

Percutaneous Coronary Intervention for Unprotected Left Main Coronary Artery Lesions

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ABSTRACT

Background: Refinements in percutaneous coronary intervention (PCI), including the use of intravascular ultrasound (IVUS) and fractional flow reserve (FFR), have allowed the treatment of complex lesions with good results. As a result, the percutaneous approach for left main coronary artery (LM) lesions has spread, including centers with a lower volume of PCI procedures. Our objective was to report the early and late outcomes of PCI in unprotected LM lesions. **Methods:** Consecutive patients treated at two different hospitals from August 2009 to July 2013 were included. The indication for the percutaneous approach was based on the clinical assessment and the calculation of Syntax score, EuroScore and on the patient's wishes. **Results:** Twenty-eight patients with mean age of 69.2 ± 10.1 years were treated, 39% were diabetic and 39% had acute coronary syndromes. Half of the patients had EuroScore ≥ 6 ; the Syntax score was 26.0 ± 8.4 and 82% had LM bifurcation lesions. Interventions were guided by IVUS and/or FFR in 71.4% of the patients, 93% were treated with drug-eluting stents, and the 1-stent technique was used in most occasions. Angiographic success was achieved in 100% of the cases. At the 19.2 ± 13.7 month follow-up, the rate of major adverse cardiac events was 21.4% in the follow-up longer than 4 years, cardiac death 14.2%, non-fatal myocardial infarction 3.5% and target-lesion revascularization 3.5%. **Conclusions:** PCI in unprotected LM lesions, guided by IVUS and/or FFR whenever possible, is safe and effective in the short and long-term, in the experience of a hospital with a moderate number of PCI procedures.

DESCRIPTORS: Coronary artery disease. Coronary stenosis. Percutaneous coronary intervention. Drug-eluting stents. Ultrasonics.

RESUMO

Intervenção Percutânea em Lesão de Tronco de Coronária Esquerda Não Protegido

Introdução: Refinamentos da intervenção coronária percutânea (ICP), entre eles a utilização do ultrassom intravascular (IVUS) e da reserva de fluxo fracionada (FFR), têm permitido o tratamento de lesões complexas com bons resultados. Como consequência, a abordagem percutânea das lesões de TCE se difundiu, incluindo hospitais de menor volume de procedimentos. Nosso objetivo foi apresentar os resultados iniciais e tardios da ICP de lesões de TCE não protegido. **Métodos:** Foram incluídos pacientes consecutivos tratados em dois centros hospitalares, de agosto de 2009 a julho de 2013. A indicação da estratégia percutânea baseou-se em avaliação clínica, cálculo do escore Syntax, EuroScore e no desejo do paciente. **Resultados:** Foram tratados 28 pacientes, com idade de $69,2 \pm 10,1$ anos, 39% eram diabéticos e 39% eram portadores síndrome coronária aguda. Metade dos pacientes tinha EuroScore ≥ 6 ; o escore Syntax foi de $26,0 \pm 8,4$ e 82% tinham lesões localizadas na bifurcação. As intervenções foram guiadas por IVUS e/ou FFR em 71,4% dos pacientes, 93% foram tratados com stents farmacológicos, predominantemente pela técnica de 1 stent, e o sucesso angiográfico foi alcançado em 100% dos casos. O acompanhamento foi de $19,2 \pm 13,7$ meses. A taxa de desfechos clínicos maiores foi de 21,4% no seguimento maior a 4 anos, óbito cardíaco de 14,2%, infarto do miocárdio não fatal de 3,5%, e revascularização da lesão-alvo em 3,5%. **Conclusões:** A ICP de TCE não protegido guiada, sempre que possível, por IVUS e/ou FFR é segura e eficaz no curto e longo prazos, na experiência em um hospital com moderado volume de procedimentos.

DESCRITORES: Doença da artéria coronariana. Estenose coronária. Intervenção coronária percutânea. Stents farmacológicos. Ultrassom.

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Received: 7/18/2013 • Accepted: 09/11/2013

Significant lesions of the left main coronary artery (LMCA) are present in about 7 % of patients undergoing coronary angiography.¹ In these lesions, percutaneous coronary intervention (PCI) may be associated with technical difficulties and, consequently, with high rates of major adverse cardiac outcomes.²⁻⁴

Coronary artery bypass graft (CABG) surgery has always been a preferred strategy for treating patients with unprotected LMCA lesion, whereas PCI has been restricted to cases at high surgical risk. However, refinements in PCI technique, the availability of drug-eluting stents, the use of intravascular ultrasound (IVUS), fractional flow reserve (FFR), and dual antiplatelet therapy have contributed to significantly reduce the rates of stent thrombosis and restenosis. Together, these advances have allowed for the expansion of the indication for PCI to subgroups of greater complexity, such as lesions of the LMCA, even in patients with conditions requiring surgery.^{5,6}

Several multicenter registries and some randomized clinical trials at centers with extensive experience and with highly trained surgeons have compared PCI and CABG surgery in LMCA lesions, demonstrating the safety and efficacy of the percutaneous procedure with use of drug-eluting stents.^{2-5,7} These results have been motivating the dissemination and application of the interventional strategy for selected LMCA disease patients in lower volume centers.

This article presents an initial experience with percutaneous treatment of patients with unprotected LMCA lesions, showing its clinical, angiographic, and procedural profile, as well as its early and late results.

METHODS

Trial population

Patients undergoing PCI were prospectively included in a conjoined registry of Hospital José Carrasco Arteaga and Hospital Santa Inés, Cuenca, Ecuador. This registry was developed for academic quality control purposes and for its medical utility. Between August 2009 and July 2013, 2,910 diagnostic trials and cardiovascular interventions by catheter were performed, of which 672 were PCIs, and in 28 (4.1%) of these, unprotected LMCA lesions were assessed. The indication of percutaneous strategy was based on clinical assessment, in a SYNTAX and EuroScore score calculation, and on the patient's and his/her family's desires. In cases of acute coronary syndrome with ST-segment elevation or acute syndromes with hemodynamic instability, the decision for CABG was taken at the time of cine-coronary angiography. The other cases were discussed with the heart team (which included a heart surgeon) to establish the best revascularization strategy. The reasons for not performing CABG included high surgical risk, advanced age, low left ventricle ejection

fraction, distal coronary beds unsuitable for grafts, and refusal of surgery by the patient. All patients signed an informed and free consent. The trial was approved by the local ethics committees.

In this trial, the inclusion criteria were patients with LMCA lesions $\geq 50\%$ accompanied by symptoms or myocardial ischemia documented by functional testing; and patients with lesions $< 50\%$ with evidence of ischemia documented by $\text{FFR} \leq 0.80$ and/or minimal lumen area $< 6.0 \text{ mm}^2$ measured by IVUS. Patients with a history of CABG with patent grafts to the left coronary artery, contraindication to the use of dual antiplatelet therapy, and those who did not consent were excluded.

Coronary Intervention

All patients received dual antiplatelet therapy before the procedure (initial dose: clopidogrel 600 mg in patients with acute coronary syndromes and 300 mg in patients with chronic ischemia). Antithrombotic therapy consisted of unfractionated heparin at doses of 100 IU/kg for chronic cases or those with acute myocardial infarction, and enoxaparin at a dose of 1 mg/kg every 12 hours for patients with coronary syndrome without ST-segment elevation. The selection of the vascular access depended on medical conditions, weight, age, gender, and degree of complexity of the coronary anatomy. Thus, the radial access was preferred in male patients weighing $\geq 60 \text{ kg}$, hemodynamically stable, and candidates to elective PCI. The femoral access was generally chosen for female patients with low weight and complex coronary anatomy, which could require a guide catheter $\geq 7\text{F}$.

IVUS was recommended in all cases, both for pre- and post-procedural assessment, and if clinically and technically possible. FFR was available after August 2010 for one of the hospitals participating in this study, and was recommended in order to determine the treatment in patients with intermediate lesions, assessed by angiography and IVUS; and also to assess the need for additional intervention to the left circumflex artery with the one-stent cross-over technique, from LMCA to the left anterior descending artery. The chosen approach for bifurcation lesions was that of a provisional stent, while the two-stent technique was restricted to patients who had one or more of the following characteristics in the left circumflex artery: severe segmental lesion at its origin before the intervention, severe residual stenosis after stent implantation, $\text{FFR} < 0.80$, and presence of dissection.

After dilation, the simultaneous kissing balloons (SKB) technique was performed in all cases of planned implantation of two stents, or with the one-stent technique if $\text{FFR} < 0.80$ or when there was a severe residual lesion in the left circumflex artery ostium. The proximal optimization technique with a larger-diameter balloon was recommended in all cases.

Definitions and clinical outcomes

Angiographic success was defined as a residual stenosis < 20% and final TIMI flow = 3. However, successful intervention was defined as the achievement of angiographic success in the absence of death or stent thrombosis during in-hospital stay. The angiographic analyses were performed by an interventionist blinded to the results of PCIs. The quantitative parameters evaluated were: minimum lumen diameter, reference vessel diameter, stenosis diameter, lesion length, acute gain, and late loss. Angiographic restenosis was defined as a lesion > 50% within the stent or within 5 mm from proximal and distal edges in relation to the stent.

Major adverse cardiac events comprised death of cardiac origin, acute myocardial infarction, stroke, and need for target lesion revascularization. Cardiac death was defined as a sudden, unexplained death, or due to heart failure or ischemic episodes. Acute myocardial infarction was defined as an increase of troponin or CK-MB ≥ 3 times the upper limit of normal, with or without symptoms, or as the development of new Q waves on the electrocardiogram in at least two contiguous leads. Stroke was defined as the finding of a neurological motor deficit, with post-intervention confirmation by computed tomography or magnetic resonance imaging. Target lesion revascularization was defined as any intervention, percutaneous or surgical, performed to treat restenosis of the stent(s) implanted, used in turn to treat the LMCA lesion. Stent thrombosis was defined according to Academic Research Consortium (ARC). All patients were clinically evaluated in the clinic after 30 days, and then every 90 days after PCI. All clinical, laboratory, and functional results were recorded in a program for digital clinical records (AS/400 system). A new angiography was performed with the return of symptoms or was suggested after six months of PCI-index in patients with asymptomatic evolution.

Continuous variables were expressed as means and standard deviations and categorical variables as absolute numbers and percentages.

RESULTS

The population studied showed a clinical profile of high complexity, comprising a significant portion of elderly patients (39% of them > 75 years), and 39% of diabetics, 14% with chronic renal failure, 21% with peripheral vascular disease, and 39% with acute coronary syndrome. In 35% of cases, the left ventricle ejection fraction was < 45%, and 50% had EuroScores ≥ 6 (Table 1).

The angiographic and procedural characteristics (Table 2 and Figures 1, 2, and 3) also revealed a complex profile, with over half of patients with LMCA + three-vessel injuries and 82% with involvement of the bifurcation. The distribution of the SYNTAX score was

39.2% for scores between 0 and 22, 42.8% for scores between 23 and 32, and 17.8% for scores ≥ 33 . The procedures were performed mostly via femoral artery (86%), in 71% of cases with the use of one stent. 2.8 ± 1.4 stents were used per patient and 93% of patients received drug-eluting stents. The interventions were guided by IVUS and/or FFR in 71.4% of the procedures, and all cases achieved angiographic success.

TABLE 1
Clinical characteristics

Characteristics	n = 28
Age, years	69.2 \pm 10.1
Male, n (%)	19 (67)
Diabetes mellitus, n (%)	11 (39)
Hypertension, n (%)	21 (75)
Dyslipidemia, n (%)	14 (50)
Smoking, n (%)	7 (25)
Family history of CAD, n (%)	6 (21)
Previous stroke, n (%)	1 (4)
Previous AMI, n (%)	9 (32)
Previous PCI, n (%)	8 (29)
Previous CABG surgery, n (%)	1 (4)
Chronic renal failure, n (%)	4 (14)
Peripheral vascular disease, n (%)	6 (21)
Clinical status, n (%)	
Stable angina FC II-IV	19 (76)
Unstable angina	3 (11)
AMI without ST-segment elevation	3 (11)
AMI with ST-segment elevation	5 (18)
Ejection fraction, %	50.9 \pm 10.6
EuroScore	5.9 \pm 3.3
Medications, n (%)	
Beta-blocker	25 (89)
ACEI or angiotensin II receptor inhibitor	22 (82)
Acetylsalicylic acid	28 (100)
Clopidogrel	28 (100)
Statins	28 (100)
Inhibitors of glycoprotein IIb/IIIa	5 (18)

CAD = coronary artery disease; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; FC = functional class; ACEI = angiotensin-converting enzyme inhibitors.

TABLE 2
Angiographic and procedural characteristics

Characteristics	n = 28
Affected vessels, n (%)	
LMCA, isolated	2 (7)
LMCA + 1 vessel	5 (18)
LMCA + 2 vessels	7 (25)
LMCA + 3 vessels	14 (56)
Location of LMCA lesion, n (%)	
Ostium	3 (11)
Body	2 (7)
Bifurcation	23 (82)
Medina rating, n (%)	
1.1.1	6 (21)
1.1.0	12 (43)
1.0.0	6 (21)
0.1.0	3 (11)
0.1.1	1 (4)
Syntax score	26.0 ± 8.4
Radial approach, n (%)	4 (14)
PCI technique used, n (%)	
One stent	20 (71)
Mini-crush	4 (14)
T-stenting	2 (7)
Culotte	1 (4)
Simultaneous kissing stenting	1 (4)
Post-dilation, n (%)	
Proximal stent optimization	23 (82)
Simultaneous kissing balloons	15 (54)
Number of stents used	2.8 ± 1.4
Total length of stents, mm	58.3 ± 32.1
Drug-eluting stent, n (%)	26 (93)
First generation	6 (21)
Second generation	20 (71)
PCI guided by IVUS, n (%)	20 (71)
PCI guided by FFR, n (%)	20 (71)
Rotational atherectomy use, n (%)	4 (14)

LMCA = left main coronary artery; PCI = percutaneous coronary intervention; IVUS = intravascular ultrasound; FFR = fractional flow reserve.

Late angiography was performed in 12 patients, due to the refusal to perform a new procedure, or to not having reached six months of evolution after PCI (Table 3). Angiographic restenosis was observed in only one patient (3.5%).

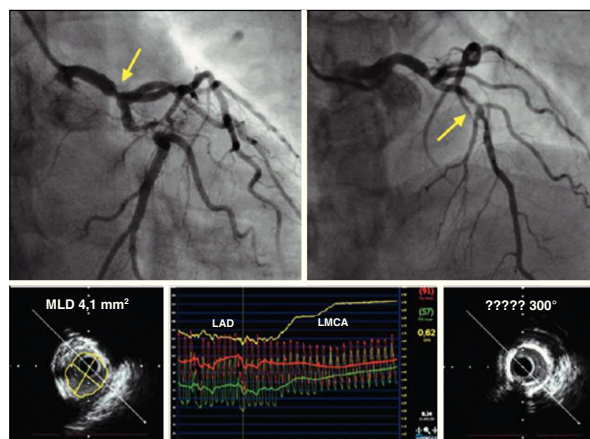


Figure 1 – Lesion in the left main coronary artery (LMCA) + three vessels, Syntax 28. The right coronary artery was previously treated during an acute coronary syndrome. Lesions of LMCA and left anterior descending artery (LAD) were assessed by intravascular ultrasound and fractional flow reserve, demonstrating a need for revascularization. Sub-occlusive lesion in the proximal third of the left circumflex artery. MLD = minimum lumen diameter.

The rate of major adverse cardiac outcomes in a follow-up of 19.2 ± 13.7 months was 21.4% greater than after four years of follow-up, due the in-hospital cardiac death of three patients who were treated in the presence of an acute myocardial infarction with ST-segment elevation, an asymptomatic acute myocardial infarction detected by elevation of cardiac enzymes three times the normal upper limit, and with a need for repeat revascularization due to restenosis of the left circumflex artery (Table 4). There were no cases of stroke or stent thrombosis.

DISCUSSION

PCI for the treatment of unprotected LMCA lesion, wherever possible guided by IVUS and FFR, is effective and safe in the short and long term, in the experience of a medical staff of a hospital with moderate procedure volume.

Technical aspects

The one-stent technique was applied in most patients; two stents were used in 29% of cases. Current evidence suggests that the provisional T-stenting strategy should be preferred in bifurcation lesions, whether or not located in the LMCA, due to the low rate of major cardiac events and lower incidence of restenosis at six months (< 6%).^{8,9} In the present registry, cases with involvement of the bifurcation were treated with the simplest technique and the best clinical results were obtained: one stent implantation directed from the LMCA to the left anterior descending artery, followed by proximal optimization, and finally, by post-dilation

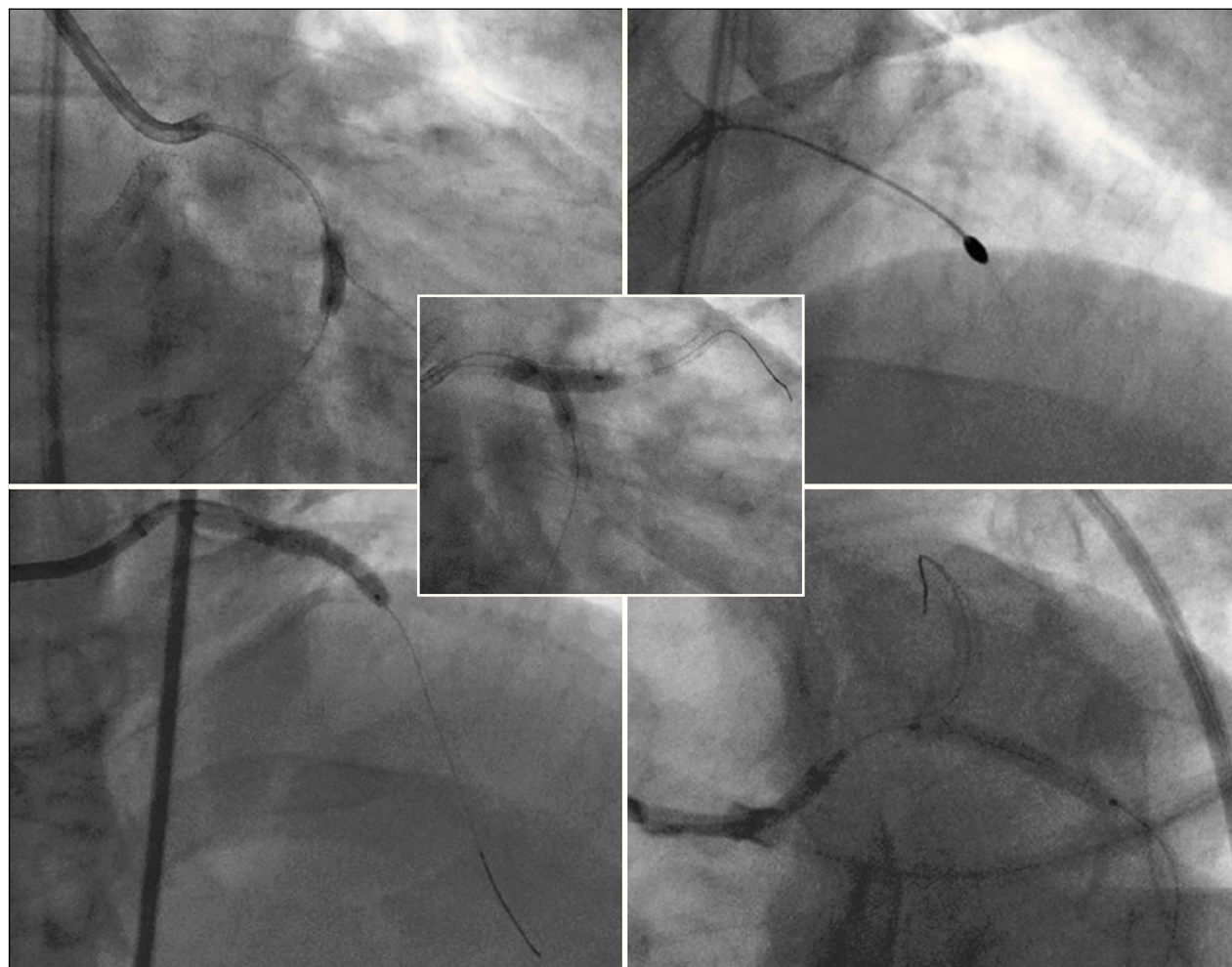


Figure 2 – Pre-dilation of lesion in left circumflex artery bifurcation and in the proximal third, followed by rotational atherectomy for the left anterior descending artery. Placement of two drug-eluting stents 3.5 × 32 mm for left anterior descending artery and of 3.0 × 24 mm for left circumflex artery with T-stenting technique. Final post-dilation with simultaneous kissing balloons technique.

with SKB when necessary (guided by FFR in one-third of cases). A second stent was used in a smaller percentage of patients, which is consistent with the findings of several randomized trials and registries.^{2,4,7} However, there are different opinions regarding the application of post-dilation. Some authors have advocated the realization of post-dilation with SKB technique in all cases of LMCA lesion, even when using one stent, in order to gain access to the lateral branch and optimize the proximal expansion.³⁻⁵ In the present analysis, 54% of patients received post-dilation with SKB, because those who received one stent showed no serious lesion in the left circumflex artery origin, dissections, changes in coronary flow, nor ischemia detected by FFR.

The usefulness of the SKB technique with one stent without involvement of the lateral branch has been explored in two trials on bifurcation, showing neutral or even harmful results.^{10,11} Gwon et al,¹⁰ in the COBIS

registry, analyzed 1,065 patients with bifurcation lesions – two-thirds with true bifurcations. Post-dilation with SKB had an unfavorable effect with respect to the need for target lesion revascularization, probably related to a deformation of the rods, which was not fully corrected with simultaneous dilation.

Given the recent availability of FFR in this service, not all patients were evaluated from a functional standpoint. However, its use has changed preconceptions regarding the treatment of bifurcations. For example, two of the cases showed LMCA lesion between 30% and 40%, but with abnormal values of FFR. Park et al.¹² confirmed this fact, verifying a discrepancy between visual estimation and functional impact of LMCA injuries. According to their results, 40% of lesions < 50% had FFR < 0.80. This discrepancy between the angiographic results and FFR was also a finding in the assessment of incarcerated lateral branch after stent implantation in

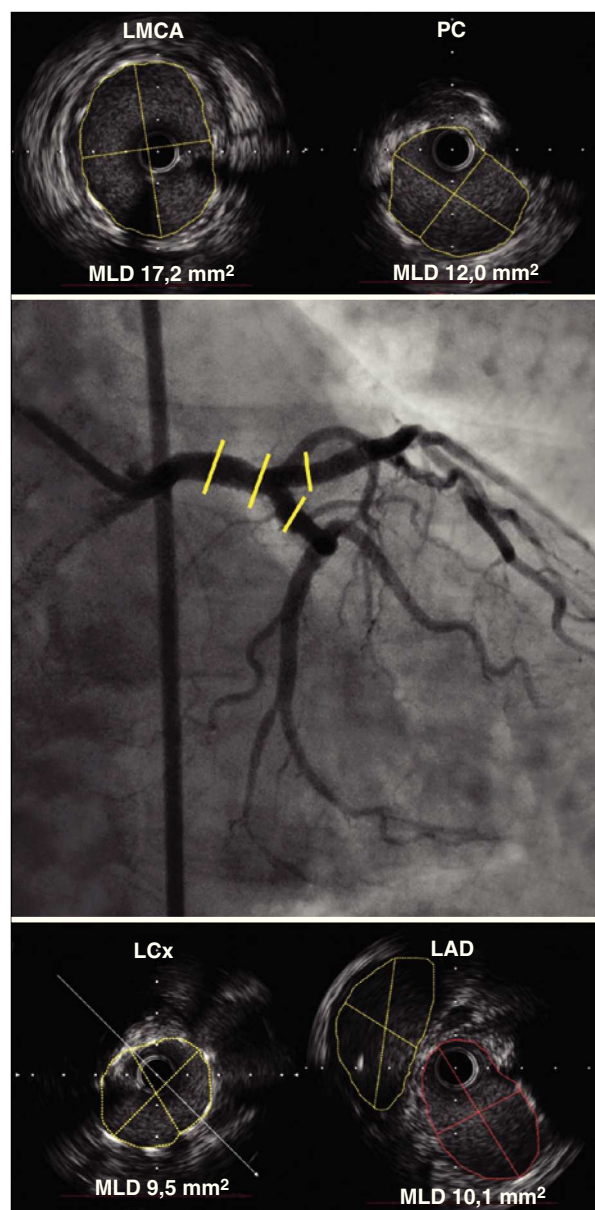


Figure 3 – Optimization achieved and verified by intravascular ultrasound through the minimal areas of the lumens in the origin of the left anterior descending artery (LAD), left circumflex artery (LCx), the polygon of confluence, and body of the left main coronary artery (LMCA). MLD = minimum lumen diameter; PC = polygon of confluence.

the main branch. Koo et al.¹³ demonstrated that only 27% of residual lesions $\geq 75\%$ had FFR < 0.75 and needed intervention.

Since there is no other segment of the coronary tree with greater interobserver variability in the assessment of lesion severity than the LMCA, the use of FFR to guide PCI can bring benefits, such as verifying the presence of hemodynamically significant lesions and the simplification of the intervention in bifurcation lesions.¹⁴ Considering that the presence of angiographic

TABLE 3
Quantitative coronary angiography

Angiographic data	n = 28
Pre-procedure	
Reference diameter, mm	3.5 ± 0.6
Minimum lumen diameter, mm	1.5 ± 0.2
Lesion length, mm	7.5 ± 2.9
Diameter of the lesion, %	57.2 ± 17.1
Post-procedure	
Reference diameter of the stent, mm	3.8 ± 0.6
Minimum diameter of the lumen of the stent, mm	3.4 ± 0.6
Stent length, mm	10.1 ± 4.3
Lesion diameter in-stent, %	10.7 ± 7.1
Acute gain, mm	1.9 ± 0.8
Late	n = 12
Reference diameter of the stent, mm	3.8 ± 0.4
Minimum diameter of the lumen of the stent, mm	3.4 ± 0.6
Lesion diameter in-stent, %	9.4 ± 2.3
Late loss, mm	-0.02 ± 0.3
Angiographic restenosis, n (%)	1 (3.5)

stenosis is one of the many factors that influence the coronary flow, the decision to intervene in an LMCA lesion should be based on clinical judgment, functional tests, and a thorough invasive evaluation, preferably by FFR and IVUS.

Clinical aspects

PCI for unprotected LMCA is increasingly emerging as a viable alternative for CABG surgery. Data collected from the SYNTAX trial, from numerous worldwide registries, and from small clinical trials have led to an evolution in the current indication of the European guideline for class IIa (level B evidence) of PCI of isolated LMCA, or in lesion involving the origin or body in association with one-vessel disease. Likewise, in the opinion of experts, PCI has been recommended for patients at high surgical risk or in the setting of acute myocardial infarction.⁶ The clinical profile of the present clinical practice registry, measured by EuroScore and Syntax, showed a population with a high potential to present major clinical outcomes (patients with acute myocardial infarction, cardiogenic shock, and low ejection fraction were included). However, the event rate was low in the short and long term. This finding may be due to two factors. Firstly, the average follow-up time is relatively short, and there is a possibility of occurrence of a significant event in the. For example, in the long term. RESEARCH

TABLE 4
Cumulative clinical outcomes

Outcomes	In-hospital	30 days	One year	Four years
Mortality, n (%)	3 (10.7)	4 (14.2)	4 (14.2)	5 (17.8)
Cardiac death	3 (10.7)	3 (10.7)	3 (10.7)	4 (14.2)
Death, non-cardiac	0	1 (3.5)	1 (3.5)	1 (3.5)
Acute myocardial infarction, n (%)	1 (3.5)	1 (3.5)	1 (3.5)	1 (3.5)
Stroke, n (%)	0	0	0	0
Revascularization, n (%)				
Target vessel	0	0	0	1 (3.5)
Target lesion	0	0	1 (3.5)	1 (3.5)
Major adverse cardiac outcomes, n (%)	4 (14.2)	4 (14.2)	5 (17.8)	6 (21.4)

registry, the subgroup of patients with unprotected LMCA lesion treated by PCI with drug-eluting stents and with high-risk clinical and angiographic profile (EuroSCORE = 4.2, Syntax = 39.4, and ejection fraction of 45.3%) presented cardiac outcomes with a significant increase in the second year of follow-up. The causes for this behavior have not been clarified.¹⁵ Second, the concomitant use of FFR and IVUS helped the interventionist to improve the cases' selection, optimizing the immediate and medium-term technical and clinical results. Although this trial represents only the experience of a medical team of two centers with moderate procedure volume, the availability of IVUS and FFR and their application in two-thirds of cases may have played an important role in obtaining good results. Park et al.¹² showed that the use of IVUS to optimize the intervention of unprotected LMCA with the use of drug-eluting stents had an impact on mortality, which was lower compared to PCI guided by angiography alone.¹⁶ The critical role of IVUS for post-procedural assessment in a setting of LMCA is evident, from a trial that demonstrated a rate of restenosis < 6% with the two-stent technique, when the authors reached minimum luminal areas of 5, 6, 7, and 8 mm² for the left circumflex artery origin, left anterior descending artery, polygon of confluence, and LMCA, respectively.¹⁷

Limitations of the study

This was a small sample of the experience of a single medical staff, in addition to presenting the inherent limitations of an observational trial. However, it is the only trial of PCI in unprotected LMCA known in Brazil.

CONCLUSIONS

Guided PCI in significant lesions of unprotected LMCA, by IVUS and FFR whenever possible, is safe and effective in the medium-term follow-up, in the experience of a medical team with moderate procedure volume.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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