Left main coronary artery percutaneous revascularization: *alea jacta est*

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**ABSTRACT**

For many years, left main coronary artery disease has remained as the last frontier resisting percutaneous coronary intervention. Until recently, the most relevant clinical studies in this regard as well as clinical practice guidelines favored surgical revascularization almost as the only treatment pathway for the management of this condition. The changes that have occurred over the last 10 to 15 years since the appearance of drug-eluting stents and their technological advances have been extraordinary. This, added to the publication of randomized clinical trials that compared both revascularization modalities, has placed percutaneous coronary interventions at a similar level to surgery in a large number of patients. The anatomical, technical, and strategic aspects are essential for the percutaneous management of left main coronary artery lesions given their tremendous clinical variability. In this article we will be reviewing their anatomy, angiography, intracoronary diagnostic techniques, and different percutaneous revascularization strategies. As long as future clinical studies do not definitively favor percutaneous over surgical revascularization or vice versa, individual discussions on each particular case by the heart team and our patients’ preferences should guide our clinical decision-making process.

**Keywords:** Coronary artery disease. Left main coronary artery. Percutaneous coronary intervention. Coronary artery bypass graft.

Revascularización percutánea del tronco coronario izquierdo: *alea jacta est*

**RESUMEN**

La enfermedad del tronco coronario izquierdo ha permanecido muchos años como la última frontera que se resistía al intervencionismo coronario percutáneo. Hasta hace poco tiempo, los estudios clínicos más relevantes en este campo, así como las guías clínicas, han sido favorables a la revascularización quirúrgica casi como forma exclusiva de tratamiento de esta patología. Los cambios ocurridos en los últimos 10-15 años, desde la aparición de los *stents* farmacoactivos y su mejora tecnológica, han sido vertiginosos. La realización de estudios aleatorizados que han comparado ambas modalidades de revascularización ha llevado al intervencionismo percutáneo a la altura de la cirugía en un alto porcentaje de pacientes. Los aspectos anatómicos, técnicos y de estrategia son fundamentales en el tratamiento percutáneo de estas lesiones, dada su enorme variabilidad clínica. En tanto los estudios clínicos futuros no se decanten definitivamente a favor de la revascularización percutánea o de la quirúrgica, la discusión individualizada de cada caso en un equipo multidisciplinario y las preferencias de los pacientes deberían guiar la decisión clínica.

**Palabras clave:** Enfermedad coronaria. Tronco coronario izquierdo. Intervencionismo coronario percutáneo. Cirugía de revascularización coronaria.

**Abbreviations**


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INTRODUCTION

Significant left main coronary artery (LMCA) disease is present in 4% to 5% of all coronary angiographies. Since the LMCA supplies over 75% of all the myocardial blood flow, the risk associated with its lesions is the highest of all possible coronary lesions. Without revascularization, its prognosis is poor and mortality rate can be up to 37% at 3-year follow-up. Revascularization can be surgical or percutaneous, each one with its corresponding advantages and limitations. Assessing anatomic spread correctly, the complexity of coronary artery disease, the patient’s comorbidities, and the operator’s expertise in complex percutaneous coronary interventions (PCI) are key factors when choosing the right revascularization strategy. There are different models and scales to guide the selection of patients. However, none of them has become the leading model yet.

HISTORIC PERSPECTIVE

Coronary artery bypass graft (CABG) has been the standard of care for the management of patients with LMCA disease based on early clinical trials that proved its prognostic benefit in patients assigned to surgery compared to medical therapy. Patients with severe LMCA disease were excluded from most of the early clinical trials and, until recently, no specific trial compared the results of surgery vs PCI as one of its endpoints. Currently, there are randomized clinical trials that have confirmed the utility of the PCI to treat LMCA disease; actually, the American and European clinical guidelines consider it the recommended strategy in certain settings. Approximately, 50% of this type of lesions are revascularized percutaneously in our setting with an annual 5% increase.

ANATOMIC CONSIDERATIONS

Anatomically speaking, the LMCA can be divided into 3 portions: ostial portion, mid-portion, and distal portion; the latter is a bifurcation with an angle that is typically wider compared to other coronary bifurcations (> 70°). It supplies at least 75% of the total coronary flow. The LMCA caliber is often 5 mm ± 0.5 mm and its mean length is 10.5 mm ± 5.3 mm. In up to 30% of the cases it originates from the ramus intermedius or bisector branch (figure 1).

LMCA atherosclerotic disease is often diffuse. When the bifurcation is affected (in 70% of cases) there is also often presence of plaque at the beginning of the left anterior descending coronary artery (LAD) and left circumflex artery (LCx). At times, the origin of both the LAD and the LCx is independent from the left coronary sinus without LMCA per se (0.41% to 0.67% of cases). In 0.03% of patients, the origin of the LMCA is anomalous describing its trajectory between the aorta and the pulmonary artery, a pattern associated with a high risk of sudden death.

LEFT MAIN CORONARY ARTERY ASSESSMENT

Angiography

The clinical practice guidelines of the European Society of Cardiology indicate that the revascularization of the LMCA is indicated for patients with angiographic stenoses > 50% and documented myocardial ischemia. The practical problem here is that coronary angiography has limitations when evaluating LMCA disease with great intra and interobserver variability. Some ostial lesions can be overestimated due to catheter-induced overlapping and artifact or the presence of an associated spasm.
Pressure wire

The pressure guidewire provides valuable information to stratify the severity of LMCA disease. In order to stop a presumably ostial disease from impacting measurement, pressures need to be equalized and measured using a guide catheter partially "desintubated" from the LMCA. Obtaining hyperemic indices from the LAD and the LCx leads to better overall assessments of the severity of LMCA disease. Also, it secures the decision-making process on the best therapeutic approach. Some authors suggest that IV adenosine is better than intracoronary adenosine to secure the condition of maximum hyperemia.

Another important aspect when assessing the LMCA with the pressure guidewire is the physiological interdependence of the coronary tree that may change the values of fractional flow reserve (FFR).

Figure 2. Key points to optimize the percutaneous coronary interventions performed on the ostial and mid-portions of the left main coronary artery through intravascular ultrasound. IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LCx, left circumflex artery; LMCA, left main coronary artery; MSA, minimum stent area. (Modified with permission from de la Torre Hernández et al.)

Figure 3. Key points to optimize the percutaneous coronary interventions performed on the distal left main coronary artery through intravascular ultrasound. IVUS, intravascular ultrasound; LAD, left anterior descending coronary artery; LCx, left circumflex artery; LMCA, left main coronary artery; MSA, minimum stent area. (Modified with permission from de la Torre Hernández et al.)
Association of Percutaneous Cardiovascular Interventions33 [figure 4]. Therefore, in ambiguous LMCA lesions, MLAs > 6 mm² would be indicative of no revascularization, MLAs < 4.5 mm² to 5 mm² would be indicative of revascularization, and MLAs between 4.5 mm-5 mm to 6 mm² would recommend the use of the FFR/iFR indices before making any decision.

REVASCULARIZATION OF THE LEFT MAIN CORONARY ARTERY

Surgical revascularization

CABG has been the standard of care for patients with LMCA disease since traditional clinical trials confirmed its prognostic benefit in patients randomized to surgery vs medical therapy.1 The CASS registry reported a 4-year survival rate in 88% of operated patients compared to 63% in non-revascularized patients.34 Other studies confirmed that the mortality rate dropped to 65% with surgery.35 This allows a complete revascularization regardless of the characteristics of proximal lesion and technical advances facilitate faster procedures without having to use extracorporeal blood pumps. The main setback is still the non-negligible peri and postoperative morbidity and mortality. Some studies have reported a mortality rate between 5.5% to 8.5%, a need for ischemia-guided revascularization of 7.1% to 9.4%, and a rate of stroke of 5.1% to 5.1% at the 3-year follow-up.36

Percutaneous revascularization

The arrival of stents improved the results of PCI on the LMCA significantly. However, at the beginning, conventional stents fared worse compared to surgery with mortality rates of 14%, a left ventricular ejection fraction (LVEF) > 40% and 78%, and a LVEF < 40% at the 9-month follow-up.37 With the arrival of drug-eluting stents, the rates of restenosis and adverse events dropped low enough to be able to compare PCI to CABG.38-41 With event-free survival rates at the 1-year follow-up of 98% in patients with LVEF < 40%.38 In patients considered non-eligible for surgery (EuroSCORE > 6 or Parsonnet > 15), the mortality and survival rates without major adverse cardiovascular events were 3.5% and 73.3%, respectively, at the 6-month follow-up.42 These studies already showed that the PCIs performed on the ostial and mid-portions of the LMCA seemed to have a better prognosis compared to those performed on the distal LMCA or that involved bifurcation. The arrival of new antiproliferative drugs, the development of better devices, and the use of new techniques and strategies to treat bifurcation improved results, efficacy, and the good prognosis of the PCIs performed on the LMCA in experienced centers.

Surgical vs percutaneous revascularization

Six landmark randomized clinical trials have compared percutaneous and surgical strategies [table 1]. The first ones (LE MANS,43 SYNTAX,44 Boudriot et al.,45 and PRECOMBAT46) were conducted with first-generation drug-eluting stents and reported similar rates of a composite of death, infarction, and stroke for both strategies. The difference in results obtained by these studies was very controversial; differences were reported in the definition of endpoint and perioperative infarction as possible determinants. Actually, unlike the EXCEL, the NOBLE trial excluded periprocedural infarction in the definition of endpoint, which may be indicative of the actual clinical practice.46,47 The difference in results obtained by these studies was very controversial; differences were reported in the definition of endpoint and perioperative infarction as possible determinants. Actually, unlike the EXCEL, the NOBLE trial excluded periprocedural infarction in the definition of endpoint, which may be indicative of the actual clinical practice.46,47

In particular, the FFR has been reportedly overestimated in the presence of diffuse disease of the LAD and the LCx and underestimated in cases of significant lateral branch disease.30 Therefore, in the presence of concomitant distal branch disease, measuring the FFR during controlled retrieval can be useful.30 Regarding the pathological threshold, it seems that delaying the PCI with FFR values > 0.8 is safe.31 Although the value of other pressure guidewire indices that don’t require hyperemia like the instantaneous wave-free ratio (iFR) has not been fully assessed in the LMCA, a study proved that using the iFR to delay the revascularization of the LMCA is safe.32 Currently, the multicenter clinical trial iLITRO (NCT03767621) is being conducted in Spain. This trial will probably shed light on the utility of the iFR and its pathological threshold in the management of LMCA lesions.

Integrating different techniques

Integrating the IVUS and the pressure guidewire in the assessment of the LMCA of angiographically dubious severity is advised as stated by an international consensus document from the European Association of Percutaneous Cardiovascular Interventions.

Figure 4. Criteria for significant left main coronary artery disease. FFR, fractional flow reserve; MLA, minimum lumen area. (Modified with permission from Johnson et al.22)
from the composite of primary events although its inclusion is recommended by the Academic Research Consortium and is part of the universal definition of myocardial infarction. It has been confirmed that periprocedural infarction is associated with a worse prognosis. Also, the large difference seen in the rate of stent thrombosis (0.7% in the EXCEL trial vs 3% in the NOBLE) is indicative of the possible influence of the different type of stent used in each of these studies.

In general, the results of these studies suggest that when complete revascularization is achieved, both surgery and the PCI achieve similar results for the composite of death, infarction, and stroke at the 5-year follow-up. However, there is an early benefit for the PCI in terms of periprocedural infarction and stroke that is compensated by the higher risk of infarction at the long-term follow-up. The risk of requiring a new revascularization is evenly higher in patients treated with PCI compared to surgical patients.

Another issue that should be taken into consideration is the correlation between the results of the PCI and the SYNTAX score. The first clinical trials conducted on this topic already suggested that the change of SYNTAX score between the SYNTAX and LMCA scores had a better prognosis with PCI compared to patients with higher SYNTAX scores. Also, patients with high SYNTAX scores showed a higher complexity of LMCA disease. Therefore, patients with low SYNTAX scores seem to be directly proportional to the angiographic mortality.

All metanalyses have described that, overall, long-term cardiovascular mortality seems to be directly proportional to the angiographic complexity of LMCA disease. Therefore, patients with low SYNTAX scores had a better prognosis with PCI compared to patients with higher scores. Also, patients with high SYNTAX scores showed a non-significant tendency towards a higher 10-year survival rate.
with surgery compared to PCI. 54-56 One of the main setbacks of this score is that it only includes anatomical variables. Currently, there are other scales including angiographical, clinical, and even functional variables, but their utility as long-term prognostic markers of LMCA disease has not been properly studied yet. 57

The current clinical practice guidelines on coronary revascularization 16 establish the indication for CABG or PCI based on the SYNTAX score (table 2). If complexity is low, the PCIs performed on the LMCA have the same indication as surgery (IA). The PCI is an alternative to surgery in patients with intermediate SYNTAX scores (II A) and greater evidence is needed in patients with high SYNTAX scores before clearly recommending PCI.

### Patient selection

The European clinical practice guidelines highlight the importance of the heart team in the decision-making process on which revascularization strategy should be used in stable patients with LMCA disease. This team should include clinical and interventional cardiologists and cardiac surgeons. However, in emergent procedures, surgery is not often a viable option due to the delay involved and the progressive worsening of prognosis in relation to ischemic time. Pappalardo et al. 52 described in-hospital mortality rates of 21% (basically due to multiorgan failure) in patients with acute myocardial infarction and acute occlusion of the LMCA. However, patients who survived hospitalization and were treated with PCI had a good prognosis with a 1-year survival rate of 89.5%.

In the remaining cases it would be desirable to avoid performing interventional procedures ad hoc after the diagnostic procedure. The different revascularization options should be discussed with the clinical cardiologist, the cardiac surgeon, and especially with the patient. The latter should also be objectively informed of the theoretical pros and cons of every technique and the specific results obtained by the treating center making him part of the decision-making process. Other clinical, anatomic and general factors should be taken into consideration too (table 3). Finally, if performing a PCI on the LMCA is considered the best option, the administration of the right predmedication, assessment by the heart team, and procedural planning on the technique and materials that will be used are all associated with higher rates of success.

Since most clinical trials have been conducted in centers with coronary care units, performing PCIs on the LMCA in centers without these units has been controversial. However, since there is evidence of the good outcome of PCIs in centers without these units, 53-55 it is widely accepted that PCIs can be performed on the LMCA in these centers safely as long as an experienced medical team is in charge and the necessary technical equipment used. Also, the patient’s informed consent needs to have been collected, and a previous protocol established for urgent transfers to hospitals with coronary care units in the hypothetical case that the patient may require urgent surgery.

### Operators and equipment

The PCIs performed on the LMCA should always be considered high-risk procedures. Actually, the experience of the operators is of paramount importance here. There is evidence that patients treated in high volume centers that perform procedures like this regularly have a better prognosis. 56

The equipment should guarantee the proper assessment of the LMCA (IVUS, pressure guidewire). All kinds of materials that may be required to perform the angioplasty and handle all possible complications should be available too. Since it is a high-risk procedure, hemodynamic support devices and resources like the intra-aortic balloon pump and the Impella device (Abiomed, United States) are very important.

#### ANGIOPLASTY OF THE LEFT MAIN CORONARY ARTERY

Prior to performing the procedure, it is essential to conduct a comprehensive analysis of the case to decide on the strategy, access route (radial or femoral), caliber of the introducer sheath (due to the presumable need for the double stenting technique, 7-Fr catheters via femoral access or “7 in 6-Fr” catheters via radial access are advised), and type of guide catheter. Although radial access has replaced femoral access in many cases, the PCIs performed on the LMCA are probably a niche where femoral access should be considered since obtaining the least support possible can be key here. Also, this access facilitates the use of larger caliber catheters and the possibility of quick hemodynamic support device implantation.

Damage to the distal LMCA or bifurcation complicates the procedure with more chances of needing 2 stents and a worse prognosis. Other factors associated with worse outcomes and prognoses are calcifications, smaller LMCA diameters, and the presence of non-ostial disease in the LAD or LCx. 57

#### Wiring and preparation of the lesion

The use of at least 2 angioplasty guidewires (for the 2 main vessels) will be the standard of use in the PCIs performed on the LMCA
with notable exceptions like protected LMCA lesions if rota
tablation is required or in some cases of isolated and ostial LMCA disease.
Using 2 guidewires slightly changes the bifurcation angle, facil-
tates access to the lateral branch and maintains flow towards it.
Using 2 guidewires also helps find this lateral branch in cases of
closure. Actually, some authors advocate the use of the bailout
technique with balloon when flow is compromised after stent
implantation into the main vessel.55 Predilatation of the main
vessel should be avoided if both vessels have not been protected
first due to the high risk of changing and moving the plaque, which
could occlude the coronary ostium of a branch complicating further
catheterizations.

The use of plaque bulking techniques (rota
tablation or laser, among other) to change the anatomy and facilitate the angioplasty can be
considered. LMCA ostial lesions often consist of abundant calcifi-
cation and large amounts of elastic muscle fibers, which is associ-
ated with a risk of elastic retraction of the lesion both after predil-
latation and stent implantation. On the other hand, the presence of
fibrocalcific plaques can condition the use of cutting balloons as
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Stent selection

Two different scenarios should be looked into when choosing the
right stent: whether only the LMCA or the bifurcation should be
treated. Treating the LMCA may be justified only in cases of
isolated ostial or mid-portion disease. In this situation, a stent of
nominal size should be picked that should reproduce the size of the
LMCA as much as possible. Another option would be to implant a
stent of a smaller size and overexpand it with a high-pressure
balloon of the right dimensions. Several platforms achieve large
degrees of expansion without jeopardizing the integrity of its struc
ture.54,55 However, there is no clear evidence that stent overexpansion
is a safe practice since it is subject to the suboptimal coverage
of the intima layer due to metal-to-artery ratio reduction. Also, it
can change the polymer or kinetics of the drug-eluting stent.

When the bifurcation should be treated, the stent implanted into the
LMCA should cover the proximal portion of 1 of the 2 main vessels.
Also, its size should match the proximal diameter of that main vessel.
Another important aspect here is having to use the proximal optimi-
tization technique (POT) with a non-compliant balloon to adapt the
stent proximal caliber to the LMCA. Recrossing towards the lateral
branch or using the double stenting technique can be an option too.

Stents implanted into the LMCA are especially prone to proximal
deformation because they are in continuous contact with the guide
catheter, due to the need for using the POT, and because they
scrape against other devices that come through after implantation.55
Therefore, the resistance of every stent to longitudinal compression
is a factor that should be taken into consideration during stent
selection. Other fundamental characteristics that should be looked
into when choosing the ideal stent to perform PCIs on the LMCA
are the safety profile and precision provided by the stent (figure 5).

Selection of the bifurcation technique

Non-complex bifurcation

When LMCA disease affects 1 bifurcation branch only or the LCx
has a small caliber (< 2.5 mm), the best strategy is the provisional
stenting technique with a single stent implanted from the LMCA
towards the main vessel. In general, the LAD is the main vessel
and only in some cases it would be the LCx. Afterwards, the use
of the POT with a non-compliant balloon of the right size is
routinely advised.

There are times when it is necessary to fully cover the length of
the LMCA. In these cases, it is extremely important to be very
precise when implanting the stent to treat the coronary ostium
properly and avoid any significant stent protrusions into the aorta.

However, there is still controversy over whether it is necessary to
always recross it towards the lateral branch and optimize it with
the kissing balloon technique in the bifurcation after using the POT
if the provisional stenting technique proves insufficient. The kissing
balloon technique should be used with suboptimal final outcomes
in the lateral branch, when the main vessel selected is the LCx,
and when the future need for a PCI on the lateral branch cannot
be discarded.4

Complex bifurcation

When disease affects both bifurcation branches significantly, the
use of the double stenting technique should be considered.
However, since different registries report that the rates of reste-
nosis and new revascularizations are lower with the single
stenting technique,56,56,57 the early approach in many centers and
in most complex bifurcations is often using the provisional
stenting technique with the possibility of finishing using the
double stenting technique, if necessary. With suboptimal results,
the expert committee of the European Bifurcation Group recom-
mends using double T stenting, the T and small protrusion (TAP)
or the culotte technique as the bailout strategy after provisional
stent implantation.67 Once the second stent has been implanted
into the lateral branch, individual dilatation in both branches is
advised using non-compliant balloons to secure the ostial expansion
of the stent of the LAD and the LCx followed by the kissing balloon
technique. If it takes over a significant portion of the LMCA, a new
proximal dilatation [re-POT] should be performed to optimize the
result.

When the double stenting technique is used right away, this selec-
tion is often based on different factors: anatomical and angiographic
variables, location of the lesion, intracoronary imaging modalities,
The imaging modality we have more evidence of in the optimization of angioplasty results of the LMCA is also IVUS that has an associated net clinical benefit. The protocolized use of IVUS for angioplasty results of the LMCA is associated with a worse clinical prognosis. The IVUS, the OCT, and the guidewire pressure optimize the result optimization

The IVUS, the OCT, and the guidewire pressure optimize the results of the angioplasties performed on the LMCA. There is evidence that the suboptimal result of these angioplasties performed on the LMCA is associated with a worse clinical prognosis. Although the OCT shows the aforementioned limitations (limited penetration depth compared to the IVUS, possible inadequate filling), the truth is that both imaging modalities can detect significant findings like stent underexpansion, strut malapposition, border dissection, and degree of lateral branch involvement, which could require result optimization.

The imaging modality we have more evidence of in the optimization of angioplasty results of the LMCA is also IVUS that has an associated net clinical benefit. The protocalized use of IVUS for optimization purposes seems to additionally improve the prognosis of these patients. However, the ongoing clinical trial OPTIMAL (NCT04111770, Optimization of left main percutaneous coronary intervention with intravascular ultrasound randomized controlled trial), that will be recruiting 800 patients, will shed light on the prognostic effect of using IVUS in PCIs performed on the LMCA compared to angiography alone.

On the other hand, several studies have been conducted on the pressure guidewire and its value as a predictor of events in cases of provisional stent implantation by estimating the flow reserve towards the lateral branch.

MEDICAL THERAPY AFTER PERCUTANEOUS CORONARY INTERVENTION AND FOLLOW-UP

Although angioplasties performed on bifurcations are a predictor of events, currently, there is no evidence available to recommend a specific antiplatelet therapy in angioplasties performed on the LMCA. Therefore, treatment should be administered based on each patient’s clinical presentation and ischemic and hemorrhagic risk profile. However, we should bear in mind that implanting a stent into the LMCA and performing a PCI on a bifurcation, especially when 2 stents are used, are criteria that add more ischemic risk to the profile of these patients.

The reappearance of suggestive symptoms or documented ischemia justifies an invasive approach. The review coronary angiography performed at the 1-year follow-up in patients with angioplasty on the LMCA has a level IIB C indication according to European clinical practice guidelines, and is not justified in all cases. The randomized clinical trial ANGELINE (Angiographic evaluation of left main coronary artery intervention) [NCT04604197] will bring more evidence on the potential advantages of the systematic angiographic review.

CONCLUSIONS

The assessment of LMCA lesions is complex, which is why acquiring different angiographic views and using imaging modalities like IVUS or pressure guidewire is advised.

Currently, the SYNTAX score, the possibility of complete revascularization, and the patient’s comorbidities are the main criteria that should guide the selection of percutaneous or surgical revascularization.

Regarding the PCIs performed on LMCA lesions, there are 2 different categories: isolated ostial or mid-portion LMCA lesions [technically easier to treat and with an excellent prognosis], and bifurcation lesions [with a more complex approach].

Optimizing the PCIs performed on the LMCA is essential using intravascular ultrasound and techniques and stents backed by the highest level of evidence in this setting followed by the proper pharmacological cover.

In conclusion, there is no doubt that PCIs performed on LMCA lesions crossed their own particular Rubicon a long time ago. Alea jacta est [which is Latin for “the die is cast”] and, in the future, new randomized clinical trials on surgical or percutaneous revascularization and technical advances in both modalities will favor one over the other. In the meantime, revascularizations based on every individual patient and in close collaboration with the heart team should guide the routine practice of clinical cardiologists and interventional and cardiac surgeons.

CONFLICTS OF INTEREST

The authors declared no financial links or conflicts of interest regarding the content of this manuscript.

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