatment. Both the ESC and the SAC inform on the role that the de-

tection of myocardial viability plays in the comprehensive assessment of patients with ischemic-necrotic HF and severe ventricular dysfunction to determine the best therapeutic strategy and what patients will benefit from such strategy.

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# Coronary transluminal angioplasty in bifurcation of the anterior descending coronary artery, using the crush stenting technique

## Angioplastia transluminal coronaria en bifurcación de arteria descendente anterior, con técnica de *crush stenting*

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### ABSTRACT

**Introduction.** Coronary angioplasty for the management of obstructive bifurcation lesions is associated with a high degree of cardiovascular complications. This article shows the immediate and mid-term results of patients with unstable angina and obstructive bifurcation lesions of the left anterior descending and first diagonal coronary arteries treated using the crush stenting technique.

**Material and methods.** Twelve consecutive patients were treated between January 2018 and July 2019. For the crush stenting technique, two Promus PREMIER™ everolimus-eluting platinum chromium stents were used.

**Results.** The mean age was 60±7 years. One third of the patients (n=4; 33.3%) showed 3-coronary vessel disease and 2 of the bifurcations treated (n=2; 16.7%) revealed in-stent restenosis. All procedures (n=12; 100%) were technically successful and the patients had no major complications during hospitalization. During the patient's mid-term disease progression, the death of a male patient (n=1; 8.3%) was reported 3 months after hospital discharge due to heart failure. The actuarial survival free of major adverse cardiovascular events (myocardial infarction, target lesion revascularization, stroke and/or death) at the 24-month follow-up was 92%.

**Conclusions.** Coronary angioplasty in a very select group of patients with unstable angina, obstructive bifurcations of the left anterior descending and first diagonal coronary arteries using the crush stenting technique followed by the implantation of 2 Promus PREMIER™ everolimus-eluting stents was safe and showed a low rate of major cardiovascular adverse events in the mid-term.

**Keywords:** coronary artery disease, bifurcation lesions, drug-eluting stents.

### RESUMEN

**Introducción.** La angioplastia coronaria de obstrucciones en bifurcación se asocia con un alto grado de complicaciones cardiovasculares. Esta publicación presenta los resultados inmediatos y a mediano plazo de pacientes con angina inestable y obstrucciones coronarias en bifurcación de arteria descendente anterior y primera diagonal, tratadas con la técnica de crush stenting.

**Material y métodos.** Se trataron 12 pacientes consecutivos entre enero de 2018 y julio de 2019. Para la técnica de crush stenting se utilizaron dos stents de cromo-platino, liberadores de everolimus, Promus PREMIER™.

**Resultados.** La edad fue de 60±7 años. Un tercio de los pacientes (n=4; 33,3%) tenía enfermedad de tres vasos coronarios y dos bifurcaciones tratadas (n=2; 16,7%) fueron reestenosis intrastent. Todos los procedimientos (n=12; 100%) fueron técnicamente exitosos y los pacientes no tuvieron complicaciones mayores durante su internación. En su evolución a mediano plazo se registró la muerte de un hombre (n=1; 8,3%) a los 3 meses del alta hospitalaria por insuficiencia cardíaca. La sobrevida actuarial libre de eventos cardiovasculares adversos mayores (infarto de miocardio, revascularización de la lesión tratada, accidente cerebro-vascular y/o muerte) a 24 meses de seguimiento fue de 92%.

**Conclusiones.** La angioplastia coronaria de un grupo muy selecto de pacientes, con angina inestable, obstrucciones de bifurcación de arteria descendente anterior y primera diagonal, con la técnica de crush stenting e implante de dos stents liberadores de everolimus Promus PREMIER™ fue segura y presentó una baja tasa de eventos cardiovasculares adversos mayores a mediano plazo.

**Palabras clave:** enfermedad arterial coronaria, lesiones en bifurcación, stents liberadores de drogas.

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### INTRODUCTION

Despite the advances made in the technique and materials used to perform the percutaneous transluminal angioplasty (PTA), the management of obstructive bifurcation lesions is associated with a high degree of cardiovascular complications. We should mention not only the possibility of periprocedural lateral branch occlusion<sup>1</sup>, but also the higher rate of restenosis anticipated in the long run<sup>2</sup>.

Bifurcation lesions represent 20% of all coronary interventions performed and are present in 30% of the patients with multivessel disease<sup>3</sup>.

The crush stenting technique is a therapeutic option that consists of implanting 2 drug-eluting stents<sup>4</sup>. The first stent is implanted into the lateral branch leaving between 2 mm to 3 mm of its proximal border inside of the main vessel lumen. Afterwards, a second stent is implanted in the main vessel crushing the proximal border of the first stent. The procedure ends with the simultaneous inflation of 2 balloons in both stents (the so-called kissing balloon technique)

This article presents the immediate and mid-term results of patients with unstable angina and obstructive bifurcation lesions of the left anterior descending and first diagonal coronary arteries treated using the crush stenting technique.

### MATERIAL AND METHODS

This was a retrospective, randomized study of 12 consecutive patients with unstable angina and obstructive bifurcation lesions of the left anterior descending and first

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**TABLE 1.** Clinical characteristics (n=12).

Age (years)	60±7
Male sex	9 (75%)
Unstable angina (Braunwald)	
Class II B	8 (66.6%)
Class III B	2 (16.7%)
Class III C	2 (16.7%)
Cardiovascular history	
Heart failure	5 (41.6%)
Acute myocardial infarction	1 (8.3%)
Coronary angioplasty	2 (16.7%)
Cardiovascular risk factors	
Family history	3 (25%)
Arterial hypertension	11 (91.7%)
Smoking	7 (58.3%)
Diabetes Mellitus	4 (33.3%)
Hypercholesterolemia	3 (25%)

diagonal coronary arteries treated using the crush stenting technique (10 patients with de novo lesions and 2 patients with in-stent restenosis). Procedures were performed after obtaining the patients' written informed consent between January 2018 and July 2019 (5 at the Hospital Nacional de Clínicas and 7 at the Clínica Chutro, Ciudad de Córdoba, Argentina).

The patients' baseline characteristics, clinical features, and coronary anatomy were studied. Their unstable angina was assessed using the Braunwald classification. Coronary obstructions  $\geq 70\%$  (as seen on the quantitative coronary angiography) were considered severe.

The Medina classification<sup>5</sup> was used to categorize coronary bifurcations, based on the 3 elements bifurcations can be divided into: proximal main vessel, distal main vessel, and secondary branch. Respecting this sequence, the Medina classification assigns a binary value (1,0) depending on whether or not the obstructions of the segments mentioned before are  $>50\%$ .

For the angiographical assessment of the myocardial mass at risk and given the chances of diagonal branch occlusion, the SNUH score was estimated<sup>6</sup>. This score analyzes 3 variables combined: diameter (size "S"), number (number "Nu") and height (highest "H") of diagonal branches with scores from 0 to 3.

The stratification of bifurcation lesions as simple or complex was based on major and minor criteria from the DEFINITION Study<sup>7</sup>. Complex lesions should meet, at least, 1 major criterion (1 diagonal branch with a 70% stenosis and/or plaque length  $\geq 10$  mm), and 2 minor criteria (lesion length of the left anterior descending coronary artery  $\geq 25$  mm; multiple obstructions; bifurcation angle type B  $\leq 45^\circ$  or  $\geq 70^\circ$ ; diameter of the left anterior descending coronary artery  $\leq 2.5$  mm; moderate-to-severe calcification; lesions with thrombotic component).

The bifurcation angle type B originated at the distal segment of the left anterior descending coronary artery and the diagonal branch was studied too. It was measured angiographically in a left anterior oblique  $30^\circ$ , cranial  $30^\circ$  projection. Low-grade B angles were  $\leq 70^\circ$  (bifurcation in "Y") and high-grade B angles were  $>70^\circ$  (bifurcation in "T").

When the obstruction-to-treat showed in-stent restenosis, the Mehran R et al classification<sup>8</sup> was used based on the location and spread of intimal hyperplasia in relation to the stent implanted. Class I: focal lesion,  $<10$  mm spread. Class II: in-stent diffuse lesion,  $>10$  mm spread.

**TABLE 2.** Cine coronary arteriography (n=12).

Coronary lesions	
De novo	10 (83.4%)
In-stent restenosis	2 (16.6%)
Number of compromised coronary arteries	
1 vessel	6 (50%)
2 vessels	2 (16.7%)
3 vessels	4 (33.3%)
Left main coronary artery	1 (8.3%)
Medina classification	
1.1.1	10 (83.4%)
0.1.1	1 (8.3%)
0.0.1	1 (8.3%)
SNUH Score	
1	3 (25%)
2	4 (33.3%)
3	5 (41.7%)
Type of coronary lesions	
Simple	5 (41.7%)
Complex	7 (58.3%)
Bifurcation angle type B	
Low grade ( $\leq 70^\circ$ )	9 (75%)
High grade ( $>70^\circ$ )	3 (25%)

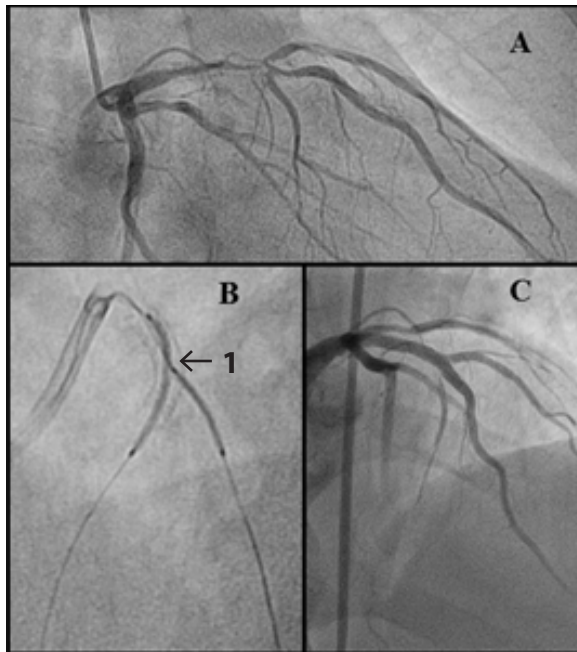
Class III: diffuse lesion in and out of the borders of the stent,  $>10$  mm spread. Class IV: complete occlusion of the stent.

All patients showed severe obstructive bifurcation lesions of the left anterior descending and first diagonal coronary arteries and were treated using the crush stenting technique with 2 Promus PREMIER™ everolimus-eluting platinum chromium stents (Boston Scientific, Ireland). In order to selectively access the diagonal branch after stent implantation into the left anterior descending coronary artery (recrossing or rewiring) the PT<sup>2</sup>™ Moderate Support coronary guidewire (Boston Scientific, Costa Rica) was used. The final kissing balloon technique was used with balloons of the same or smaller diameter compared to the balloons of the stents implanted. Only non compliant coronary balloons were used in cases of suboptimal stent expansion according to the StentBoost™ technique (the StentBoost™ is a simple, easy-to-use imaging modality that improves the visualization of the stent after eliminating background noise and anatomical structures).

Before the PTA, the patients were already on aspirin 100 mg/day PO and clopidogrel 75 mg/day PO or prasugrel 10 mg/day PO. The clinical, electrocardiographic, and laboratory parameters were assessed the next day. Patients with prolonged angina pectoris ( $>30$  minutes), new Q-waves on the electrocardiogram, and high CPK-MB levels (7-25 IU/L) were diagnosed with acute myocardial infarction post-PTA.

Angiographic success was defined as the implantation of both stents in the bifurcation area using the crush stenting technique with residual stenosis  $<30\%$  and TIMI grade 3 flow. Clinical success was defined as patients with angiographic success who were discharged from the hospital without any major cardiovascular complications (hematomas at the puncture site requiring blood transfusion, acute myocardial infarction, coronary revascularizations, stroke and/or death). After hospital discharge all patients remained on aspirin 100 mg/day PO continuously and clopidogrel 75 mg/day PO or prasugrel 10 mg/day PO for, at least, 12 months.

The patient's mid-term disease progression (between 6 and 24 months after hospital discharge) was clinically assessed as actuarial survival free of major adverse cardio-



**Figure 1.** Crush stenting technique for the management of in-stent restenosis (4 months after the PTA to the left anterior descending coronary artery). A: Image before the angioplasty (Medina 1.1.1). B: Positioning of the stents in the diagonal (Promus PREMIERTM 2.5 mm x 20 mm) and left anterior descending coronary arteries (Promus PREMIERTM 3.0 mm x 28 mm). (1) Stent into the left anterior descending coronary artery previously implanted. C: Final outcome.

vascular events (acute myocardial infarction, target lesion revascularization, stroke and/or death). Data were obtained from the patients' clinical histories or through direct consultation with general physicians. Angiographic restenosis was defined as percent diameter stenosis  $\geq 50\%$  in the stents implanted (inside the stent and/or in the 5 mm outside the proximal or distal borders).

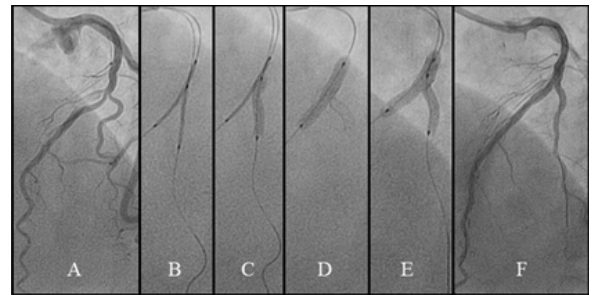
Continuous variables were expressed as mean  $\pm$  standard deviation (SD) and qualitative variables were expressed as percentage (%). The actuarial life tables and the Kaplan-Meier approach for survival analysis were used. Survival that was expressed as mean survival.

## RESULTS

The patients' baseline characteristics are shown on Table 1. The mean age of the patients was  $60 \pm 7$  years and most of them had clinical signs of unstable angina Class II B (n=8; 66.6%).

Angiographic characteristics are shown on Table 2. A third of the patients (n=4; 33.3%) showed 3-vessel disease. Two of the bifurcations treated (n=2; 16.7%) revealed in-stent restenosis (Figure 1). Both cases were treated using a conventional coronary stent (bare-metal stent) previously implanted in the left anterior descending coronary artery. One stent was implanted after 4 months (Mehran Class III) and the other after 12 months (Mehran Class IV) prior to the date of the procedure.

Table 3 shows the characteristics of the PTA. All procedures were performed via femoral access using a 7-Fr guide catheter and 2 Promus PREMIERTM everolimus-eluting platinum chromium stents (Boston Scientific, Ireland). The diameter of the stent implanted in the left anterior descending coronary artery was usually 3 mm



**Figure 2.** Crush stenting technique without predilatation (direct). A: Image before the angioplasty (Medina classification 0.1.1). B: Positioning of the stents in diagonal (Promus PREMIERTM 2.5 mm x 12 mm) and left anterior descending coronary arteries (Promus PREMIERTM 3.0 mm x 16 mm). C: Stent implantation into diagonal artery. D: Stent implantation into the left anterior descending coronary artery (crush). E: Kissing balloon. F: Final outcome.

**TABLE 3.** Percutaneous transluminal angioplasty (n=12).

Diameter of the stents implanted into the left anterior descending coronary artery	
2.75 mm	2 (16.7%)
3.00 mm	9 (75%)
3.50 mm	1 (8.3%)
Diameter of the stents implanted into the first diagonal artery	
2.25 mm	2 (16.7%)
2.50 mm	6 (50%)
2.75 mm	3 (25%)
3.00 mm	1 (8.3%)
Additional stents	
Implanted into the left anterior descending coronary artery	2 (16.7%)
Implanted into the first diagonal artery	1 (8.3%)
Combined angioplasty	
To left circumflex artery	1 (8.3%)
To left main coronary artery	1 (8.3%)
Crush without predilatation	2 (16.7%)
Final kissing balloon	12 (100%)
StentBoost	5 (41.7%)
Angiographic success	12 (100%)
Clinical success	12 (100%)

(n=9; 75%), 2.5 mm when implanted in the first diagonal artery (n=6; 50%). In 2 patients (n=2; 16.7%) with proximal dissection of the left anterior descending coronary artery an additional 3.5 mm x 16 mm Rebel™ platinum chromium stent (Boston Scientific, Ireland) was implanted. In another patient (n=1; 8.3%), an additional 2.5 mm x 20 mm Promus PREMIERTM stent (Boston Scientific, Ireland) was implanted in the first diagonal artery due to distal dissection. In another patient (n=1; 8.3%) a PTA was performed in the left circumflex artery with a 3.0 mm x 18 mm Waltz™ cobalt chromium stent (Microport Inc. Shanghai, China). In another patient (n=1; 8.3%), a 4.0 mm x 16 mm Promus PREMIERTM stent (Boston Scientific, Ireland) was implanted in the left main coronary artery due to a previous obstructive lesion. The crush stenting technique without predilatation (direct) was used in 2 patients (n=2; 16.7%) (Figure 2).

Angiographic success was confirmed in all of the lesions treated and no patient had major cardiovascular complications during the hospital stay. Eleven patients (n=11; 91.6%) were discharged from the hospital the day after the procedure and none of them had high CPK-MB levels. Only 1 patient (n=1; 8.3%) remained hospitalized for 5 days for the implantation of a new definitive pacemaker due to atrioventricular conduction block (prior to the PTA).

**TABLE 4.** Disease progression after hospital discharge at the 24-month follow-up (n=12).

Acute myocardial infarction	0 (0%)
Revascularization	
of the lesions treated	0 (0%)
of other lesions	1 (8,3%)
Death	1 (8,3%)
Actuarial survival free of MACE	92%
Control cine coronary arteriography	3 (25%)
Angiographic restenosis	0 (0%)

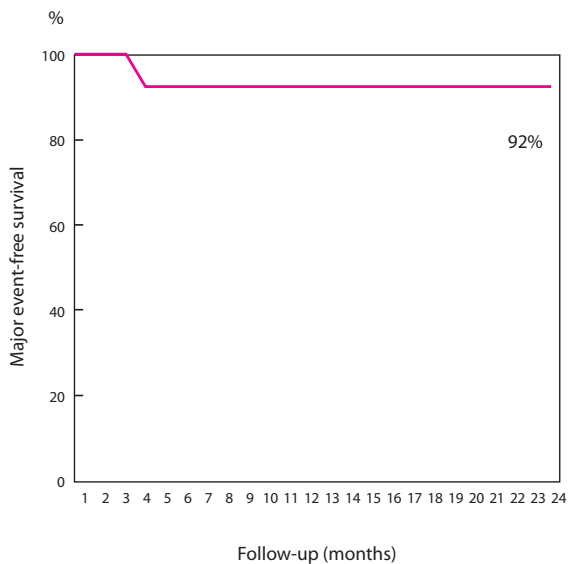
MACE, major adverse cardiovascular events.

Clinical follow-up was conducted in all of the patients (n=12; 100%) for an average  $15.6 \pm 5.8$  months after hospital discharge (Table 4). A 56-year-old male (n=1; 8.3%) with a past medical history of angina following an acute myocardial infarction (Class III C), 3-vessel disease, and cardiogenic shock died 3 months after hospital discharge due to heart failure. The actuarial survival free of major cardiovascular adverse events at the 24-month follow-up was 92% (Figure 3).

Three patients (n=3; 25%) underwent control cine coronary arteriographies at the follow-up. None of them showed angiographically significant restenosis of bifurcation stents in the left anterior descending and first diagonal coronary arteries. The first patient was a 55-year-old male who underwent a control angiography at the 7-month follow-up in the course of an eligible PTA of the left circumflex artery. The second patient was a 70-year-old male who underwent a cine coronary arteriography at the 10-month follow-up due to unstable angina class II B and a myocardial perfusion imaging modality with thallium 201 that tested positive for the presence of myocardial ischemia at inferior, inferior-lateral, and LV apex level. The cine coronary arteriography confirmed the patency of bifurcation stents in the left anterior descending and first diagonal coronary arteries. However, due to a severe de novo obstruction of the left main coronary artery the patient was treated with myocardial revascularization surgery (coronary artery bypass graft). The third patient was a 69-year-old male who underwent a control angiography at the 19-month follow-up due to atypical precordial pain (without a previous myocardial perfusion study). The angiography showed a patent stent inside the left anterior descending coronary artery and in-stent proliferation of the diagonal artery with a 40% lumen compromise (the patient remained on medical treatment).

## DISCUSSION

The strategies for the percutaneous management of coronary bifurcations are varied. They are often divided into simple or complex. Basically, simple strategies refer to the provisional stenting technique that consists of initial stent implantation into the main vessel followed by second stent implantation into the lateral branch in case of occlusion or significant stenosis of this vessel. Complex strategies include a group of techniques that initially use the elective double stenting technique by implanting 1 stent into the main vessel followed by a second stent into the lateral branch<sup>9</sup>. It is reasonable to use the initial double stenting technique in patients with complex coronary bifurcation anatomies that compromise a large caliber lateral branch with high risk of occlusion



**Figure 3.** Actuarial survival free of major cardiovascular adverse events (myocardial infarction, target lesion revascularization, stroke, and/or death) at the 24-month follow-up.

and low chances of recovery (Class IIa; level of evidence: B)<sup>10</sup>. In line with this concept, it is imperative to define what is considered a complex bifurcation lesion. After the analysis of 1500 procedures strictly controlled (training group), the DEFINITION Study established the differences between simple and complex coronary bifurcation lesions based on easily applicable angiographic parameters<sup>7</sup>. They reported on 3660 patients (study group) with complex lesions (7 out of 12 patients in our own experience, 58.3%). In these patients the double stenting technique had a significantly lower annual mortality rate compared to the use of the provisional stenting technique (2.8% vs. 5.3%;  $P=0.047$ ). The DEFINITION II is a recently published study that provides evidence in favor of the early double stenting technique for the management of complex coronary bifurcations. This study compared the double and provisional stenting techniques in 653 patients from 49 international centers. Within the double stenting group, most of the lesions treated were bifurcations of the left anterior descending and diagonal coronary arteries (62.5%). The final composite endpoint was target lesion failure at the 1-year follow-up [6.1% for the double stenting technique and 11.4% for the provisional stenting technique ( $P=0.019$ )]. No significant differences were seen in the mortality rate reported between both techniques (2.1% vs. 2.5%;  $P=0.772$ ), meaning that the benefit mainly came from the lower rates of target vessel related myocardial infarction (3.0% vs. 7.1%;  $P=0.025$ ) and clinically guided target lesion revascularization (2.4% vs. 5.5%;  $P=0.049$ ) of the double stenting group<sup>11</sup>.

The crush stenting technique is a double stenting technique that was first described by Colombo A et al.<sup>4</sup> This technique is used to make sure that the ostium of the lateral branch is circumferentially covered by the metal mesh of the stents to avoid its occlusion during or immediately after the procedure. Also, if drug-eluting stents are implanted, the release of higher doses of the drug per square millimeter is guaranteed<sup>5</sup>.

In our study bifurcations were studied using the Medina

classification since it is an easy-to-use and generally accepted classification tool. However, one of its limitations is that it does not measure the size of the territory irrigated by the diagonal branch and the distal left anterior descending coronary artery outflow tract (bifurcation angle type B).

Louvard Y et al.<sup>12</sup> say that, basically, a significant lateral branch is the one you don't want to lose at all in a patient. It is important to define what diagonal branch diameters may be considered significant since their occlusion can trigger acute myocardial infarctions. This definition is arbitrary, but most studies speak of significant lateral branches >2.2 mm in diameter<sup>13,14</sup>. In our own experience, this parameter could be seen in the diameter of the stent implanted into the diagonal branch ( $\geq 2.25$  mm in every patient). However, Koo B-K et al.<sup>6</sup> proved that the sensitivity of the diagonal branch diameter to assess myocardial masses at risk is low. They claim that after selectively inflating an occlusion balloon for 1 minute in 1 vessel  $\geq 2.5$  mm, only 48% of the cases showed ST-segment elevation. On the contrary, with SNUH scores  $\geq 2$  (75% in our own experience) including the diameter, number, and distribution of diagonal branches, sensitivity went up from 58% to 83%. Afterwards, the SNUH score was changed (m-SNUH score) including a new variable: the presence, or not, of a dominant circumflex artery or an obtuse marginal branch irrigating the cardiac apex<sup>15</sup>. Similarly, the ERACI score weighs in on the risk of patients with multiple vessel coronary artery disease who are eligible for coronary angioplasty or coronary artery bypass graft surgery. It does not include patients with small vessel lesions (<2.0 mm) or intermediate obstructions (from 50% to 69%). As Rodríguez A et al.<sup>16</sup> pointed out, the ERACI score reduces to less than 20% the patients considered of high-risk to undergo a PTA according to the original SYNTAX score. Although it is an angiographic score, the ERACI generates clinical results similar to those of patients with FFR-guided (guided by fractional flow reserve) revascularizations considered "functional revascularizations".

The bifurcation angle type B is another determinant factor to plan the strategy that should be used. When the B-angle is  $\leq 70^\circ$  (9 patients in our series, 75%), the initial use of a double stent technique is advised because these stents can cover the ostium of the lateral branch ostium completely facilitating the inflation of the final kissing balloon. However, when the B-angle is almost  $90^\circ$  (as it was the case with 3 of our 12 patients, 25%), the T-stent technique is advised. However, with this technique we run the risk of an incomplete coverage of the ostium of the diagonal branch with the corresponding risk of acute thrombosis and higher rate of restenosis during disease progression after hospital discharge<sup>17</sup>.

In order to achieve better immediate and mid-term results the kissing balloon technique needs to be used. In our own experience it was used in all the procedures. After implanting the stent into the left anterior descending coronary artery, the ostium of the diagonal branch is jailed by a double mesh of stents. The challenge here is to recross it with a coronary guidewire followed by dilatation with a low-profile balloon and eventually postdilatation with a double balloon. Several studies report failure rates between 8% to 28% when trying to do this<sup>5,10,18,19</sup>. As Ge L et al.<sup>20</sup> proved when they compared patients treated using the crush stenting technique and divided them into

2 groups depending on whether the final kissing balloon technique was used. Clinical success was lower in the group without final postdilatation with double balloon and the rate of restenosis and major adverse cardiovascular events at the 9-month follow-up was higher (38.5% vs 19.8%;  $P=.008$ ). Although the reasons that made the final kissing balloon technique fail are not clear, the studies attribute as potential factors the structure and diameter of the stent of the main vessel and the distortion caused by the crushing<sup>21</sup>. To overcome this, back in 2005, Chen S-L et al.<sup>22</sup> published a modification of the crush stenting technique that they called double kissing crush (DK crush) technique. After implanting the stent into the lateral branch, the crushing is performed with a balloon, instead of a stent, into the main vessel. Then, the first kissing balloon causes the circumferential displacement of the lateral branch stent struts facilitating the coronary guidewire re-crossing and the final kissing balloon technique. Afterwards, the DK crush technique improved with the use of noncompliant coronary balloons inflated at high pressure in each kissing balloon and the proximal optimization technique (POT) that consists of dilating the proximal border of the stent implanted into the main vessel using a high-pressure balloon<sup>23</sup>.

The DKCRUSH-I<sup>24</sup> study compared the traditional crush stenting technique (156 patients) and the DK crush technique (155 patients) and reported a final kissing balloon inflation rate of 76% and 100%, respectively ( $P<.001$ ), and a significant reduction of in-stent thrombosis, restenosis, and major adverse cardiovascular events at the 8-month follow-up favorable to the new technique. The authors say that one of the limitations of the study is the non-routine use of intravascular ultrasound (IVUS) considered the standard of care to diagnose stent underexpansion<sup>25</sup>. In our own experience, the IVUS was not used. However, the StentBoost<sup>TM</sup> was used in 5 procedures (41.7%). StentBoost<sup>TM</sup> is a software developed by Philips to improve the angiographic visualization of stent expansion. It is easy to use, helps detect stent underexpansion, stimulates postdilatation, does not delay the procedure, and can reduce the risk of stent thrombosis and in-stent restenosis<sup>26,27</sup>.

The management of patients with in-stent restenosis is still challenging. In-stent restenosis is often due to aggressive neointimal proliferation. Also, there is evidence of a process of neo atherosclerosis histologically characterized by the accumulation of lipid-laden macrophages with "foamy" appearance in up to 16% of conventional in-stent restenoses<sup>28</sup>. The ISAR-DESIRE<sup>29</sup> and RIBS II clinical trials<sup>30</sup> proved that treating in-stent restenosis with sirolimus or paclitaxel-eluting stents lowers significantly the rate of restenosis compared to balloon angioplasty.

The implantation of a new stent into the main vessel displaces the neointimal proliferation tissue towards the ostium of the lateral branch triggering its occlusion. Also, the presence of the metal mesh of the stent previously implanted covering its origin makes keeping its patency more difficult<sup>31</sup>. In this setting, the angioplasty using the crush stenting technique is completed with 2 layers of stents implanted into the left anterior descending coronary artery except for 1 proximal short segment adjacent to the origin of the diagonal artery where 4 of them overlap. As it occurred with our 2 patients, Jim M-H et al.<sup>32</sup> presented their successful experience with the mana-

gement of 5 patients with in-stent restenosis in bifurcations of the left anterior descending and diagonal coronary arteries.

Since 1982 when Simpson J et al.<sup>33</sup> published the new coronary angioplasty technique we currently use today that consists of advancing a balloon catheter mounted over a removable coronary guidewire, the latter have evolved to become a crucial element to achieve success in different settings. In the management of bifurcation lesions treated using the crush stenting technique, once the stent has been implanted into the main vessel, the ostium of the lateral branch is jailed by the double metal mesh of the stents. Re-crossing it means selecting a coronary guidewire with several characteristics that go from having a flexible yet not easily deformable floppy tip with a slippery coverage and a sufficiently rigid structure to allow the passage of a dilatation balloon.<sup>34</sup> The PT<sup>2</sup>™ Moderate Support guidewire (Boston Scientific, Costa Rica) used in our own experience reached this target in all the cases. It has a nitinol core (a nickel and titanium alloy), hydrophilic coverage, a shaping ribbon design, and a tip load toughness of 2.9 g.

As it occurs in the management of coronary lesions, the management of bifurcations has worked better with drug-eluting stents compared to conventional stents (also called bare-metal stents) reducing the rate of restenosis and repeating coronary revascularization in the mid-<sup>35</sup> and long-term<sup>36</sup>. The CACTUS clinical trial used a first-generation sirolimus-eluting stent (Cypher, Johnson & Johnson, Miami Lakes, FL, United States) for the management of bifurcation lesions and compared 2 different strategies: the crush stenting vs the provisional stenting technique<sup>18</sup>. The study recruited 350 patients, and the provisional stenting group needed the implantation of a second stent into the lateral branch in 31% of the lesions treated. No significant differences were seen in the rate of major adverse cardiovascular events at the 6-month follow-up (15.8% in the crush stenting group vs 15% in the provisional stenting group; P=NS).

The Promus PREMIER™ (Boston Scientific, Ireland) is a second-generation everolimus-eluting stent with a permanent biocompatible biopolymer. Eighty percent of the drug is released within the 30 days following stent implantation<sup>37</sup>. Everolimus is an immunosuppressant macrolide

that blocks the progression of the cell cycle in the G1 phase (cytostatic). Both the safety and efficacy profile of the PROMUS stent has been confirmed by the PLATINUM studies. The PLATINUM QCA study<sup>38</sup> analyzed 73 patients with 9-month angiographic monitoring and reported on an in-stent late lumen loss of 0.17 mm ± 0.25 mm. The PLATINUM trial<sup>39</sup> that included 1530 patients with up to 2 de novo coronary lesions reported a rate of revascularization of 1.9% in the lesion treated at the 1-year follow-up. The mesh of the stent is a radiopaque alloy based on additions of chrome and platinum with several rings united by 2 connectors. Unlike the Promus ELEMENT™ Plus (Boston Scientific, Natick, Massachusetts, United States), the 2 proximal rings of the Promus PREMIER stent are united by 4 connectors that make it more solid giving it more longitudinal integrity too<sup>40,41</sup>. Its structure is made up of open cells and thin struts (81 μm) to allow access to lateral branches<sup>42</sup>. The Promus PREMIER™ stent was assessed in the NG PROMUS clinical trial<sup>43</sup>. This study included a total of 100 patients with de novo coronary lesions and reference diameters from 2.5 mm to 4 mm and lengths <34 mm. Technical success (residual lesion <30% and TIMI grade flow 3) was achieved in 99.2% of the cases. No longitudinal deformations of the stent were reported. The stent proved safe and effective at the 30-day follow-up in the absence of target lesion revascularization or stent thrombosis.

## CONCLUSIONS

Despite its limitations due to the small number of patients included, technical issues like the omission of IVUS or POT and the lack of systematic angiographic follow-up, this study exposes the results of coronary angioplasty in a very select group of patients. All showed unstable angina, obstructive bifurcation lesions of the left anterior descending and first diagonal coronary arteries treated with the crush stenting technique and always implanted with 2 Promus PREMIER™ everolimus-eluting stents (Boston Scientific, Ireland). Results were consistent with those previously reported in medical literature and show that the technique used was safe and triggered fewer cardiovascular events in the mid-term.

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# Neutrophil-lymphocyte ratio for the diagnosis of type 4a myocardial infarction

## Índice neutrófilo-linfocitario en el diagnóstico de infarto de miocardio tipo 4a

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### ABSTRACT

**Introduction.** Periprocedural type 4a myocardial infarction is among the complications associated with percutaneous coronary interventions. The important role played by inflammation in cardiovascular disease is well-known, and a better expression of this inflammatory state is the neutrophil-lymphocyte ratio.

**Objective.** To assess the association between the neutrophil-lymphocyte ratio and the appearance of type 4a myocardial infarction and the potential diagnostic value of this biological marker.

**Methodology.** Applied, descriptive-correlational, and prospective study. The neutrophil-lymphocyte ratio was obtained six hours after coronary intervention at the "Hermanos Ameijeiras" Hospital, Havana, Cuba, between November 2018 and January 2020.

**Results.** A total of 184 patients were studied, 25 of whom developed type 4a infarction. In patients with heart attack, the ratio increased after the procedure [ $4.26 \pm 0.95$ ; (3.87-4.65)] vs [ $3.19 \pm 0.86$ ; (2.83-3.54)]. Ratios  $>2.63$  were associated with the diagnosis of the complication, with an area under the ROC curve for diagnosis of 0.932 (95%CI: 0.868-0.995;  $p < 0.001$ ).

**Conclusions.** The neutrophil-lymphocyte ratio has high sensitivity, high specificity, and high positive and negative predictive values in the diagnosis of type 4a myocardial infarction.

**Keywords:** neutrophil-lymphocyte ratio, periprocedural type 4a myocardial infarction.

### RESUMEN

**Introducción.** Dentro de las complicaciones relacionadas con el intervencionismo coronario percutáneo se encuentra el infarto del miocardio periprocedimiento tipo 4a. Se conoce el importante papel que juega la inflamación en las enfermedades cardiovasculares, y una mejor expresión de este estado inflamatorio es el índice neutrófilo-linfocitario (INL).

**Objetivo.** Evaluar la asociación entre el índice neutrófilo-linfocitario y la aparición del infarto del miocardio tipo 4a así como el potencial valor diagnóstico de este marcador biológico.

**Metodología.** Investigación aplicada, descriptiva-correlacional y prospectiva. En el Hospital Hermanos Ameijeiras, La Habana, Cuba, entre noviembre de 2018 y enero de 2020, se determinó el INL a las seis horas de la intervención coronaria.

**Resultados.** Se estudiaron 184 pacientes, 25 de estos desarrollaron infarto tipo 4a. En los pacientes con infarto se incrementó el índice después del proceder [ $4,26 \pm 0,95$ ; (3,87-4,65)] vs [ $3,19 \pm 0,86$  (2,83-3,54)]. Un índice mayor de 2,63 se asoció al diagnóstico de la complicación, con un área bajo la curva ROC para el diagnóstico de 0,932 (IC95%: 0,868-0,995;  $p < 0,001$ ).

**Conclusiones.** El índice neutrófilo-linfocitario tiene alta sensibilidad, alta especificidad y altos valores predictivos positivos y negativos en el diagnóstico de infarto del miocardio tipo 4a.

**Palabras claves:** índice neutrófilo-linfocitario, infarto de miocardio periprocedimiento tipo 4a.

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## INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality worldwide<sup>1</sup>. Ischemic heart disease ranks #1 as the leading cause of death and disability<sup>2</sup>. In Europe, this condition represents 19% of deaths in males and 20% in women<sup>3</sup>; in the United States an acute myocardial infarction is reported every 40 seconds with a mean age of 65 years for males and 72 years for women<sup>4</sup>. In Cuba, cardiovascular disease is the leading cause of death. Back in 2018, ischemic heart disease killed 16,260 people (63.31%) and is the most common single cause of death among Cubans<sup>5</sup>. In order to fight it several advances have been made by developing the main therapeutic tools available today: optimal medical treatment with drugs that starts by preventing cardiovascular risk factors and training the population to change these factors at all levels of healthcare; rehab; coronary revascularization surgery; and percutaneous coronary intervention (PCI)<sup>6</sup>.

## HISTORY

Percutaneous coronary intervention is one of the most widely developed areas in contemporary cardiology<sup>7</sup>. Several advances made in the techniques and materials used have gradually brought PCI to more and more complex settings such as bifurcation lesions, thin vessels, calcified lesions, angulated lesions, left main coronary artery lesions, chronic total coronary occlusions, and other<sup>8,9</sup>. Periprocedural type 4a myocardial infarction (type 4a MI) is a complication associated with PCI. One of the diagnostic criteria for type 4a MI is the release of proteins from myocardial cells in a certain amount<sup>10,11</sup>. In cardiology the definition of this complication is controversial since there is no agreement on the diagnostic criteria and, most important of all, the availability and accessibility of validated markers is scarce<sup>10</sup>. The rate of type 4a MI reported is highly variable going from 2.6% all the way up to 30%<sup>12,13</sup> and has implications in the prognosis of patients, which is why its detection and stratification is essential to guide treatment<sup>12</sup>.

The role of inflammation in cardiovascular disease is important as well as the role it plays in atherosclerotic plaque progression and destabilization, the leading cause of coronary artery disease (CAD)<sup>14-16</sup>. The CANTOS clinical trial showed how interleukin-1 beta inhibition lowers the C-reactive protein levels and the occurrence of cardiovascular events beyond the 30 day-mark in patients with acute coronary syndrome<sup>17</sup>. White blood cells and their different subtypes are among the various inflammatory markers that exist; inflammatory pro-

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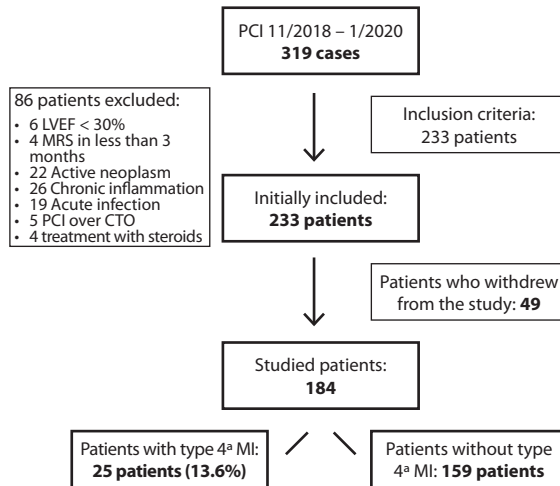


Figure 1. Study flow chart.

cess raises the levels of neutrophils, reduces the levels of lymphocytes, and is associated with more cardiovascular risk factors<sup>18,19</sup>. Neutrophils secrete inflammatory mediators like the proteolytic enzyme elastase that degrades the vascular basement membrane and causes endothelial damage<sup>20</sup>. On the other hand, lymphocytes regulate the inflammatory response and have inhibitory effects on atherosclerosis<sup>21</sup>.

A better expression of this inflammatory state is the neutrophil-lymphocyte ratio (NLR). The NLR is easy to obtain, cost-effective, commonly used, reproducible, and widely available in all centers in our country; increases of the NLR are associated with adverse cardiovascular events, mortality included, in patients with myocardial infarction (MI) and adverse clinical results in patients treated with elective coronary revascularization<sup>19,22</sup>.

Type 4a MI as a complication of PCI is associated with a torpid course of the disease in this subgroup of patients. A possible correlation between the NLR and type 4a MI, with high sensitivity and specificity, and high predictive values would place the NLR as a cheaper and more available diagnostic marker of type 4a MI to benefit patients who undergo this procedure.

## OBJECTIVE

To assess the correlation between the NLR and the appearance of type 4a MI and the diagnostic value of this biological marker.

## PARTICIPANTS AND METHOD

Applied, descriptive-correlational, and prospective study of a total of 148 consecutive patients treated at the cath lab of the Hospital “Hermanos Ameijeiras” in Havana, Cuba, between November 2018 and January 2020. A total of 233 of 319 patients treated with PCI during this period were initially included. Forty-nine of these patients were eventually excluded due to incomplete data in the clinical history (Figure 1).

### Percutaneous coronary intervention and drugs

Both the PCI technique and the decision on the type of stent to be used were left to the operator’s criterion. Unfractionated heparin was used in all the patients during the procedure to achieve activated clotting times >250 seconds during the procedure; the patients were on dual antiplatelet therapy.

TABLE 1. Características sociodemográficas y antecedentes personales de la población estudiada.

Social and demographic characteristics and past medical history	Type 4a MI			P
	Total (n=184) n (%)	Yes (n=25) n (%)	No (n=159) n (%)	
Age (mean ± SD)	61,4±14,2	57,6±12,2	62,0±14,4	0,097 <sup>a</sup>
Sex				
Male	123 (66,8)	16 (64,0)	107 (67,3)	0,923 <sup>b</sup>
Female	61 (33,2)	9 (36,0)	52 (32,7)	
Personal past medical history				
AHT	129 (70,1)	16 (64,0)	113 (71,1)	0,629 <sup>b</sup>
DM	66 (35,9)	14 (56,0)	52 (32,7)	0,042 <sup>b</sup>
CKD	24 (13,0)	7 (28,0)	17 (10,7)	0,026 <sup>c</sup>
Previous MI	93 (50,5)	13 (52,0)	80 (50,3)	1,000 <sup>b</sup>
Previous revascularization				
No	142 (77,2)	17 (68,0)	125 (78,6)	d
PCI	37 (20,1)	4 (16,0)	33 (20,89)	
MRS	4 (2,2)	4 (16,0)	0 (0,0)	
Hybrid	1 (0,5)	1 (0,6)	0 (0,0)	
Smoking				
Does not smoke	76 (41,3)	7 (28,0)	69 (43,4)	0,215 <sup>e</sup>
Smoker	70 (38,0)	10 (40,0)	60 (37,7)	
Former smoker	38 (20,7)	87 (32,0)	30 (18,9)	

AHT, arterial hypertension; CKD, chronic kidney disease; DM, diabetes mellitus; MI, myocardial infarction; MRS, myocardial revascularization surgery; PCI, percutaneous coronary intervention; SD, standard deviation; a, Mann-Whitney U test; b, chi-square test with correction; c, Fisher’s exact test; d, not valid chi-square test since 50.0% of the anticipated frequencies were < 5; e, chi-square test ( $\chi^2$ )

## Neutrophil-lymphocyte ratio

The NLR was defined as the ratio between the absolute value of neutrophils and the absolute value of lymphocytes. It was obtained before the PCI (within the previous 7 days) and 6 hours after the PCI. The leukogram was performed using the Pentra-DX NEXUS analyzer. This is a fully automatic hematology analyzer for the in-vitro diagnosis of whole blood samples anticoagulated with EDTA at 10% capable of testing 120 samples an hour. The following parameters were analyzed:

- Lymphocytes: [LYN], expressed as absolute value (#).
- Neutrophils: [NEU], expressed as absolute value (#).

## Ethical considerations

This clinical study was conducted according to the last review of the Declaration of Helsinki. All the patients involved in the study were informed of the characteristics of the study and procedures used and gave their written informed consent prior to their participation.

## Techniques used for statistical analysis

In order to identify the factors associated with the appearance of type 4a MI, the logistic regression function that models the probability of suffering this disease was estimated.

The model was adjusted with variables based on scientific evidence and on the researchers’ experience in such a way that the variables would not be correlated and the sizes of the samples within each group allowed the most accurate estimate possible of the parameters in the logistic regression equation. The point estimates of odds ratios (OR) and 95% confidence intervals (95%CI) were calculated for every variable; Hosmer-Lemeshow goodness-of-fit statistical test was used to assess the quality of adjustment of the logistic regression model.

## RESULTS

The social, demographic, clinical, anatomical, and procedural characteristics are all shown on Tables 1, 2, and 3.

**TABLE 2.** Characteristics of the patients based on clinical and anatomical variables.

Clinical variables	Type 4a MI <sup>a</sup>			p
	Total (n=184) n (%)	Si (n=25) n (%)	No (n=159) n (%)	
LVEF 30% - 50%	63 (34,2)	15 (64,0)	48 (31,4)	<b>0,003<sup>a</sup></b>
LVEF mayor 50 %	121 (65,8)	10 (40,0)	111 (69,8)	<b>0,097<sup>a</sup></b>
Diagnosis				
CSAE	72 (39,1)	11 (44,0)	61 (38,4)	<b>0,749<sup>b</sup></b>
NSTEACS	99 (53,8)	13 (52,0)	86 (54,1)	
STEACS	13 (7,1)	1 (4,0)	12 (7,5)	
Anatomical variables				
Multivessel CAD	89 (48,4)	15 (60,0)	74 (46,5)	<b>0,300<sup>c</sup></b>
SYNTAX (median/IQR)	11,0/15,0	21,0/15,0	11,0/12,0	<b>&lt;0,001<sup>c</sup></b>
Multi-arterial PCI	52 (28,3)	14 (56,0)	38 (23,9)	<b>0,002<sup>c</sup></b>
Type of lesion treated				
Type A	121 (65,82)	10 (40,0)	111 (69,8)	<b>d</b>
Type B1	16 (8,7)	7 (28,0)	9 (5,7)	
Type B2	46 (25,0)	7 (28,0)	39 (24,5)	
Type C	1 (0,5)	1 (4,0)	0 (0,0)	
Thrombus	5 (2,7)	4 (16,0)	1 (0,6)	<b>0,001<sup>e</sup></b>
Severe calcification	43 (23,4)	5 (20,0)	38 (23,9)	<b>0,862<sup>a</sup></b>
Bifurcation lesion	85 (46,2)	17 (68,0)	68 (42,8)	<b>0,033<sup>a</sup></b>
Bifurcverd	54 (29,3)	16 (64,0)	38 (23,9)	<b>&lt;0,001<sup>a</sup></b>

CAD, coronary artery disease; CSAE, chronic stable angina provoked by exertion; IQR, interquartile range; LVEF, left ventricular ejection fraction; NSTEACS, non-ST-elevation acute coronary syndrome; STEACS, ST-elevation acute coronary syndrome; SYNTAX, score according to the SYNTAX scale; a, chi-square test with correction; b, chi-square test; c, Mann-Whitney U test; d, chi-square test not valid since 37.5% of the anticipated frequencies are <5; e, Fisher's exact test.

There are significant differences ( $p < .001$ ) between the absolute neutrophil count and absolute lymphocyte count and the NLR before and after the procedure. The values of these absolute counts and the NLR increased after the procedure was performed on the patients (**Table 4**).

Between the 2 groups of patients (with type 4a MI and without infarction), except for the absolute neutrophil count before the procedure ( $5.46 \pm 1.21$  vs.  $5.53 \pm 1.15$ ;  $p = .599$ ), there were very significant differences ( $p < .001$ ) in the absolute neutrophil count after the procedure ( $8.26 \pm 0.99$  vs.  $6.32 \pm 0.66$ ), the absolute lymphocyte count before ( $1.68 \pm 0.48$  vs.  $2.26 \pm 0.40$ ) and after ( $2.03 \pm 0.47$  vs.  $2.62 \pm 0.31$ ) the procedure, and the NLR before ( $3.19 \pm 0.86$  vs.  $2.51 \pm 0.50$ ) and after the procedure ( $4.26 \pm 0.95$  vs.  $2.40 \pm 0.28$ ). Both in the group of patients with type 4a MI and in the group of patients without infarction, there were very significant differences ( $p < .001$ ) between the absolute neutrophil count, the absolute lymphocyte count and NLR before and after the procedure. These results are shown on **Chart 1**.

The area under the ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the procedure was 0.932 (95%CI: 0.868-0.995;  $p < .001$ ) (**Chart 2**).

For the NLR cut-off value  $\geq 2.63$ , sensitivity was 84.0% (95%CI: 67.6-100%), meaning that it can detect 84.0% of the patients with an actual diagnosis of type 4a MI. Specificity was 74.2% (95%CI, 67.1-81.3%), meaning that it can identify 74.2% of the patients without infarction (**Table 5**). The PPV was 33.9% (21.3%-46.5%) meaning that the percentage of patients with type 4a MI within those with NLR  $\geq 2.63$  was 33.9%. The NPV was 96.7% (95%CI: 93.2%-100%), meaning that the percentage of patients without type 4a MI within those with NLR  $< 2.63$  was 96.7% (**Table 5**). The VR+ was 3.3 (95%CI: 2.4-4.5) and the VR- was 0.2 (95%CI: 0.1-0.5), meaning that NLRs  $\geq 2.63$  are nearly 3 times more likely in patients with type 4a MI compared to patients without type 4a MI and NLRs  $< 2.63$  are 5 times more likely (1/0.2)

**TABLE 3.** Characteristics of the patients based on their hemodynamic variables.

Hemodynamic variables	Type 4a MI			p
	Total (n=184) n (%)	Si (n=25) n (%)	No (n=159) n (%)	
Simple bifurcation technique	81 (56,0)	13 (52,0)	68 (42,8)	<b>0,517<sup>a</sup></b>
Complex bifurcation technique	4 (2,2)	4 (16,0)	0 (0,0)	<b>&lt;0,001<sup>b</sup></b>
Type of complex technique				
No	180 (97,8)	21 (84,0)	159 (100)	<b>c</b>
Culotte	3 (1,1)	2 (8,0)	1 (0,6)	
TAP	1 (0,5)	1 (4,0)	0 (0,0)	
DK-crush	2 (0,5)	1 (4,0)	1 (0,6)	
Double kissing balloon	26 (14,1)	6 (24,0)	20 (12,6)	<b>&lt;0,001<sup>b</sup></b>
Type of stent				
Drug-eluting	136 (73,9)	18 (72,0)	118 (74,4)	<b>1,000<sup>a</sup></b>
Conventional	48 (26,1)	3 (14,3)	45 (27,6)	
# Implanted stents (median/IQR)	1,5/2,0	2,0/2,0	1,0/1,0	<b>0,006<sup>d</sup></b>
Total length of stented segment	23,0/16,0	28,0/12,0	23,0/10,0	<b>0,001<sup>d</sup></b>
Diameter of the stent	3,0/1,0	3,0/1,0	3,0/1,0	<b>0,273<sup>d</sup></b>
Angiographic success	159 (86,4)	9 (36,0)	150 (94,3)	<b>0,081<sup>b</sup></b>

DK-crush, double kissing crush technique; IQR, interquartile range; TAP, stenting and small protrusion technique; a, chi-square test with correction; b, Fisher's exact test; c, chi-square test not valid since 75.0% of the anticipated frequencies are <5; d, Mann-Whitney U test.

**TABLE 4.** Descriptive statistics of the absolute neutrophil count, absolute lymphocyte count, and NLR before and after the procedure.

Statistics	ANC pre	ANC post	ALC pre	ALC post	NLR pre	NLR post
Median $\pm$ SD	5,5 $\pm$ 1,2	6,6 $\pm$ 1,0	2,2 $\pm$ 0,5	2,5 $\pm$ 0,4	2,6 $\pm$ 0,6	2,7 $\pm$ 0,8
95%CI	5,4-5,7	6,4-6,7	2,1-2,2	2,4-2,6	2,5-2,7	2,5-2,8
Minimum	2,0	4,1	1,1	1,1	1,5	1,0
Maximum	8,0	10,2	3,0	3,5	4,9	6,2
$p^a$	<b>&lt;0,001</b>		<b>&lt;0,001</b>		<b>0,060</b>	

95%CI, 95% confidence interval; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; NLR, neutrophil-lymphocyte ratio; SD, standard deviation; a, Wilcoxon signed-rank test.

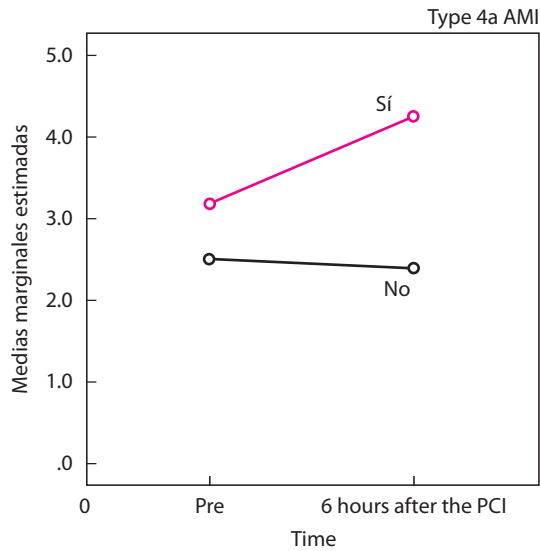
in patients without type 4a MI compared to patients with this disease (**Table 5**).

The variables that play an independent role in the presence of type 4a infarction were the past medical history of CKD, previous revascularization, and the NLR obtained 6 hours after the procedure.

The OR for CKD was 10.515 (95%CI: 1.123-98.471), the OR (chance or opportunity) of having type 4a MI is nearly 10 times higher in patients with a past medical history of CKD compared to patients without this disease. The OR of previous revascularization was 4.117 (95%CI: 1.115-15.199), the OR of having type 4a MI is nearly 4 times higher in patients with previous revascularization compared to patients without it. The OR for NLRs obtained 6 hours after the procedure was 81.395 (11.933-555.210). Finally, the OR of having type 4a MI increases parallel to the increase of such variable (**Table 6**).

## DISCUSSION

The fourth universal definition of myocardial infarction describes MI as related to the PCI with higher concentrations in the markers of myocardial damage above the 99th percentile of the upper reference limit within the first few hours after the intervention. To this day, the most highly specific and sensi-



**Chart 1.** Means of NLR before and after the procedure based on the presence of type 4a MI.

**TABLE 5.** Indicators of the validity of the NLR 6 hours after the procedure for the diagnosis of type 4a MI.

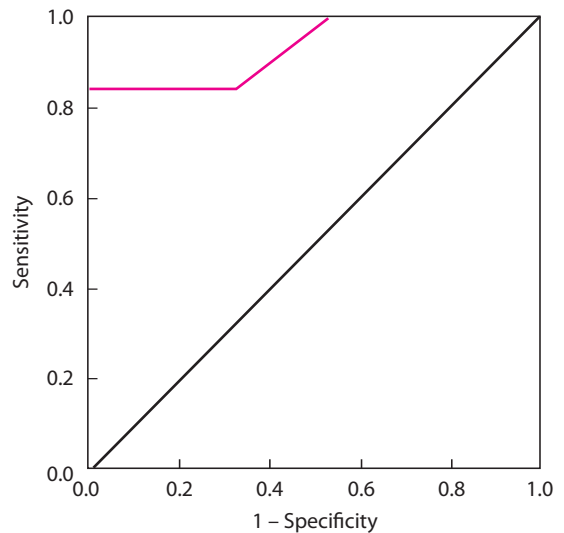
Indicators	NLR 6 hours after the procedure ( $\geq 2.63$ )	
	Point estimates (%)	95%CI
Sensitivity	84,0	67,6-100
Specificity	74,2	67,1-81,3
PPV <sup>a</sup>	33,9	21,3-46,5
NPV <sup>a</sup>	96,7	93,2-100
LR+	3,3	2,4-4,5
LR-	0,2	0,1-0,5

95%CI, 95% confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NLR, neutrophil-lymphocyte ratio; NPV, negative predictive value; PPV, positive predictive value; a, prevalence of type 4a MI=13.6%, 95%CI: 8.4%-18.8%.

ve validated markers are cardiac troponins T and I, the creatine kinase MB isoenzyme (CK-MB)—the most specific isoform of the heart muscle—plus clinical evidence or images of ischemia or angiographic alterations<sup>11</sup>. In this study, the frequency of type 4a MIs is similar to that reported in the medical literature<sup>13,14,23</sup>.

The sudden decrease of blood flow to a myocardial territory during the PCI can be due to several causes like loss of blood flow or slow flow to a secondary branch, distal embolization of thrombus or material from the atherosclerotic plaque, the transient occlusion of a vessel, no-reflow or slow flow in the main vessel, and residual dissection, among others. This coronary flow disorder is associated with metabolic changes accompanied by an acute inflammatory state both in the myocardium damaged and in the location of the coronary anatomy damaged. Myocardial necrosis induces the generation and activation of free radicals, starts the cytokine storm, and releases the tumor necrosis factor- $\alpha$ <sup>18</sup>.

The role of inflammation in the pathophysiology of growth and instability of atherosclerotic coronary artery disease has been established by scientific evidence<sup>24,25</sup>. The inflammatory response is associated with a prothrombotic state that increases fibrinogen levels, coagulation factors, and platelet reactivity<sup>26</sup>. The results of this study show that the clinical, anatomical, and procedural elements involved with a greater inflammatory state are significantly associated with the presence of type 4a MI.



**Chart 2.** ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the procedure.

**TABLE 6.** Results of multivariate analysis for the presence of type 4a MI.

Variables	OR	95%CI	P
CKD	10,515	1,123-98,471	<b>0,039</b>
DM	1,032	0,126-8,419	0,977
Previous revascularization	4,117	1,115-15,199	<b>0,034</b>
NLR 6 hours after the procedure	81,395	11,933-555,210	<b>&lt;0,001</b>

95%CI, 95% confidence interval; CKD, chronic kidney disease; DM, diabetes mellitus; NLR, neutrophil-lymphocyte ratio; OR, odds ratio.

Diabetes mellitus, chronic kidney disease (CKD), and left ventricular systolic dysfunction establish a systemic inflammatory state. Diabetic macroangiopathy causes more vulnerable and extensive coronary lesions in diffusely diseased coronary vessels, anatomical conditions that increase the risk of having a type 4a MI<sup>27</sup> and other complications during the PCI; CKD and left ventricular systolic dysfunction are associated with inflammation and can be the cause of extensive and complex coronary disease<sup>28-30</sup>. Inflammation increases the vulnerability of coronary plaque followed by risk of rupture and dissection during the PCI<sup>28</sup>; Kurtul A et al.<sup>31</sup> showed that an inflammatory state before the primary PCI, expressed as a high NLR, is associated with no-reflow.

In this study, the anatomical characteristics of coronary arteries indicative of a higher atherosclerotic burden like moderately high scores, presence of thrombus, true bifurcation lesions, and the complex double coronary bifurcation stenting technique were associated with the presence of type 4a MI. Atherosclerotic burden is associated with the inflammatory state; in a former study, the author found that higher NLRs prior to an invasive coronary angiography was associated with significantly higher SYNTAX scores<sup>32</sup>. The presence of thrombus increases the risk of distal embolization, severe spasm, and no-reflow or slow reflow during the procedure and is associated with higher NLRs<sup>33</sup>.

The NLR is a biomarker that expresses the emergent systemic and coronary inflammatory state. Percutaneous coronary interventions cause inflammation after the cannulation of coronary ostia, the injection of iodinated contrast, the insertion and expansion of intracoronary devices, among others. The NLR as an expression of inflammation increases after the in-

vative procedure<sup>34,35</sup>. No significant increase was seen in this series, but an absolute neutrophil count increase was reported. The biomarkers established for the diagnosis of type 4a MI are the TnT and the CK-MB<sup>11,12</sup> and they express cardiac inflammation. There is not enough evidence on the association between the NLR and the presence of myocardial damage during the PCI. In this study, 6 hours after the PCI, the NLR was >2.63 and it was associated with the occurrence of periprocedural infarction. With an acceptable sensitivity and specificity, and a high NPV, the area under the ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the PCI is rather good since it is >0.8. Also, based on the 95%CI, it could be up to 0.995. The study conducted by Verdoia et al. reported similar results in patients treated with a PCI in a stable clinical context where NLRs  $\geq 3$  were associated with the occurrence of type 4a MI.

On the utility of the NLR for the diagnosis of type 4a MI, the values of estimated sensitivity and specificity in this series can be considered good because they are high. Actually, they are close to 100%. However, the PPV is not good because predictive values are influenced by the prevalence of the disease they

are trying to diagnose. That is why the NPV is high, because the lower the prevalence of the disease the higher the NPV and the lower the PPV.

Likelihood ratios are also accepted. It has been considered that diagnostic means (in this case the NLR) have good diagnostic efficacy with LR+ as high as they can be and LR- as close to 0 as possible.

In the multivariate analysis, CKD, previous revascularization, and the NLR obtained 6 hours after the procedure were independently associated with type 4a MI. This result is telling us that the NLR is an inflammatory biomarker that can be useful for the risk stratification of patients treated with PCI to predict and diagnose type 4a MI.

## CONCLUSIONS

The neutrophil-lymphocyte ratio obtained 6 hours after a percutaneous coronary intervention is significantly higher compared to the baseline NLR of patients with type 4a MI. This ratio has high sensitivity, high specificity, and high positive and negative predictive values for the diagnosis of type 4a MI

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# First National Survey on Training in Interventional Cardio-Angiology in the Argentine Republic (ENFOCIRA I)

## Primera Encuesta Nacional sobre Formación en Cardioangiología Intervencionista en la República Argentina (ENFOCIRA I)

Ignacio M. Seropian

### ABSTRACT

**Introduction.** Interventional cardiology is a medical specialty listed in the Argentine Ministry of Sanitation. In order to be licensed, a course including a theoretical and a practical part needs to be passed.

**Objective:** To evaluate the characteristics of practical training in interventional cardiology.

**Methods.** Retrospective, cross-sectional study of a voluntary anonymous survey on 3 characteristics of the doctors in training: demographics, training, and working conditions.

**Results.** The survey included 65 participants aged 34 years old (33-37), mostly males (94%), 80% from Argentina and most of them practicing in the City of Buenos Aires (55%) and the Province of Buenos Aires (20%). The trainees performed different endovascular interventions including coronary interventions (96%), arterial peripheral procedures (92%), and structural heart disease procedures (82%). Differences were seen in the learning curve and in the degree to independence among the trainees. Working conditions were not the right ones and 21% of the trainees never got paid. Eighty-five percent of them needed a second or third job to make it through the month. Only 34% had health insurance (only 39% had an occupational accident insurance and only 19% malpractice insurance).

**Conclusion.** In Argentina, interventional cardiology trainees undergo extensive training, have different learning curves, and lack proper working conditions.

**Keywords:** medical education, fellowships and scholarships, endovascular procedures.

### RESUMEN

**Introducción.** La Cardioangiología Intervencionista es una subespecialidad médica reconocida por el Ministerio de Salud. Se obtiene el título a través de un curso teórico-práctico.

**Objetivos.** Evaluar las características de la formación práctica en Cardioangiología Intervencionista.

**Métodos.** Estudio descriptivo de corte transversal a partir de una encuesta voluntaria y anónima a médicos en formación, con tres ejes: datos demográficos, formación práctica y condiciones laborales.

**Resultados.** Sesenta y cinco encuestados, de 34 (33-37) años, casi todos (94%) de sexo masculino, 80% argentinos y en su mayoría en formación en la Ciudad Autónoma de Buenos Aires (55%) y Provincia de Buenos Aires (20%). Los centros donde se formaron realizaron distintos tipos de procedimientos: coronarios (96%), periféricos arteriales (92%) y estructurales valvulares (82%). Existió heterogeneidad en la curva de aprendizaje y el grado de independencia. Se observó precarización laboral sin recibir honorarios en el 21%, y el 85% realizó otras tareas laborales para subsistir. Solo el 34% fue provisto de cobertura de salud, el 39% de aseguradora de riesgos de trabajo y el 19% de seguro de mala praxis.

**Conclusión.** Los médicos en formación en Cardioangiología Intervencionista se exponen a diversos tipos de estudios, presentan distintas curvas de aprendizaje y alta precarización laboral.

**Palabras claves:** educación médica, residencias, procedimientos endovasculares.

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## INTRODUCTION

Interventional cardiology is a medical subspecialty within the list of subspecialties recognized by the Argentine Ministry of Sanitation. It is often referred to as “General Angiology and Vascular Surgery” (Annex I of the Resolution 1418/2015 of the Argentine Ministry of Sanitation). The Argentinian College of Interventional Cardioangiologists (CACI) and the University of Buenos Aires School of Medicine (UBA) created a 3-year long medical specialty called General and Interventional Cardiology/Angiology (Res CD #1043/90) back in 1990. Seven years later, in 1997, it was renamed as “Hemodynamics, Angiology, and Interventional Cardiology” (Res CD #5751/97). Although it is a theoretical-practical specialty, training takes place in several Argentinian cath labs that need to be approved by CACI guaranteeing the quality and biosafety of patients, trainees, and

operators. Also, several prerequisites are required to be able to graduate such as the submission of statistical data from the cath lab to CACI, attending the theoretical workshops, passing the exams, conducting scientific activities, and performing a minimum number of procedures as lead operator. However, there is heterogeneity on the different ways practical training should be conducted and the working conditions effective during this training. Something similar happens in other countries where medical societies establish the prerequisites needed to obtain a degree as medical specialist, but they do not regulate practical training<sup>1,2</sup>. Yet despite these differences, there is no report or regulation in the medical literature available today establishing practical training in interventional cardiology in Argentina or any other country. The objective of this study is to describe the characteristics of practical training in interventional cardiology in the Argentine Republic.

## MATERIAL AND METHODS

This is a descriptive, cross-sectional study from data obtained through a survey. An online, anonymous, semi-structured and voluntary survey was conducted. Three items were considered (appendix) to conduct this survey: demographic data, practical training, and working conditions. The survey was conducted using the free of charge survey administration application app Goo-

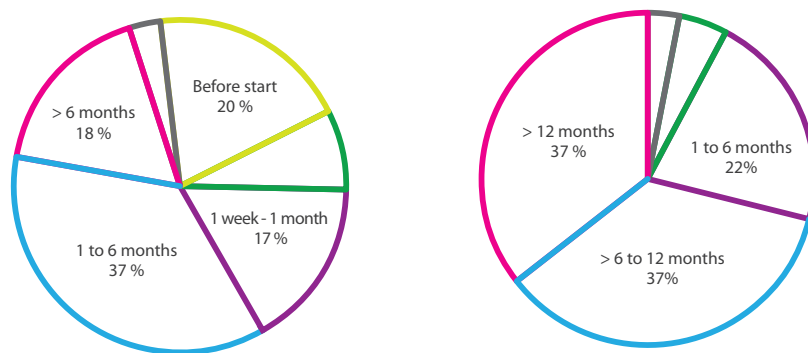
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**Figure 1.** Learning curve assessed based on the time it took trainees to become lead operators in diagnostic (cine coronary arteriography) and therapeutic procedures (angioplasty).

**TABLE 1.** Different procedures the respondents were exposed to during their training.

Procedures	Number (n)	Percentage
Coronary	62	95%
Structural heart disease (valvular)	53	82%
Structural heart disease (non-valvular)	39	59%
Arterial peripheral	60	92%
Venous peripheral	41	63%
Splanchnic vessels	36	55%
Pediatric	19	29%
Neurological	15	23%

gle Forms (Google LLC, CA, United States). Some squares were “free text” squares (respondents could write anything they wanted) while others showed just a menu. Some questions were one-answer only while other were multiple-answer questions (this was always specified in the heading to avoid misunderstanding). Regarding the location of training, the different participant provinces were divided based on the geographical regions of the Argentine Republic into the Autonomous City of Buenos Aires and the Buenos Aires Province given the geographical density of this city. When the trainee would study in different locations, the main study center was considered as the central center for geographical location purposes.

The survey was submitted from the cell phone of the author of this article using WhatsApp Messenger (Facebook Inc, CA, United States) to a group called CACI 17 that was created in September 8th, 2017, by students of this medical specialty that started studying that year and had over 50 members by the time the survey was submitted to the respondents. Since starting June 2018 training in his medical specialty stopped happening every 3 years, meaning that residents could join every year, the WhatsApp group included mostly students who started in 2017 and students who started in 2018 and 2019. The survey was submitted on August 15th, 2019 through a message linked to the survey. Permission to submit the survey to other contacts of the medical specialty was requested too. Also, it was requested that the survey be submitted to a few more contacts (around 5 people) who had completed their medical specialty between 2014 and 2017. At all time we tried to submit the survey to more and more trainees for the sake of increasing representativity. No databases were used or centers involved in

the submission of the survey. The survey was considered complete on October 15th, 2019, two months after being implemented.

Data were exported to a spread sheet (Excel, Microsoft Corporation, WA, United States) that was later used for analysis and to make the charts. Qualitative variables were expressed as frequency (percentage) and the quantitative ones as mean and interquartile range (IQR). In the case of frequencies, no decimals were used. Instead, rounding was used towards the immediately higher number if the next decimal was  $\geq 5$ .

## RESULTS

From August to October 2019, a total of 65 trainees responded to the survey. Eighty-five percent of them completed it within 48 hours after submission of the survey to the WhatsApp group; the last registry received was obtained 19 days later. The median age was 34 years (IQR: 33-37) and 94% (61/65) were males. Eighty-three percent (54/65) were born in Argentina and 80% (51/65) had obtained their medical degree in an Argentinian school of medicine. The rest had graduated in other Latin American countries that were not specified in the survey. Eighty-eight percent studied their medical specialty at UBA-CACI and 60% of these (34/57) entered the specialty back in 2017. The remaining trainees entered their specialty in different years [2011 (11%), 2014 (15%), 2018 (7%), and 2019 (6%)]. The training medical center was located in the Autonomous City of Buenos Aires (54%) followed by the Buenos Aires Province (19%), Central region (11%), Cuyo (8%), Northwest Argentina (5%), and Northeast Argentina (3%). Patagonia was not represented. Eighty-one percent of the training happened in private centers and 34% in public hospitals. Regarding the number of health centers where training took place, 49% of the trainees studied in one center only, 22% in 2 centers, and 29% in 3 or more centers. Regarding the number of cath labs used, 49% used 1 or 2 labs, 45% used 3 or 4 cath labs, and only 6% used 5 or more labs. Centers were defined as medical institutions. Cath labs were defined as PCI-capable facilities. Ultimately, trainees were exposed to a large variety of procedures (Table 1), not only coronary, but also structural and from other medical specialties.

Afterwards, practical training was assessed until the trainee would become knowledgeable enough to be able to perform a procedure as lead operator (Figure 1). As ex-

**TABLE 2.** Supplementary working activities performed by trainees.

Activity	Number (n)	Percentage
Calls (external/CLU)	48	84%
Cardiology consultation	29	46%
Cardiology monitoring	8	14%
Ambulance/General practitioner	6	10%
Other	16	28%

CU, Coronary unit.

pected, most trainees (82%) performed a cine coronary arteriography as lead operators within 6 months after starting training (**Figure 1A**) while only 25% performed coronary angioplasties during this time (**Figure 1B**). It was considered that a coronary angioplasty had been performed as a lead operator when a 0.014 in guidewire had crossed an obstruction and balloon predilatation had been performed if appropriate. Then, the degree of independence was assessed by asking whether the procedure had been performed without direct supervision defined as the presence of a doctor with specific training on interventional cardiology near at the cath lab. At this point, we saw that 72% of trainees (66% were positive on the answer while 6% said "maybe") performed a cine coronary arteriography without direct supervision during their training and even 65% (60% were sure about the procedure while 5% had some reservations) performed a coronary angioplasty without direct supervision. Within the latter group that performed a therapeutic procedure 50% (21/42) did so during their 3rd year of training, 31% (13/42) during their 2nd year, and 19% (8/42) during their 1st year of training. Since medical practices required doctors to remain on passive calls for emergency reasons, this point was assessed too. It was seen that 41% were on call without direct supervision during their training. This basically happened during the trainees' 3rd year of training (58% of them did remain on call), 38% during their 2nd year, and even 1 respondent (4%) during his 1st year of training. In the Autonomous City of Buenos Aires, where medical practices are run by the Argentinian Ministry of Health, it was reported that 71% of trainees (25/35) performed a therapeutic procedure while 43% (15/34) remained on call without direct supervision. Finally, 65% of trainees said that the duration of the training received was appropriate, 28% said training went very slow, and 2% said it went very fast (5% did not know/did not answer).

Lastly, the working conditions implemented during training were studied as well. In the first place, we saw that working conditions were self-employment in 63% of the respondents. The remaining trainees signed contracts as residents or on dependency conditions without any distinctions between the two. Twenty percent received no income during their training and even 1 respondent (2%) said he had to pay for his practical training. Eighty percent of the respondents who were actually being paid said they did not make enough money and 85% said that they had to look for another job to make it through the month as shown on **Table 2**. Regarding working benefits (**Table 3**) nearly 1 of every 3 respondents had occupational accident insurance (OAI) or personal health insurance while 1 of every 5 had malpractice insurance or paid emergency calls. Finally, 62% of respondents had a dosimeter to measure exposure at the different centers where they were doing their practices. Thirty percent said

**TABLE 3.** Beneficios laborales recibidos por los profesionales en formación.

Benefits	Number (n)	Percentage
Health insurance (social security or private)	22	34%
Occupational accident insurance (OAI)	25	39%
Malpractice insurance	12	19%
Transportation for ER calls (paid calls)	13	20%

they actually had a dosimeter but not in every center while 8% had no dosimeter at all. Sixty-five percent of those who did have a dosimeter (92%) were aware of their dose levels.

## DISCUSSION

Unlike other countries in the region, the Argentine Republic offers a medical specialty regulated by CACI and UBA required to obtain the degree of specialist to be able to practice this medical specialty. Since it is listed as one of the medical subspecialties of the Argentine Ministry of Sanitation this degree provides the necessary qualification at least in the Autonomous City of Buenos Aires. This specialist degree includes a theoretical part and a practical part that should both be conducted at the corresponding training center. Although the participant centers need to be qualified and meet the necessary standards, the special characteristics of practical training and working conditions vary from one center to the next. Despite this heterogeneity in practical training, no data have been published reporting on this issue. That is why we decided to submit a survey precisely to know more about the issue at stake. The modality selected was the medical survey, similar to what had been done in the Argentine Republic with cardiology residences<sup>3</sup>.

This first medical survey was submitted to 65 respondents, which is an important and representative number of respondents in our setting. According to CACI official website ([www.caci.org.ar](http://www.caci.org.ar)), the 2017-2020 medical degree includes 72 students, meaning that in this cross-sectional cut-off value, 90% of those who completed the course at that time could have surveyed. These numbers are similar to those reported by other countries. Back in 2015, Spain reported a total number of trainees of 76<sup>4</sup>. The number of respondents is also higher compared to the 20 surveys completed in Europe<sup>5</sup>, 26 in Canada<sup>6</sup>, and 50 in the United States<sup>7</sup> on a study regarding procedural training to treat structural heart disease. However, in these surveys the training center was assessed by surveying the director in charge and not the trainee himself. In our survey, trainees had to complete the survey themselves, which is why the centers with the largest number of doctors could alter the final results. However, this same modality was used in the survey submitted to cardiology residents and it can identify differences among trainees of the same center, if any. Unfortunately, in our survey the degree of acceptance of the survey could not be estimated, that is, the number of people who actually received the questionnaire but decided not to fill it out.

Regarding the population surveyed, most respondents were Argentinian male doctors who were studying their medical specialty at UBA-CACI 2017-2020 and who were working in large metropolitan areas in the Autonomous City of Buenos Aires and the Buenos Aires Province, mostly in the private sector. The number of centers and cath labs was more diverse. Half of the respon-

dents did their practices in 1 center and in 1 to 2 cath labs. In the first place we saw that the practices the trainees were exposed to were very diverse including a higher percentage of peripheral procedures and structural heart disease procedures (valvular and non-valvular). There is no doubt that this is beneficial since it expands the trainee's field of expertise. As expected, respondents were less exposed to neurological and pediatric procedures since these are often performed by other health professionals. However, almost a third was exposed to these procedures, which is acceptable considering the heterogeneity of respondents.

Afterwards, we saw the learning curve and found heterogeneity in it with some respondents performing diagnostic studies as lead operators even before starting their training and angioplasties within the first month. However, other trainees performed their first angioplasty after one year. At this point, we should mention that the variable "time" and not the variable "number of cases" was used, which is a limitation regarding analysis since those who performed earlier procedures may have been exposed to more cases. Unfortunately, since we do not know the participant center in each case, we cannot establish a correlation between time and volume of cases per center. On the other hand, we also studied the degree of independence and found that two thirds of the respondents performed a therapeutic procedure without any supervision from expert physicians. Although the number of procedures performed by respondents before becoming self-sufficient cannot be established, we believe that during training a registered expert physician should have been near the cath lab at all time to help the trainee should any complications arise. At this point, the survey was very clear on the concept of presence of a registered expert physician "near the cath lab." Technically, this physician was required to be close enough to the cath lab (not actually inside the cath lab) to take charge should any complications arise. It is even more surprising to see that almost half of the respondents performed unsupervised emergency procedures (in the modality of passive calls). This group of patients has higher risks, morbidity, and mortality, which is why they are expected to benefit from the procedures performed by health professionals with more experience. Since until 2017 the medical specialty was opened for registration every 3 years and several trainees would often join the practical training programs every the year, trainees may have been involved in unsupervised practices after completing their 3-year practical training without obtaining an official degree from the Argentine Ministry of Sanitation. For this reason, the survey was very specific on the years passed since the start of practical training regardless of the training period as a specialist. We should mention that one respondent said that he worked at the ER without even being exposed to interventional procedures for 1 full year and 17% without having completed a 2-year training program.

However, this was not perceived negatively by the trainees since only 2% thought that their learning curve had been too fast.

Then, the working conditions were studied. Considering that trainees already have a medical degree and their specialty on cardiology, we found that the working conditions of two thirds the trainees were not residencies or dependency conditions since very few of these trainees had working benefits as occupational accident insurance (OAI) or health insurance. This means that these were more precarious working conditions compared to cardiology residencies in our country where 60% had health insurance and 67% OAI<sup>3</sup>. Also, on top of the fact that many trainees were doing unsupervised emergency procedures, all costs had to be paid by the trainees in almost all of the cases. Lastly, over 80% had to take other jobs to be able to make it through the month, which is > 60% compared to cardiology residents<sup>3</sup>.

This study has some limitations. In the first place, this survey was only submitted to a group of interventional cardiology medical students from UBA-CACI between 2017 and 2019. Secondly, the survey is representative of an even more select group since no databases were used for its submission. Only a WhatsApp group was created for other purposes. Still, the questionnaire was submitted to most students from that batch. Thirdly, in order to prioritize anonymity, the form did not request any personal information so anybody could have accessed the questionnaire several times and answered it. Also, the veracity of the answers can only be attributed to the honorability of respondents since no internal control was implemented for confirmation purposes. However, we believe anonymity is an essential part of this type of surveys to avoid any possible retaliation against the respondents. It is the only way to answer freely to questions that otherwise may be detrimental those involved in the training programs. Fourthly, this was the first survey ever conducted in Argentina to learn about the characteristics of interventional cardiology training. This means that no chronological comparisons can be established to know whether this training has improved or not through time. In order to solve this, whenever possible, comparisons with cardiology residencies were drawn. Lastly, the questionnaire was designed without using any other valid surveys including 3 areas of interest that were arbitrarily considered for both the respondents and the medical community in general paying special interest in that the survey should be brief so it could be completed easily. It is expected that future iterations of this survey will include other suggestions and comments from the parties and regulatory entities involved so this questionnaire can become a useful tool with room for improvement.

In conclusion, in this first survey on training programs in cardioangiopathy in the Argentine Republic we see a huge diversity of procedures, heterogeneity in training times, self-sufficiency and independence, and precarious working conditions.

## CONFLICTS OF INTEREST

None reported. No funding received either.

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# Chronic thromboembolic pulmonary hypertension: uneventful pregnancy after pulmonary balloon angioplasty treatment. Case report

Hipertensión pulmonar tromboembólica crónica: embarazo sin incidentes después del tratamiento de angioplastia pulmonar con balón. Reporte de un caso

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## ABSTRACT

Pulmonary hypertension is associated with a significant risk for both mother and child during pregnancy. While pulmonary endarterectomy is the treatment of choice for patients with chronic thromboembolic pulmonary hypertension, balloon pulmonary angioplasty has emerged as an alternative for patients who are not eligible for surgery. This is the case of a 33-year-old patient with chronic thromboembolic pulmonary hypertension who was considered inoperable and who became pregnant after balloon pulmonary angioplasty treatment. The delivery was achieved without complications under strict multidisciplinary monitoring.

**Keywords:** chronic thromboembolic pulmonary hypertension, balloon pulmonary angioplasty, pregnancy outcome.

## RESUMEN

La hipertensión pulmonar durante el embarazo implica un riesgo significativo tanto para la madre como para el recién nacido. Mientras que la endarterectomía pulmonar es el tratamiento de elección en pacientes con hipertensión pulmonar tromboembólica crónica, la angioplastia pulmonar con balón se convirtió en una alternativa válida para los pacientes que no son candidatos a cirugía. Presentamos el caso de una mujer de 33 años con hipertensión pulmonar tromboembólica crónica, no candidata para resolución quirúrgica, que cursó su embarazo después de ser tratada con angioplastia pulmonar con balón, lográndose un parto sin complicaciones bajo un monitoreo estricto multidisciplinario.

**Palabras claves:** hipertensión pulmonar tromboembólica crónica, angioplastia pulmonar con balón, resultado del embarazo.

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## INTRODUCTION

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare complication of acute pulmonary thromboembolism. Its incidence rate is between 0.1% and 9.1% and its long-term mortality rate is high<sup>1</sup>.

Although pulmonary endarterectomy (PE) is the treatment of choice in patients who are not eligible for surgery, medical treatment or balloon angioplasty should be both considered since they are both good alternatives<sup>1</sup>.

The expert clinical practice guidelines on the management of pulmonary hypertension (PH) recommend avoiding pregnancy<sup>1</sup>. However, when this is the case, both the mother and the fetus have a high mortality rate during pregnancy and delivery<sup>2-4</sup>. This is the case of a patient with CTEPH who became pregnant after receiving treatment with balloon pulmonary angioplasty (BPA).

## CLINICAL CASE

This is the case of a 33-year-old woman with a past medical history of multiple fractures in hip, femur, and left knee-

pad after a motorcycle accident occurred in 2006. The patient's health status became complicated with chronic osteomyelitis that required the insertion of a permanent central venous catheter for prolonged antibiotic therapy. Back in 2017, she was admitted to a different center after presenting with progressive dyspnea. An acute pulmonary thromboembolism was diagnosed and oral anticoagulation with acenocoumarol was started. After completing a 3-month course of treatment, the patient failed to show any symptom improvement (functional class III according to the World Health Organization) and she had to be transferred to our hospital.

The physical examination confirmed the presence of tachypnea and tachycardia. The oxygen saturation level on room air was 90%. The electrocardiogram confirmed the presence of sinus tachycardia with right bundle branch block (RBBB). At the lab, the most significant finding was a proBNP of 4310 pg/mL. The presence of deep venous thrombosis was discarded on the venous Doppler ultrasound. The transthoracic echocardiography performed revealed the presence of right atrial and ventricular dilatation, moderate right ventricular systolic dysfunction, and a right ventricular systolic pressure of 80 mmHg. No signs of cardiac vegetations were seen. The ventilation/perfusion lung scan performed revealed the presence of bilateral mismatch with multiple areas of hypoperfusion at baseline level. These findings were confirmed on a CCTA with contrast that revealed the presence of thromboembolic disease at the level of subsegmental branches with both lower lobe predominance. These were the parameters obtained

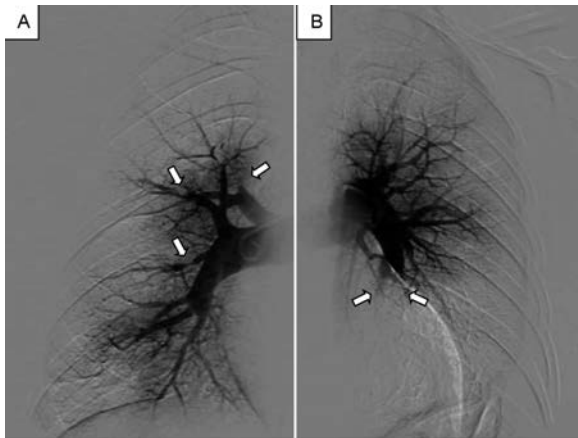
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The author declared no conflicts of interest whatsoever.

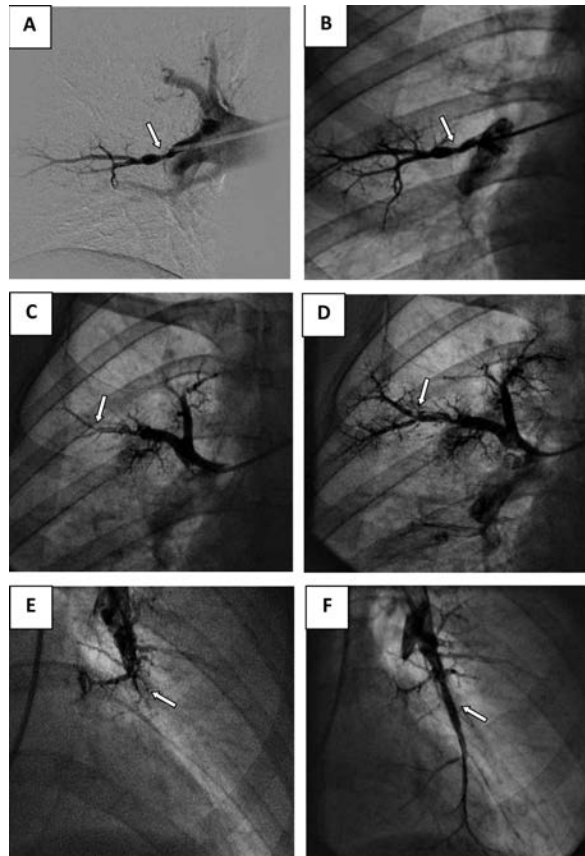
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**Figure 1.** Bilateral pulmonary angioplasty. White arrows: significant lesions of segmental and subsegmental vessels.

during right cardiac catheterization: pulmonary artery pressure (PAP), 62/25 (50) mmHg; pulmonary capillary wedge pressure (PCWP), 7 mmHg; volume per minute (VM): 4.1 L/min; pulmonary vascular resistance (PVR), 878 dyn·s·cm<sup>-5</sup> (10.9 Wood units). The pulmonary angiography showed web-like and annular lesions with subsegmental predominance (**Figure 1**). The case was discussed with the CTEPH heart team and the patient was considered non-eligible for PE because her lesions were at peripheral pulmonary vasculature level. Treatment with riociguat and multiple sessions of BPA were prescribed.

Eight sessions of BPA were conducted in the cath lab. A 7-Fr Flexor guiding sheath (Cook France S.A.R.L, Charenton-le-Pont, France) was used via left or right femoral vein in each procedure. A 0.014 in guidewire (Runthrough NS PTCA Guide Wire, Terumo, Japan) or Choice PT Floppy guidewire (Boston Scientific, Marlborough, Massachusetts, United States) mounted over a JR4 7-Fr guide catheter (Boston Scientific Marlborough, Massachusetts, United States) was advanced. The lesions were crossed unevenly. Successive dilatations were performed with Emerge balloons (Boston Scientific, Marlborough, Massachusetts, United States) of between 2.0 mm and 4.0 mm in diameter. Measurements were decided based on the size of the blood vessel in a 1:1 ratio (**Figure 2**). Inflations lasted from 30 to 60 seconds. After 8 sessions without serious complications or symptoms during the procedure, the hemodynamic parameters improved significantly: PAP decreased to 50/20 (30) mmHg and PVR dropped to 417 dyn·s·cm<sup>-5</sup> (5.2 Wood units). The oxygen saturation levels were 95%. Although treatment with BPA had not been completed the patient became pregnant and it had to be suspended. The risks associated with the pregnancy were explained to the patient who, nevertheless, decided to go on with it. Accoumarol was combined with subcutaneous enoxaparin twice a day and riociguat was withdrawn. The patient was closely monitored by a multidisciplinary team. Full-term pregnancy came without complications and a C-section was scheduled for the 37th week of pregnancy. Prior to surgery a Swan Ganz catheter was inserted for strict hemodynamic monitoring purposes (mean PAP, 37 mmHg; VM, 4.3 L/min; PVR, 465 dyn·s·cm<sup>-5</sup>) and under epidural anesthesia the baby was born without complications. The newborn baby weighed 2600 grams and scored 9/10 in the Apgar scale. Both the mother and the baby were discharged



**Figure 2.** Pulmonary angiography during balloon pulmonary angioplasty. (A) Annular lesion in the A5 right segment before and (B) after the BPA. (C) Web-type lesion in the A4 right segment before and (D) after de BPA. (E) Subocclusive lesion in the A9 left segment before and (F) after the BPA.

from the hospital after 5 days showing good clinical conditions at the 30-day follow-up.

## DISCUSSION

During pregnancy, the body of women undergo physiological changes; at the end of pregnancy blood volume can increase over 50%<sup>5</sup>.

Through changes in systemic vascular resistance and heart rate, the cardiac output can increase up to 50% compared to non-pregnant women<sup>5</sup>. Patients with PH have an increased PVR due to vascular remodeling. Therefore, these patients may not tolerate increased heart rates and blood volume overloads. Our patient may have tolerated well the physiological hemodynamic changes thanks to previous improvement after treatment with BPA.

The increased mean PAP during right cardiac catheterization prior to delivery may be associated with reduced pulmonary artery compliance as reported by Magon et al.<sup>6</sup> Epidural anesthesia was used. Local anesthesia is the preferred one because general anesthesia is often associated with an up to a 4 times higher maternal mortality rate due to reduced cardiac contractility and increased PVR and PAP<sup>7</sup>. Discussion on the optimal type of delivery is still controversial. Although vaginal delivery is associated with fewer significant changes in blood volume, fewer complications of coagulation or hemorrhage, and a lower risk of infection<sup>7</sup>, the C-section was decided to avoid a second prolonged stage of labor and a possible and uncontrollable vaginal bleed-

ding<sup>5</sup>. Very few cases of pregnant women with CTEPH have been reported in the medical literature. Both Ikeda et al.<sup>8</sup> and Kopec et al.<sup>9</sup> reported on cases of patients with CTEPH treated with BPA who became pregnant. In both cases, treatment with BPA was considered completed. This was shown in the final mean PAP obtained. Our patient became pregnant before all the sessions scheduled for her would ever be completed. This may explain the high mean PAP seen before pregnancy was ever confirmed.

## CONCLUSION

Pregnancy in patients with PH is a very high-risk situation both for the mother and the baby. After the BPA our patient improved significantly on both the hemodynamic and clinical levels. We believe that these interventions facilitated an uneventful pregnancy and delivery. Close monitoring by the multidisciplinary team should be the standard of care in high-risk patients like these.

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# What are we learning during the COVID-19 pandemic

## Qué estamos aprendiendo durante la pandemia COVID-19

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Dear colleagues,

I wish to tell you about an interesting activity that members from CACI had with friends and colleagues of different countries regarding their experiences during the COVID-19 pandemic. We conducted a webinar with Dr. Juan Granada of New York City (United States), Dr. Miguel Montero Baker of the city of Houston (United States), and Dr. Eduardo Apteocar of Paris (France).

We discussed the importance of keeping the strategies of cardiovascular healthcare in large cities and the management of acute coronary syndrome during the COVID-19 pandemic. Several doctors from Argentina and Latin America shared their thoughts with us.

Dr. Granada started by describing his experience in New York, a city that had a sudden and high rate of infection where the healthcare system collapsed immediately after to the huge number of cases reported. He said it was almost impossible to implement any strategies to reduce cardiovascular mortality following this collapse. In this context, he said it was important to use thrombolytic agents to treat the infarctions of critically ill patients with COVID-19 (+) to stop these coronary presentations right away as long as there were beds available since the cath labs remained closed in some cases. Dr. Granada insisted that during the peak of the pandemic it was impossible to access a cath lab in New York City and that patients simply did not seek medical attention with infarction-like symptoms.

On the other hand, those who actually sought medical attention did not receive proper care in the cath lab since the performance of primary angioplasties became almost nonexistent at one time or another during the pandemic.

Dr. Montero Baker said that in the City of Houston and the state of Texas this was never the case. The impact of COVID-19 was lower regarding health centers and had nothing to do with the situation lived in New York. However, the citizens of Houston also experienced massive hysteria, fear, and uncertainty that played a significant role causing delays when seeking medical attention, increasing mortality, and reducing the rate of success of these procedures.

Dr. Apteocar made a comparison between Paris and the city of Buenos Aires. Paris and its surroundings extend over 12000 square kilometers. Two million people live in the city and another 12 million live in the suburbs. The Buenos Aires metropolitan area extends over 14000 square kilometers with 2.7million people living in CABA and 13million people living in the Greater Buenos Aires conurbation. During the pandemic, in Paris it was necessary to double the number of beds from 1100 to 2600 by April 8. Even patients with non-COVID-19 related conditions were transferred by train to other regions to receive medical attention. He said that the French Group of Atheroma and Interventional Cardiology (GACI) conducted a survey that showed that angioplasty procedures for the management of infarctions reduced 50% in 2020 compared to the same three months of 2019.

In our country, data published by CACI and Stent-Savea Life show similar numbers with drops between 50% and 60% in the number of primary angioplasties performed over the months of April, May, and June and increases between 70% and 80% in July and August. However, this increase in the number of primary angioplasties performed was followed by consultation time delays, which translated into a higher mortality rate (from 5.5% to 11%), basically due to Killip-Kimball Classification C and D myocardial infarctions, cardiac ruptures, ISR, and severe arrhythmias. All these are conditions associated with time delays when seeking medical attention on fear of going to the health center.

Finally, on coadjuvant schemes or the management of myocardial infarction, the primary angioplasty remained as the standard of care and all panelists suggested continuing with the usual management of this condition as long as the healthcare system would allow it. Similarly, they discarded making big changes in the use of peri-

procedural drugs. Under uncertain conditions like the ones posed by this pandemic, it does NOT seem appropriate to change routines and treatments that have proven effective in the management of myocardial infarction.

For this reason, our own best judgment as physician and that of each health center should be used during the current COVID-19 pandemic. And when we start seeing light at the end of the tunnel, we'll have to raise our hopes. Nothing will be the same, but it will be the right time to rebuild. A better patient-doctor relation will be essential as well as clearer information to the people, more discipline, respect among colleagues at all time, and keeping a very cautious attitude about the information that is disclosed and the way it is exposed in the social media.

We should stress out that the cardiovascular mortality rate is still higher compared to the COVID-19 related mortality rate, which is why the population needs to know about the importance of seeking medical attention in the presence of infarction or stroke-like symptoms. Also, they should still go see their cardiologists to learn how to control their risk factors.

**Diego Grinfeld**  
President of CACI 2020 – 2021  
**Sebastián Peralta**  
Sanatorio Güemes, CABA, Argentina

# Publication Guidelines of the *Revista Argentina de Cardioangiología Intervencionista*

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

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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](http://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](http://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](mailto: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.

A maximum of eight (8) authors shall be allowed in each paper and they must follow the authorship standards established by the IMCJE. Each manuscript received is examined by the Editorial Committee and one or two external reviewers. Afterwards, the lead author will be notified on the acceptance (with or without corrections and changes) or rejection of the manuscript. After the article has been approved for publication, RACI has the copyright for its total or partial reproduction.

### SECTIONS (See Preparation of the manuscript)

#### Original articles

These are scientific or educational papers of original basic or clinical studies. Requisites: a) general text, up to 5000 words including references; b) abstract, up to 250 words; c) tables + figures, up to 8; d) authors, up to 10.

### Brief communications

The studies published under this section follow the same criteria established for original articles, but do not have enough patients to be considered as such.

### Review articles

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.

### Continuing medical education

These are articles on the rational and protocolized management of the different circumstances that can occur in the routine clinical practice. They are reviewed and agreed previously with subject matter experts and include a flow chart on the diagnostic and therapeutic management of the disease. The following requisites have been established by the Editorial Committee. Requisites: a) general text, up to 2500 words excluding the references; b) abstract, up to 150 words; c) tables + figures, up to 6; d) references, up to 20; e) authors, up to 4.

### Clinical case

This is the description of a clinical case of unusual characteristics with its diagnostic and therapeutic management, and final resolution. It needs to include a brief reference search. Requisites: a) general text, up to 1200 words; b) abstract, up to 100 words; c) tables + figures, up to 4; d) references, up to 10; e) authors, up to 5.

### How did I approach it?

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-mail will 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.

### Interventional cardiology images

The publication of images describing exceptional cases that the Editorial Committee and external reviewers consider significant for the journal will be accepted for publication. They will need to be followed by an explanatory text and a brief summary of the clinical history. Requisites: a) general text, up to 300 words; b) 2 original figures only; c) references, up to 3; d) authors, up to 5.

### Research protocols

The publication of research protocols—preferably multicenter—will be accepted and published by the journal as special articles as long as these protocols do not include the study partial or total results.

### Editorials

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.

### Letters to the editor

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.

## PREPARATION OF THE MANUSCRIPT

The article will be written in Spanish language using a Microsoft® Word text processor and saved under the \*.doc file extension. The size of the page will be A4 or letter with double-spacing, 25 mm margins, fully justified text, and 12-point Times New Roman or Arial font. Pages will be numbered consecutively starting with the cover. The manuscript (original article) needs to follow the so-called IMRAD structure: Introduction, Material and method, Results, and Discussion (see the ICMJE Publication Guidelines). Also, it will include Title, Abstract, Conflicts of Interest, and References. In some cases, it will be necessary to add a Conclusion, Acknowledgements, and an Appendix. The metric system will be the standard system of measurement used with comas to write the decimals. All clinical, hematologic, and chemical parameters will be expressed in units of measure from the metric system and/or IU. Only common abbreviations will be used except for the title and the abstract. The first time these abbreviations are used they will be preceded by the whole term except for the use of standard units of measure.

Tables must be presented in individual sheets and they need to be numbered consecutively with Arabic numbers (0, 1, 2, etc.) according to the order in which they were quoted in the text with a short title for each and every one of them. All of the non-standardized abbreviations of the table need to be explained and developed. Explanatory notes will be placed at the foot of the table using the following symbols in this sequence: \*, †, ‡, §, ¶, \*\*, ††, ‡‡, etc. Figures need to be submitted in TIFF, PSD or JPEG format and each figure will be submitted in a separate file with a resolution of 300 dpi in its final format. Each of them will be numbered consecutively together with the explanatory legend in a separate file. The normal size of the photographs will be 127 mm x 173 mm. Titles and detailed explanations will be included in the text of the legend, not the illustration. References will be numbered consecutively with Arabic numbers between brackets. All of the authors will be included if they are six or fewer; if there are more authors involved, the third one will be followed by the expression «, et al.». The titles of the journals will be shortened based on the style used in Index Medicus. These are a few examples:

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