ORIGINAL ARTICLE

Unprotected Left Main Percutaneous Coronary Intervention: One and 3-Year Evolution. Event Prediction

Angioplastia de tronco de la coronaria izquierda no protegido: evolución clínica al año y a los 3 años. Predictores de eventos

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ABSTRACT

Background: Left main percutaneous coronary intervention is a therapeutic option for patients with favorable anatomy.
Objectives: The aim of this study was to report our experience in the treatment of these patients, their clinical evolution and the variables associated with clinical events during follow-up.
Methods: This was a retrospective analysis of patients that underwent percutaneous coronary artery intervention for left main obstructive disease between 2011 and 2017 at Clínica Bazterrica and Clínica Santa Isabel. The incidence of clinical events was evaluated at one year and at long-term follow-up (at least 3 years after the intervention). A univariate and multivariate analysis (Cox proportional risk model) was performed to identify event-associated variables (death and myocardial infarction).
Results: Among a total of 95 patients included in the study, 39 (41.1%) underwent a non-elective procedure. The rate of overall mortality was 9.3% at 12 months and 13.6% at long-term follow-up, and that of non-fatal myocardial infarction 7.2% and 14.5%, respectively. On the other hand, the rate of stroke and coronary artery bypass grafting was 2.1% and 10.4% at 12 months, respectively. On multivariate analysis, the only independent predictors of adverse clinical events were non-elective intervention at 12 months ($p=0.003$) and age >70 years after the first year ($p<0.0001$).
Conclusions: Our results of left main percutaneous coronary intervention correspond with those reported by other authors. The incidence of one-year and long-term clinical events was associated with identifiable conditions, as procedural indication and age of the patients at the time of intervention.

Keywords: Left Main Coronary Artery Disease - Percutaneous Coronary Intervention - Stent

RESUMEN

Introducción: La angioplastia de Tronco de la Coronaria Izquierda es una opción terapéutica en pacientes con anatomía favorable.
Objetivos: Reportar nuestra experiencia en el tratamiento de estos pacientes, así como su evolución clínica y evaluar los predictores de eventos clínicos durante el seguimiento.
Material y Métodos: Análisis retrospectivo de pacientes intervenidos entre 2011 y 2017 por obstrucción significativa del Tronco de la Coronaria Izquierda (Clínica Bazterrica y Clínica Santa Isabel). Se registró la incidencia de eventos clínicos al año y alejados (3 años como mínimo). Se realizó un análisis univariado y multivariado (modelo de riesgos proporcionales de Cox) para identificar aquellas variables asociadas a la ocurrencia de eventos (muerte e infarto).
Resultados: Se incluyeron consecutivamente 95 pacientes, de los cuales en 39 el procedimiento fue no electivo (41,1%). La mortalidad global fue 9,3 % a los 12 meses y 13,6% alejada. La tasa de infarto de miocardio no fatal fue 7,2 % al año y 14,5% alejada. La tasa de accidente cerebrovascular fue 2,1% y la de revascularización fue 10,4% a los 12 meses. El único predictor multivariado de eventos a 12 meses fue la indicación no electiva del procedimiento ($p=0,003$). Cuando consideramos los eventos ocurridos luego del primer año, el único predictor multivariado fue la edad >70 años ($p<0,0001$).
Conclusiones: Nuestros resultados de la angioplastia del Tronco de la Coronaria Izquierda corresponden a los reportados por otros autores. La ocurrencia de eventos al año y eventos alejados se relacionó con condiciones identificables como la indicación del procedimiento y la edad de los pacientes.

Palabras Clave: Obstrucción del Tronco de la Coronaria Izquierda - Angioplastia Transluminal percutánea - Stent

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INTRODUCTION

Left main coronary artery (LMCA) obstructive disease is a predictor of poor prognosis in patients with coronary heart disease, and its revascularization is therefore a frequent indication. (1)

In coronary angiography registries, its prevalence is 5% in patients with suspected coronary heart disease. (2)

At present, unprotected left main percutaneous coronary intervention (PCI) is a therapeutic option in patients with favorable anatomy, and is also growing in cases with contraindications for surgery. (3, 4)

Multicenter studies, as EXCEL (5) and NOBLE (6), as well as numerous international registries (7) have demonstrated the feasibility and safety of this therapeutic modality compared with coronary artery bypass graft surgery.

Considering our previous experience in unprotected left main PCI treatment, (8) the aim of this report was to present our most recent results both in elective and non-elective patients, and to evaluate predictors of clinical events during short- and long-term follow-up in different clinical scenarios: chronic stable angina, ST- segment elevation and non-ST-segment elevation acute myocardial infarction (AMI), and cardiogenic shock.

METHODS

A retrospective analysis was performed evaluating patients who consecutively underwent left main PCI with bare-metal (BMS) or drug-eluting (DES) stents in two medical centers of the City of Buenos Aires (Clínica Bazterrica and Clínica Santa Isabel).

Patients with history of coronary artery bypass graft surgery with a patent graft distal to the LMCA (protected procedure) were excluded from the study.

The following operational definitions were considered:

A. Significant LMCA obstruction: ≥50% obstruction with respect to angiographic reference diameter. When the diagnosis of severity was established by intravascular ultrasound (IVUS), a minimum luminal area <6 mm2 was used.
B. Medina bifurcation obstruction 1.1.1 (The Medina classification was designed to typify coronary bifurcation obstructions, according to the presence or not of atheroma in the main or secondary branch, "1.1.1" being the one in which all coronary segments are compromised): obstruction involving the distal LMCA segment, with significant obstruction of the anterior descending and circumflex artery origin.
C. Procedure indication: A non-elective procedure was defined as that performed following a coronary angiography due to hemodynamic instability (including cardiogenic shock) or persistent myocardial ischemia secondary to a significant LMCA obstruction.
   Any procedure that did not match the aforementioned definition was considered elective, regardless of the clinical presentation (stable angina, ST-segment elevation or non-ST-segment elevation acute coronary syndromes).
D. Technical success: It was defined as left main coronary artery residual obstruction <30%. In the case of distal LMCA obstruction treatment, the residual obstruction of the secondary branch should be <50%.
E. Overall mortality: All deaths that occurred during follow-up, independently of their etiology.
F. Cardiovascular mortality: All deaths of evident cardiovascular origin (for example: AMI, heart failure, arrhythmia), those related with the procedure and those whose cause could not be established.
G. Stroke: Any acute or recent motor or sensitive deficit, with evident cerebral ischemia by computed tomography or nuclear magnetic resonance imaging of the brain.
H. Non-fatal AMI: Significant elevation of myocardial injury markers associated with at least a sign or symptom of myocardial ischemia (angina, ECG ST-T segment abnormalities or new segmental wall motion abnormality by imaging study). (9)
I. Revascularization: Any percutaneous or coronary artery bypass graft surgery procedure performed during the follow-up period. The procedure indication should be by ischemia occurrence in a functional test or acute coronary syndrome relapse. Procedures performed on the LMCA or other coronary arteries were considered.

Percutaneous coronary intervention procedure

Prior to the intervention, all patients received acetylsalicylic acid (ASA) (100 mg/day orally) and heparin sodium (100 units/kg), except for treatment with IIb/IIIa glycoprotein inhibitors, in which case 75 units/kg were administered.

The choice of arterial access, use of IIb/IIIa glycoprotein inhibitors, DES, adjuvant atherectomy, intra-aortic balloon counterpulsation, IVUS and angiographic control during follow-up was left at the operators' discretion.

Concomitantly, all patients received P2Y12 receptor antagonists, as clopidogrel (loading dose of 300 mg and then 75 mg per day) or ticagrelor (loading dose of 180 mg and then 90 mg per day), with at least 12-month recommended treatment duration.

Follow-up

Follow-up was performed by the authors, either by personal contact, telephone call, through contact with their general practitioner, or medical history or hospitalization summary review. The occurrence of all-cause death, cardiovascular death, non-fatal AMI, stroke and new coronary artery bypass graft surgery was recorded.

Statistical analysis

Continuous variables were expressed as mean and standard deviation and categorical variables as percentage. Difference between groups were evaluated using the Mann-Whitney test or Fisher´s exact test, according to continuous or categorical variables.

Percentages corresponding to the different events were reported with their 95% confidence interval (95% CI).

A univariate analysis for overall mortality and non-fatal infarction (death/AMI) at one-year and during follow-up was performed using the Kaplan-Meir method. Patients with events during the first year were excluded from the long-term evolution analysis.

All variables associated with the occurrence of death/AMI (with significance level <0.05) were included in a Cox proportional hazards model, with stepwise multivariate analysis.

Medical 19.1.3 and EPI INFO 7.2.3.1 for Windows software packages were used for the statistical analysis.

RESULTS

A total of 95 patients were consecutively included in

the study between January 2011 and December 2017. Table 1 shows baseline population characteristics. Technical success was achieved in 100% of patients.

In 59% of cases, procedures were elective and in 41% non-elective. Significant differences in the clinical presentation were found depending on the type of procedure indication, elective patients presenting stable or stabilized conditions, without evidence of cardiogenic shock (Table 1).

Only 3.2% of patients received ticagrelor and the rest clopidogrel as adjuvant treatment to acetylsalicylic acid (ASA). Drug-eluting stents were used in most cases. Table 2 shows angiographic and procedural characteristics.

Mean follow-up was 3.2±1.6 years. Figure 1 shows rate of events during follow-up in elective and non-elective patients.

The incidence of death/AMI was 17.5% (n=16) at 12 months. In univariate analysis, non-elective condition (RR: 5.4, 95% CI 1.9-15.6, p=0.002) and chronic kidney failure (RR: 6.4, 95% CI 1.1-36.4, p=0.04) were predictors of events and in multivariate analysis, the only independent predictor was non-elective condition (p=0.003).

Beyond one year follow-up, the incidence of death/AMI was 13.4% (n=13). In univariate analysis, age ≥70 years at the time of intervention (RR: 12.3, 95% CI 3.8-39.8, p <0.0001). and use of BMS (RR: 10.7, 95% CI 2.3-49.7, p=0.0025) were predictors of events and in multivariate analysis, the only independent predictor was age ≥70 years at the time of intervention (p=0.0001).

Figure 2 shows Kaplan-Meier curves for death/AMI combining multivariate predictors at one and 3 years after the procedure.

DISCUSSION

In 2010, the authors of the REMART-T registry reported that the "advent of DES, together with encouraging results of several multicentric registries and randomized studies have generated a growing interest in unprotected left main PCI". (10)

However, as shown in the RAdAC 2 registry presented in the last 2021 47th Congress of the Argentine

Table 1. Clinical characteristics of elective and non-elective patients

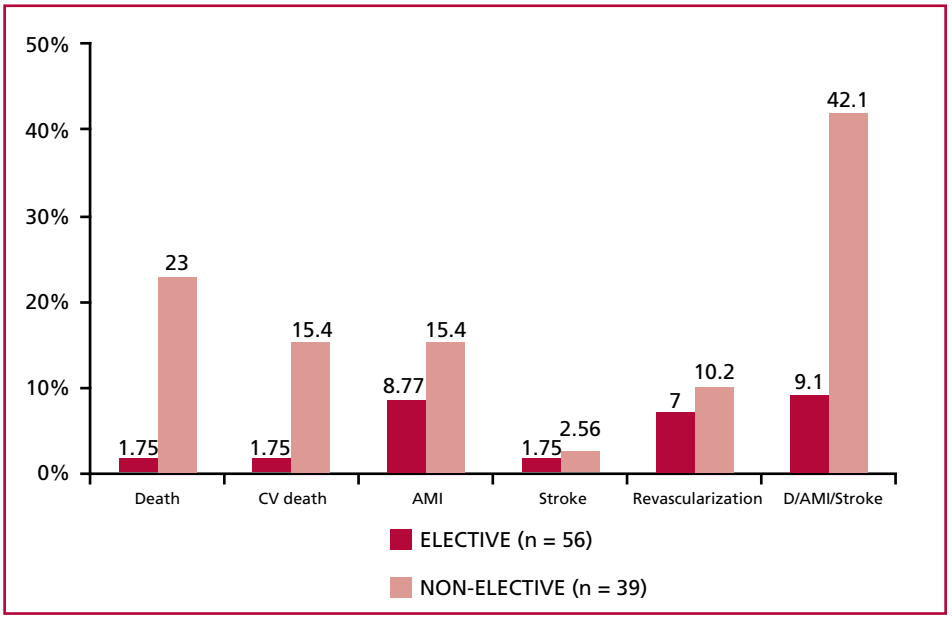
Variable	Total (n=95)	Elective (n=56)	Non-elective (n=39)	p
Male gender	77.7%	83.6%	69.2%	ns
Age	68.3 ± 13.4	68.8 ± 14.6	67.6 ± 11.6	ns
Age >70 years	45.7%	50.9%	38.5%	ns
HTN	69.9%	72.7%	65.6%	ns
Smoking	19.4%	14.6%	26.3%	ns
DBT	23.7%	20.0%	23.7%	ns
CKF	9.7%	9.1%	10.5%	ns
COPD	17.2%	20.0%	13.2%	ns
PVD	5.4%	3.6%	7.9%	ns
Previous infarction	50.5%	54.6%	44.7%	ns
Previous stent	40.9%	40.0%	42.1%	ns
Moderate/severe LVEF	28.7%	16.4%	46.2%	0.002
Clinical condition				<0.0001
Chronic angina	44.2%	72.7%	5.1%	
Non-ST-elevation ACS	37.9%	21.8%	59.0%	
ST-elevation ACS	17.9%	5.5%	35.9%	
Cardiogenic shock	9.5%	0%	23.1%	

HTN: Hypertension. DBT: Diabetes. CKF: Chronic kidney failure. COPD: Chronic obstructive pulmonary disease. PVD: Peripheral vascular disease. LVEF: Left ventricular ejection fraction. ACS: Acute coronary syndrome.

Table 2. Angiographic and procedural characteristics in elective and non-elective patients

Variable	Total (n=95)	Elective (n=56)	Non-elective (n=39)	p
SYNTAX score	24.4 ± 9.4	22.4 ± 9.1	27.2 ± 9.4	0.008
SYNTAX <23	43.6%	58.2%	23.1%	0.0008
Distal LMCA disease	40.4%	41.8%	38.9%	ns
Use of ≥2 stents	35.1%	40.0%	28.2%	ns
DES	78.7%	87.2%	66.7%	0.02
Cutting balloon (atherectomy)	59.6%	65.5%	51.3%	ns
IVUS	28.7%	45.5%	5.1%	<0.0001

LMCA: Left Main Coronary Artery DES: Drug-eluting stent. IVUS: Intravascular ultrasound.



CV: Cardiovascular. AMI: Acute myocardial infarction. D: Death

Fig. 1. Clinical events during follow-up in elective and non-elective patients

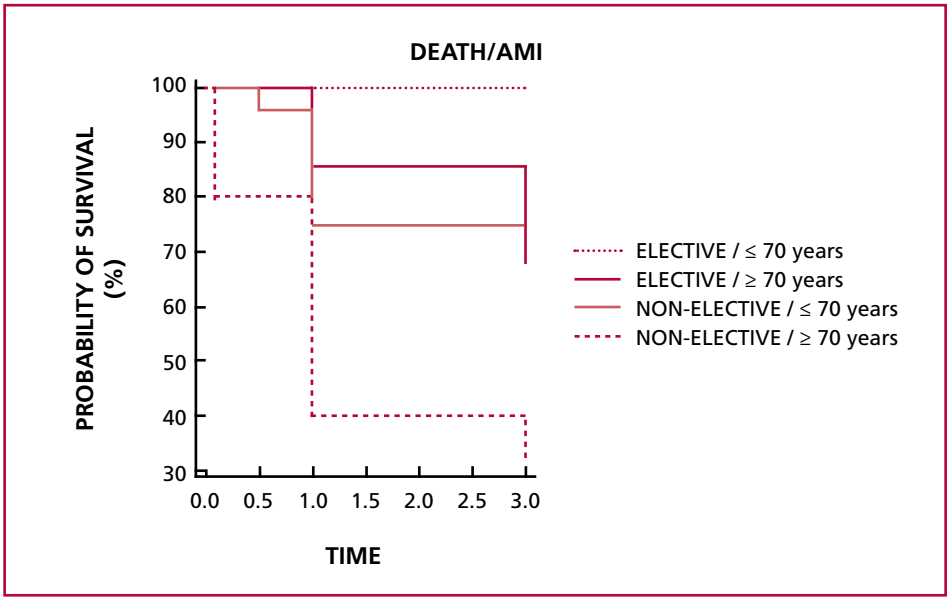


Fig. 2. Incidence of death or non-fatal AMI (considering procedure indication and age >70 years).

	Death/AMI 1 year	Death/AMI 3 years
ELECTIVE / ≤70 years (n=27)	0%	0%
NON-ELECTIVE / ≤70 years (n=25)	24.0%	24.0%
ELECTIVE / >70 years (n=28)	14.2%	35.7%
NON-ELECTIVE / >70 years (n=15)	60.0%	66.7%
p	<0.0001	<0.0001

Society of Cardiology, PCI indication in this group of patients is still scarce in our country (3.98% of all procedures performed). (11) If we consider our publication, we obtain an average of 14 patients per year.

In the BCIS registry, more than half of the patients requiring stent in unprotected left main PCI presented an acute coronary syndrome (15% with ST-segment elevation and 47% without ST-segment elevation), and mortality was significantly higher in acute patients compared with stable ones (adjusted OR 29.5). (12)

The AMIS Plus registry studied the evolution of patients with LMCA disease and ST-segment elevation AMI. The incidence of death and in-hospital events was higher in those with LMCA and other vessel disease, intermediate in isolated LMCA disease and mild in the rest of cases. (13)

The SHOCK study showed that 15.5% of patients presented ≥50% LMCA obstruction and 53.3% 3-vessel disease, with particularly elevated in-hospital mortality in patients with LMCA disease (62.8% vs. 49.9%). (14)

In our series, 40% of patients underwent a non-elective procedure, including patients with cardiogenic shock. These have been systematically excluded from randomized studies comparing PCI with stent and coronary artery bypass graft surgery (5, 6, 15), either due to their clinical condition (ST-segment elevation AMI), hemodynamic instability or presence of multiple comorbidities.

Regarding the influence of age on the long-term evolution, our results are in agreement with those of the REMAR-T registry. (10) In the SHOCK study, patients ≥75 years presented higher 30-day and long-term mortality. (16)

Limitations

Since this work was a registry, there was an implicit selection bias that does not allow establishing the reasons for patient orientation to a certain therapeutic modality (PCI or coronary artery bypass graft surgery).

Our center has a large experience in the treatment with stent of unprotected left main PCI. This aspect limits the extrapolation to other groups that occasionally perform this kind of treatment.

Of relevance, there was less use of DES and IVUS in patients with non-elective treatment. According to a recent meta-analysis, use of IVUS would be associated with lower long-term mortality.

In univariate analysis, use of DES was related with lower incidence of death and AMI. However, this association did not persist in multivariate analysis, which could be attributed to the number of patients included. There are no randomized studies comparing DES and BMS in the percutaneous treatment of unprotected LMCA. A longitudinal analysis of the IRIS-MAIN registry showed a significant decrease of long-term events (death, reintervention and composite events) after the systematic incorporation of DES. (18)

CONCLUSIONS

Our experience in the treatment with stent of the left main coronary artery is compatible with results reported by other authors. The occurrence of one-year and long-term events was associated to easily identifiable conditions as indication of elective or non-elective procedure, and patient age.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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