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Intravascular ultrasound in the evaluation and treatment of left main coronary artery disease: a consensus statement from the European Bifurcation Club

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KEYWORDS

- bifurcation
- left main
- intravascular ultrasound

Abstract

Interventional cardiology and coronary stent insertion have an increasing role in the optimal management of left main coronary artery (LMCA) stenosis. Assessing the extent of obstructive disease of the LMCA by angiography alone can be challenging. However, in contrast to the two-dimensional, shadow graphic nature of coronary angiography, intravascular ultrasound (IVUS) is an accurate tomographic technique for assessing both the coronary lumen and the vessel wall characteristics. Consequently, it is a particularly useful technique in imaging the LMCA before, during and after intervention. The European Bifurcation Club (EBC) recommends the use of IVUS during most LMCA interventions. The purpose of this consensus document is to review the available IVUS data on LMCA disease evaluation and treatment. It is a practical guide to show "how and when" to use the imaging modality. It is hoped that a standardisation of the practical approach to imaging may allow consolidation of learning and, ultimately, improve patient outcomes.

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Abbreviations

AUC	area under the curve
CI	confidence interval
DS	diameter stenosis
FFR	fractional flow reserve
ISR	in-stent restenosis
IVUS	intravascular ultrasound
LAD	left anterior descending
LCx	left circumflex
LMCA	left main coronary artery
MACE	major adverse cardiac events
MLA	minimum lumen area
MLD	minimum lumen diameter
MI	myocardial infarction
MSA	minimal stent area
OR	odds ratio
RR	relative risk
SB	side branch
ST	stent thrombosis
TLR	target lesion revascularisation

Introduction

Atherosclerotic obstruction of the left main coronary artery (LMCA) is worthy of particular consideration compared to stenoses elsewhere in the coronary tree as it usually provides blood supply to >75% of the left ventricle; untreated patients with obstructive LMCA disease have a particularly poor prognosis. Recent trial data have highlighted the potential role of coronary stenting in the LMCA setting, particularly in patients with less complex LMCA disease and patients unsuitable for surgery[1]. LMCA disease is difficult to assess angiographically because of the possible lack of a proximal reference; atherosclerosis within the LMCA is usually diffuse, with frequent involvement of the bifurcation. Calcific disease is also common in the LMCA making lesions more difficult to dilate; consequently, optimal stent expansion is more challenging. Notably, acute complications occurring during LMCA intervention may have a rapid progression towards haemodynamic instability.

Even when using modern equipment, LMCA assessment by angiography can be challenging[2,3]. For example, in a series of 38 patients with an angiographically normal or nearly normal LMCA, 10 patients had intravascular ultrasound (IVUS) evidence of diffuse LMCA disease[4].

In contrast to the two-dimensional, shadow graphic nature of coronary angiography, IVUS is an accurate, tomographic technique for assessing both the coronary lumen and wall characteristics; it has a higher tissue penetration compared to optical coherence tomography (OCT) which uses infrared light. Consequently, IVUS is a particularly useful technique in imaging the LMCA.

The European Bifurcation Club (EBC) recommends the use of IVUS during most LMCA interventions. The purpose of this consensus document is to review the available IVUS data on LMCA disease evaluation and treatment.

THE NORMAL LMCA, PATHOGENESIS, AND PLAQUE DISTRIBUTION

The sizing of the normal LMCA and its bifurcation into the LAD and LCx is predictable using fractal geometry and Murray's Law[5]. IVUS dimensions for a normal (or minimally diseased) LMCA and the subtended LAD and LCx are remarkably consistent[4,6,7] and have been confirmed in cross-sectional data from the PROSPECT study **(Supplementary Table 1)**.

PROSPECT[8] also suggests that, when atheroma develops, the LMCA undergoes positive remodelling in response to plaque deposition to preserve lumen dimensions, a process originally described by Glagov et al[9]. Conversely, an ostial stenosis may be a consequence of negative remodelling (sometimes without significant plaque) and can occur at all three segments – ostial LMCA, ostial LAD, and ostial LCx[10-12]. Shorter anatomic LMCAs tend to develop ostial narrowings while longer anatomic LMCAs tend to develop distal bifurcation stenoses[10].

Careful IVUS imaging from both the LAD and the LCx back to the LMCA have demonstrated that bifurcation disease is rarely focal: in 140 patients and irrespective of angiographic Medina classification[13], the carina and both sides of the flow divider were almost always disease-free. Continuous plaque from the LMCA into the proximal LAD was seen in 90% and from the LMCA into the LCx in 66%, with disease from the LMCA into both the LAD and LCx in 62% **(Figure 1, Figure 2)**[14]. Importantly, plaque localised to either the LAD or LCx ostium and not involving the distal LMCA was seen in only 9% of LAD and 17% of LCx arteries. In practice, a stent in the proximal LAD can move as much as 5.5 mm between systole and diastole[15]. This reality, together with recognition of typical atheroma distribution, explains why attempting to place a stent accurately at the true LAD ostium is usually unsuccessful and results in angiographic and clinical results which are commonly suboptimal.

Examples of complete IVUS assessment are shown in **Figure 2** and **Figure 3**.

Summary statements/recommendations

- Sizing of the normal LMCA is predictable using fractal geometry.
- LMCA bifurcation disease is rarely focal and almost always extends from the LMCA to the LAD (with variable involvement of the LCx), but the carina and both sides of the flow divider are commonly disease-free.

IVUS ASSESSMENT OF LMCA STENOSIS: INDICATION FOR TREATMENT

There have been six published IVUS studies assessing LMCA severity, including three with clinical follow-up[7,16,17]. These are reviewed in **Supplementary Appendix 1** and **Figure 4**.

IVUS ASSESSMENT OF THE LMCA: PRACTICAL GUIDE

Three considerations are important from a technical standpoint when evaluating LMCA lesion severity. First, when studying an ostial LMCA stenosis, it is important to disengage the guiding catheter to avoid confusing the guiding catheter with an ostial stenosis,

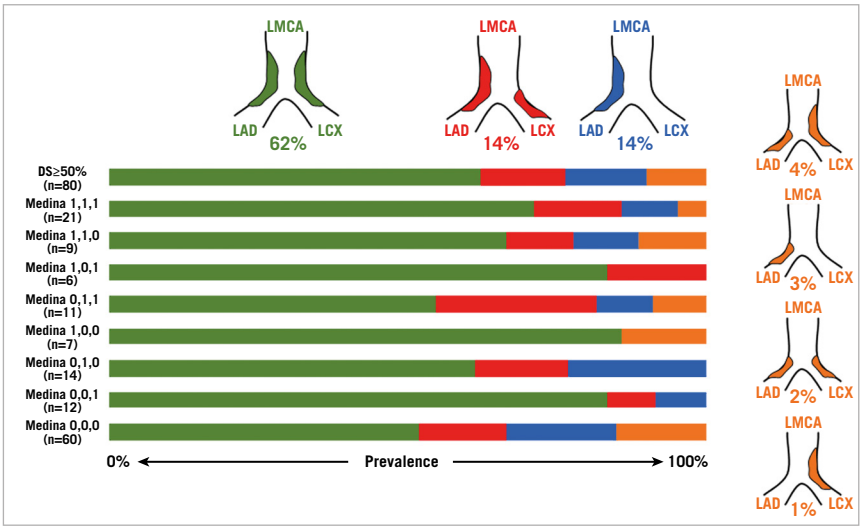

Figure 1. *Irrespective of the Medina classification[13], plaque in the distal LMCA is continuous into the ostium of the LAD and LCX in 62%. The other patterns are less common comprising only 10% of distal LMCA lesions. (Adapted with permission from Oviedo et al[14]).*

and it is important to maintain a coaxial relationship between the IVUS catheter and the LMCA ostium. Secondly, it is not reliable to use IVUS imaging of either the LCx or the LAD to infer the status of the other vessel tangentially during pullback, as either ostial lumen dimension or plaque burden assessment can be misleading[18]. Third, a discrepancy between the minimum lumen area (MLA) in the LMCA when imaging from the LAD or LCx can be generated by the oblique plane of the IVUS beam when the transducer turns from the daughter vessel with the greatest angle into the LMCA. This oblique transducer position can create an artificially large

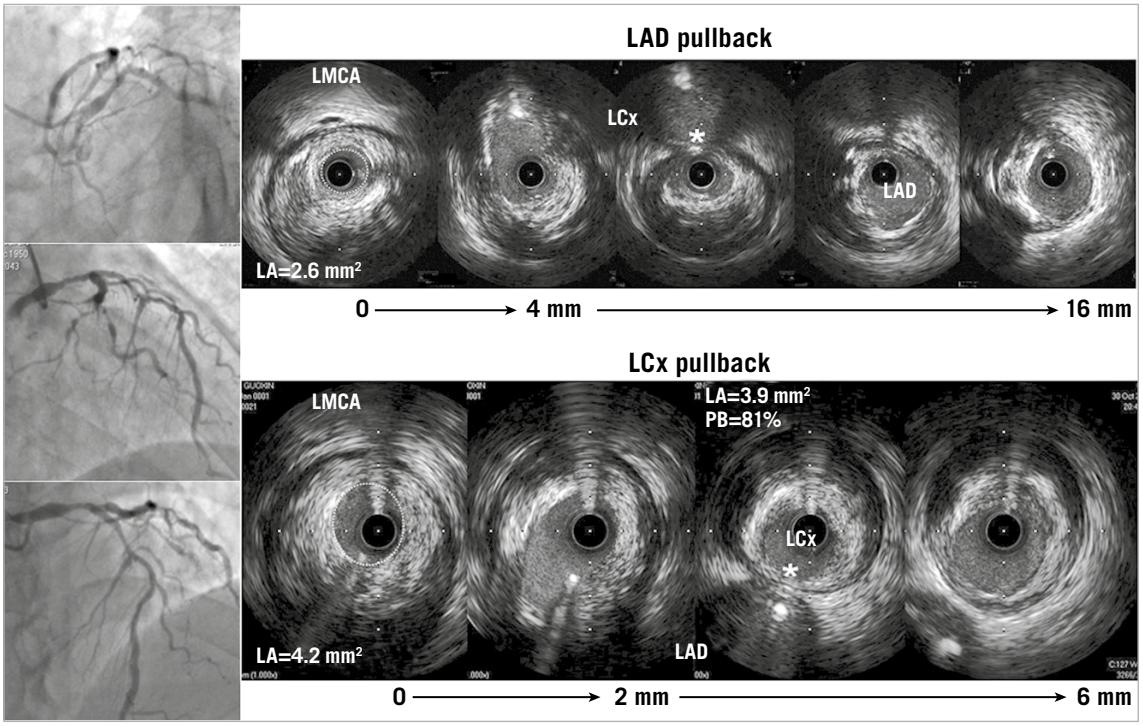

Figure 2. *In this patient with a distal LMCA stenosis, the MLA in the LMCA measured during the LAD pullback was round and smaller (dotted line, 2.6 mm²) than the oval-shaped MLA when imaged during the LCx pullback (dotted line, 4.2 mm²) because of the sharp turn from the LCx into the LMCA creating an oblique IVUS image, an oval-shaped lumen, and a larger and oval-shaped artery compared to the LAD pullback. Despite the apparently normal-looking LCx on the angiogram (as well as in the LMCA to LAD pullback), the plaque burden at the ostium of the LCx measured 81%. In addition, and irrespective of the angiographic appearance, plaque at the ostium of the LAD and LCx is opposite the flow divider, and the carina (shown as a white asterisk in both pullbacks) is disease-free.*

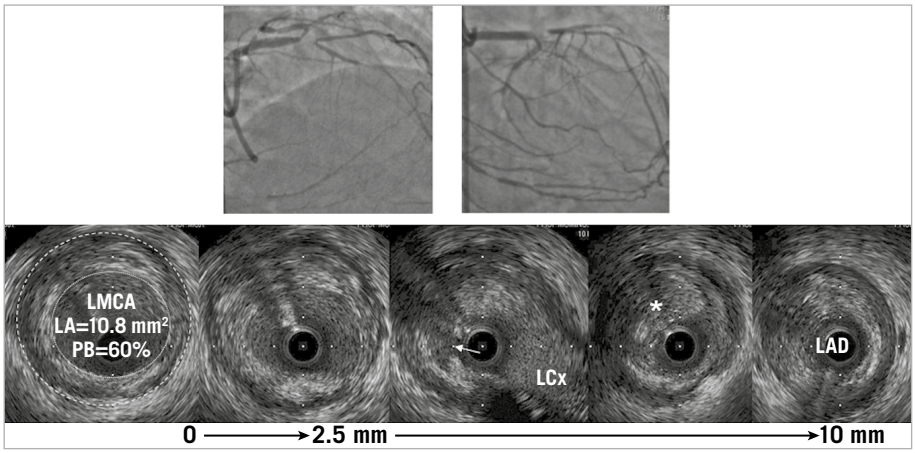

Figure 3. *A patient who presented with a chronic total occlusion (CTO) of the LAD. IVUS imaging indicated that the cause was plaque rupture at the polygon of confluence (white arrow) with chronic thrombus at the LAD ostium (asterisk) and plaque in the distal LMCA (lumen: dotted white line and external elastic membrane dashed white line) where the plaque burden measured 60%.*

MLA, but not one that is artificially small; therefore, the smallest MLA is the most accurate. An example is shown in **Figure 2**.

As part of procedure planning, IVUS can be used before stent implantation to assess the following:

1) Risk of side branch (SB) compromise. Lesions proximal or distal to the SB or ostial SB stenoses affect the risk of SB compromise after main vessel stenting. Patients who have a "vulnerable" carina – the eyebrow sign[19]) or significant calcium[20] identified by IVUS longitudinal reconstruction – are at particular risk of adverse carina shift towards the LCx.
2) Stent length. When using automated pullback, proposed stent length can be measured to limit residual stenosis in adjoining segments (i.e., geographic miss).
3) Stent diameters. Segmental stent diameters can be based on proximal and distal reference size measurements.
4) Reference size and length measurements can be used to plan the size and length of the "proximal optimisation technique (POT) balloon" to ensure that it fits within the stent from carina to the proximal stent edge.

Summary statements/recommendations

– The EBC recommends IVUS guidance for patients undergoing LMCA intervention.
– Given the unique prognostic implications of LMCA disease, the EBC recommends using a threshold MLA cut-off of 6 mm² to indicate an LMCA that should be treated with revascularisation in a European population.
– Disengage the guiding catheter prior to image acquisition and ideally image from both the LAD and LCx to the LMCA with at least one pullback to the aorta.
– The vessel with the angiographically least apparent disease should be imaged back to the LMCA as a minimum guide for bifurcation strategy.

EVIDENCE THAT USING IVUS GUIDANCE DURING LMCA INTERVENTION IMPROVES OUTCOMES

The EBC recommends IVUS in all elective LMCA cases especially when clinical practice is evolving and especially when procedural complications occur or there is uncertainty.

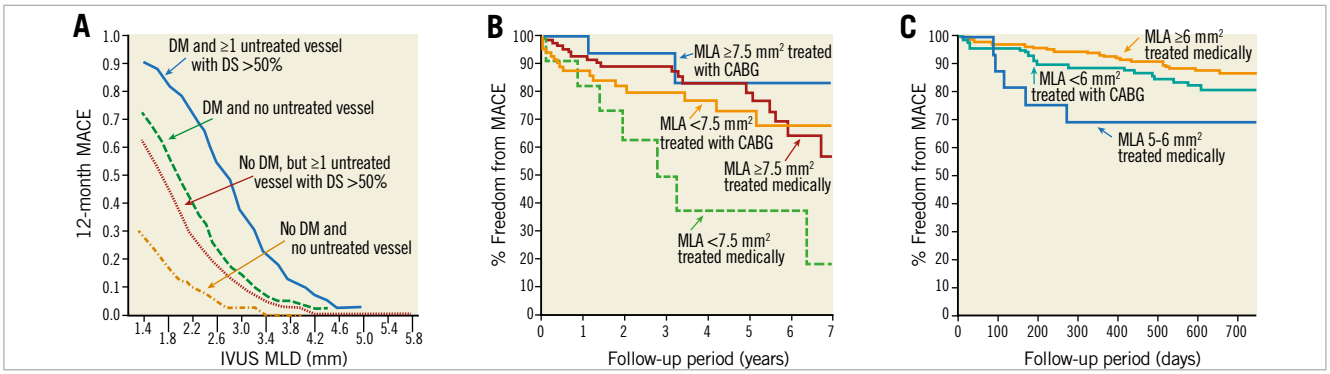

Figure 4. *Three studies have related IVUS minimum lumen area (MLA) in the left main coronary artery to long-term clinical events. Abizaid et al (A, with permission[16]); Fassa et al (B) (adapted with permission[7]); and C) an update of the LITRO Registry[17] in a presentation by de la Torre Hernandez at TCT2017.*

Single-centre data suggest that higher-volume operators get better outcomes when stenting patients with LMCA disease with less benefit from IVUS guidance, replicating some historical randomised trial data that did not clearly support IVUS imaging in every case[21]. However, Ye et al performed a meta-analysis of 10 studies indicating that IVUS guidance of LMCA stenting reduced the risk of all-cause mortality by 40% and cardiac death by 53% compared with conventional angiography-guided procedures[22]. In addition, IVUS guidance was associated with lower risks of TLR and definite or probable stent thrombosis but not MI or TVR. Among these included studies, one was a small randomised trial[23]; the others were either single-centre or multicentre registries[24-28]. Five were conference abstracts and only one study was later published as a manuscript[28]. This analysis was performed by the same group that assessed the impact of operator volume[21].

These data were supported by a complex lesion meta-analysis performed by Fan et al[29]. In a propensity score-matched substudy including three of the four LMCA articles that were also included by Ye[24-26] plus one additional study[30], they also showed a significantly lower incidence of all-cause mortality, MI, ST, and MACE when LMCA intervention was informed by IVUS.

Most studies included in both meta-analyses had a significant number of distal LMCA lesions, but only the propensity score-matched IVUS-TRONCO-ICP looked at this subgroup specifically[25]. In the subgroup of distal lesions irrespective of treatment, IVUS guidance reduced the composite of death+MI+TLR from 19% to 11% (p=0.03), a difference that was magnified in distal LMCA lesions treated with two stents. Most recently, Andell et al (using registry data) have reported a reduced incidence of a combined primary endpoint of mortality, ST, and restenosis over a period of five years when LMCA intervention was IVUS-guided[27].

SPECIFIC PROCEDURAL OPTIMISATION: ONE VERSUS TWO STENTS

A "provisional" approach is recommended by the EBC for bifurcation treatment, including treatment of the LMCA. A trial comparing this approach with a systematic two-stent strategy has been initiated by the EBC and is currently recruiting. The provisional approach when applied to the LMCA will involve wiring both the LAD and the LCx. Stenting towards the LAD will be the usual strategy with a stent sized according to the LAD diameter. However, occasionally when the LAD appears to be spared from disease on IVUS and the LCx is large and/or dominant, stenting to the LCx may be the initial strategy. The type of stent selected should allow post-dilation to a diameter suitable for the LMCA – commonly >5 mm. POT should precede rewiring of the SB; rewiring through a distal strut is optimal.

After stent implantation, IVUS can be used to rule out residual edge stenosis or edge dissection (geographic miss), evaluate stent expansion and apposition, rule out accidental abluminal rewiring, assess complications, and in some cases verify guidewire position after SB recrossing. When a second stent must be implanted, kissing balloon inflation with two balloons is mandatory. A final POT is recommended. IVUS can then be used to evaluate the SB ostium, assess stent expansion (particularly important at the LCx ostium) and apposition, and rule out longitudinal compression.

Kang et al attempted to inform on the likelihood of needing a second stent after initial stenting to the LAD across the LCx. They reported 23 LMCA bifurcation lesions with a preprocedural angiographic DS <50% at the LCx ostium evaluated using pre- and post-stenting IVUS in both the LAD and the LCx[31]. The MLA within the LCx ostium significantly decreased from 5.4 mm^2 to 4.0 mm^2 post stenting (p<0.001). This was associated with a significant decrease in vessel area and increase in vessel eccentricity, but no increase in plaque mass (although there was an increase in plaque burden related to the decrease in vessel area), indicating that the main mechanism of lumen area loss at the LCx ostium was carina shift during crossover stenting. Importantly, in 43 patients with a pre-PCI ostial LCx angiographic DS <50%, a post-stent crossover FFR <0.80 in the LCx was predicted by a preprocedural ostial LCx MLA <3.7 mm^2 or a preprocedural plaque burden of >56%[32]. Sato et al reported on patients who underwent single stent crossover and IVUS pullback of only the LAD to LMCA[20]. Post-stenting narrowing at the LCx ostium (defined as a >50% angiographic DS) occurred in 27 patients (35%) who more frequently had IVUS-identified calcified plaque at the culprit with a greater arc of calcium. On multivariable analysis, a calcium arc >60° was an independent predictor of LCx ostium narrowing. In two-stent procedures, whether or not pre-planned, IVUS evaluation after each rewiring may be useful.

An example of how to use pre-intervention IVUS for treatment planning is shown in **Figure 5**.

Summary statements/ recommendations

- A "provisional" approach is the default treatment strategy for the LMCA.
- Sizing of the stent should be based on the diameter of the branch vessel. The selected stent type should allow POT as the final dilation of all LMCA procedures (POT or re-POT).
- IVUS can be used before stenting to inform the operator about the likelihood of needing a two-stent technique.
- POT and kissing balloon post-dilation are mandatory in two-stent bifurcation procedures.

SPECIFIC PROCEDURAL OPTIMISATION: RISK OF RESTENOSIS/THROMBOSIS

These data are discussed in **Supplementary Appendix 2** and summarised above and in **Figure 6**.

Conclusions

The EBC believes that IVUS guidance is useful at each step of an LMCA interventional procedure: (1) to decide whether or not revascularisation is necessary, (2) to decide whether a one-stent crossover technique (the default strategy) is sufficient or whether a two-stent technique may be more appropriate, (3) to size the stent (diameter and length) and select the optimum landing zones, and (4) to optimise the final result (expansion, apposition, and geographic miss). While randomised trials are limited, data suggest that IVUS guidance is superior to angiographic guidance in terms of death, MI, TLR, ISR, and ST.

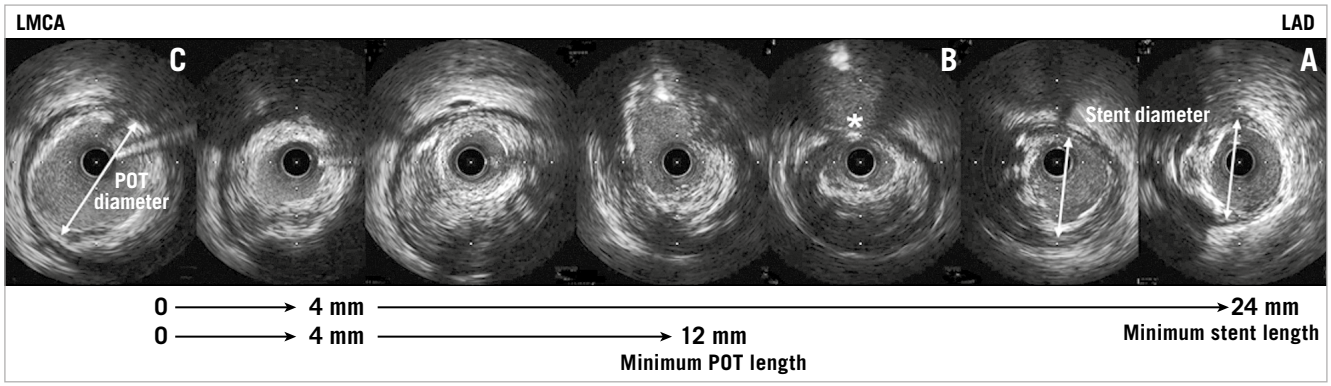

Figure 5. *IVUS imaging to select the stent and POT balloon size and length using the case shown in Figure 2. A) The distal landing zone in the LAD. B) The carina (white asterisk). C) The proximal landing zone in the LMCA. Stent size should be 3.5 mm in diameter (based on the LAD mid wall measurements, double-headed arrow in panel A as well as the nearby cross-section) and at least 24 mm in length (to cover LMCA disease [C]). The POT balloon should be 5 mm in diameter (based on the LMCA measurements, double-headed arrow in panel C) and at least 12 mm in length.*

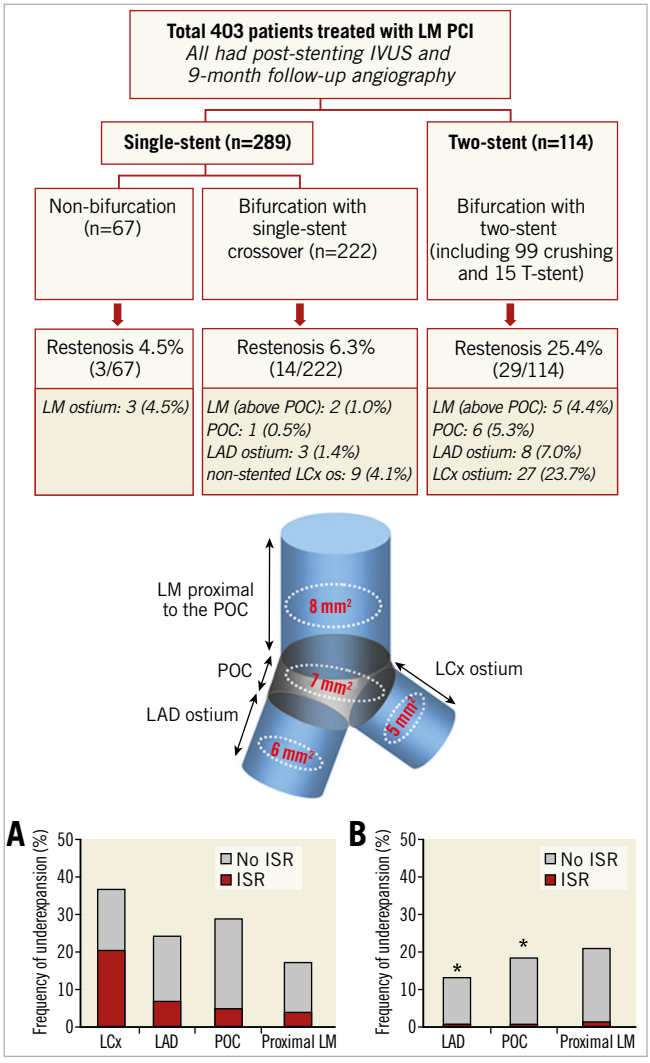

Figure 6. *A comprehensive analysis of LMCA lesions performed by Kang et al. A) Two stents; B) one stent. They related the frequency of angiographic restenosis to underexpansion at one of four sites (cartoon): LMCA, polygon of confluence (POC), ostial LAD, and ostial LCX (adapted with permission from Kang et al[33]).*

Impact on daily practice

Treatment of the left main with stents is an increasing part of our interventional practice. Use of IVUS within the left main has a strong evidence base but there is limited practical guidance about how to use it. This practical guideline based on principles from the European Bifurcation Club provides important clinical information for interventional cardiologists and provides momentum towards changes in clinical practice that might improve outcomes.

Conflict of interest statement

G. Mintz has received honoraria from Boston Scientific, Volcano, and Infraredx. The CRF receives grant/fellowship support from Boston Scientific and Volcano. A. Banning has received honoraria from Boston Scientific, Volcano and partial funding from NIHR Oxford BRC. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. IVUS assessment of LMCA stenosis: indication for treatment.

Supplementary Appendix 2. Specific procedural optimisation: risk of restenosis/thrombosis.

Supplementary Table 1. Measurements of a normal or minimally diseased LMCA and the corresponding proximal LAD and LCx.

The supplementary data are published online at: http://www.pcronline.com/eurointervention/137th_issue/81

Supplementary data

Supplementary Appendix 1. IVUS assessment of LMCA stenosis: indication for treatment.

Abizaid et al initially reported 122 patients who were followed for one year [16]. Logistic regression identified three predictors of events: diabetes mellitus, presence of one or more major epicardial vessels or bypass grafts with >50% angiographic diameter stenosis (DS) that was not treated, and IVUS minimum lumen diameter (MLD) **(Figure 4A)**. The event rate was 60% for an IVUS MLD <2.0 mm, 24% for an MLD of 2.0-2.5 mm, 16% for an MLD of 2.5-3.0 mm, and 3% for an MLD >3.0 mm. Fassa et al reported that the mean minimum lumen area (MLA) of 121 patients with an angiographically normal or minimally diseased LMCA was 16.25±4.30 mm^2 with a "lower limit of normal" (based on mean minus two standard deviations) of 7.65 mm^2 [7]. Among a second group of 214 patients with intermediate LMCA disease, 83 (38%) had an MLA <7.5 mm^2, most underwent surgical revascularisation, but 12/83 who did not have surgery for various reasons had an extremely high rate of events **(Figure 4B)**. Conversely, patients with an MLA ≥7.5 mm^2 who were treated medically or surgically or patients with an MLA <7.5 mm^2 who were treated surgically had a similar outcome. Performing multivariate analysis, age, smoking status, and the number of diseased non-LMCA vessels remained the only significant predictors of adverse events. The LITRO Registry reported 354 patients in whom LMCA revascularisation was performed in 90.5% (152/168) with an IVUS MLA <6 mm^2 and was deferred in 96% (179/186) with an MLA ≥6 mm^2; two-year cardiac death-free survival was 97.7% in the deferred group vs. 94.5% in the revascularisation group (p=0.5) with event-free survival of 87.3% vs. 80.6%, respectively (p=0.3) [17]. However, as shown in **Figure 4C**, among 16 patients with an IVUS MLA of 5-6 mm^2 who did not undergo revascularisation because of operator and/or patient

preferences, cardiac death-free survival was 86% with only a 62.5% survival free of cardiac death, myocardial infarction (MI), or revascularisation.

Comparing IVUS to fractional flow reserve (FFR) in three groups of patients has been inconsistent [34-36]. Jasti et al reported that an IVUS MLA <5.9 mm^2 and an MLD <2.8 mm predicted an FFR <0.75 [34]. Subsequently, Kang et al reported that the IVUS MLA that best predicted FFR <0.80 was <4.8 mm^2 (89% sensitivity, 83% specificity, area under the curve [AUC] 0.90, p<0.001) [35]. In addition, the cut-off value of plaque burden to predict FFR <0.80 was ≥72% (sensitivity 73%, specificity 79%, AUC 0.79, p<0.001). Of note, the FFR was significantly lower in 18 lesions with plaque rupture versus 37 lesions without plaque rupture (0.76±0.09 vs. 0.82±0.09, p=0.018). In a follow-up study in an expanded group of 112 patients, the independent predictors of an FFR ≤0.80 were plaque rupture (odds ratio [OR] 4.47, p=0.014), body mass index (OR 1.19, p=0.05), patient age (OR 0.95, p=0.031), and IVUS MLA (OR 0.37, p<0.001) [36]. The optimal IVUS MLA cut-off for FFR ≤0.80 was 4.5 mm^2 (77% sensitivity, 82% specificity, AUC 0.83, p<0.001) with an optimal IVUS plaque burden cut-off of 77% (70% sensitivity, 82% specificity, and AUC 0.80). The prevalence of ostial/shaft versus distal bifurcation lesions varied among the studies of Jasti, Kang, and Park; however, the most plausible explanation for the differences between the MLA cut-offs appeared to be the ethnicity of the patient populations as a comparison of white North American versus Asian patients showed a smaller MLA in Asian patients (5.2±1.8 mm^2 vs. 6.2±1.4 mm^2, p<0.0001) [37].

Supplementary Appendix 2. Specific procedural optimisation: risk of restenosis/thrombosis.

Kang et al reported 403 patients with LMCA disease who had post-drug-eluting stent (DES) IVUS and 9-month follow-up angiography [33]. Post-stenting minimal stent area (MSA) was measured in each of four segments: ostial LAD, ostial LCx, POC (confluence zone of LAD and LCx), and LMCA proximal to the POC. Overall, 46 (11.4%) showed angiographic in-stent restenosis (ISR): 3/67 (4.5%) non-bifurcation lesions treated with a single stent, 14/222 (6.3%) bifurcation lesions treated with single-stent crossover, and 29/114 (25.4%) bifurcation lesions treated with various two-stent techniques. The MSA cut-offs that best predicted restenosis were 5.0 mm^2 (ostial LCx ISR), 6.3 mm^2 (ostial LAD ISR), 7.2 mm^2 (POC ISR), and 8.2 mm^2 (LMCA ISR above the POC). Using these criteria, 133/403 (33.8%) had underexpansion of at least one segment, more commonly in the two-stent versus the one-stent group (54% vs. 27%, p<0.001); ISR (at any location) was more frequent in lesions with any underexpanded segment versus no underexpansion (24.1% vs. 5.4%, p<0.001). The two-year MACE-free survival rate was significantly lower in patients with any underexpansion versus no underexpansion (90% vs. 98%, p<0.001); post-stenting underexpansion was an independent predictor for MACE (adjusted hazard ratio 5.56, 95% CI: 1.99-15.49, p=0.001). These are shown in **Figure 5**. Although acute stent-vessel wall malapposition was observed in 28 lesions, in this study it was not related to ISR or MACE at follow-up [33]. It is not clear whether these cut-offs obtained in Korean patients should also be used for DES implantation in Western patients or whether stent area cut-offs should be larger.

In a follow-up study by Kang et al, the LMCA ostium was assessed in more detail [38]. Strut protrusion into the aorta measured 3.4±1.7 mm in length. Among 169 lesions with >2 mm

strut protrusion, only 5 (3.0%) showed ostial restenosis; among 109 lesions with >3 mm of strut protrusion, only 3 (2.8%) showed ostial restenosis. On the other hand, 53 patients (23%) had an unstented ostium measuring 2.3±1.3 mm in length with no significant difference in ostial restenosis between patients with versus without an uncovered ostium (3 of 126 [2.4%] vs. 10 of 333 [3.0%], p=0.10) and restenosis in only 2/57 patients (3.5%) having a >2 mm long uncovered ostial LMCA segment. Overall, the residual plaque burden within the uncovered ostial segment measured 38.1±11.9%, 50.0±9.4% in patients with vs. 41.3±11.3% in patients without restenosis (p=0.17). Finally, acute malapposition at the LMCA ostium was seen in 43 of 229 patients [18.8%]), but ostial restenosis was found in only one (2.3%), similar to patients without malapposition (1.6%, p=0.6).

These studies did not assess the risk of distal edge restenosis, i.e., the edge of the stent in the LAD or LCx with a two-stent technique or the edge of the stent in the LAD with a one-stent crossover technique. In a large series of 987 lesions [39], the threshold for distal edge plaque burden predicting distal edge restenosis was 51.9% (sensitivity 86%, specificity 81%, AUC 0.86) and for distal edge lumen area was 4.8 mm^2 (sensitivity 86%, specificity 55%, AUC 0.75). Similarly, in a large series of 2,433 lesions from ADAPT-DES, only the effective lumen CSA at a stent edge dissection site predicted TLR at one year with a cut-off of 5.1 mm^2 (sensitivity 66.3%, specificity 65.8%, AUC 0.73) [40].

Inaba et al reported three patterns of longitudinal stent deformation in patients treated with second-generation DES: (1) deformation with intra-stent wrinkling and overlapping of the proximal and distal stent fragments, (2) deformation with elongation, and (3) deformation with shortening [41]. Most of the deformations were located near the

proximal stent edge; 8.3% of 96 LMCA stented lesions had evidence of deformation. These deformations presumably reflected physical interaction with the guiding catheter (or guiding catheter extension devices), although interaction with post-dilation balloons was also a possibility. From the EXCEL experience, Kim et al reported longitudinal stent deformation in 33/506 (6.5%) - 81.8% at the LMCA ostium, 15.2% in the LMCA shaft, and 3.0% in the LAD, but none in the POC or LCx. At three years of follow-up, LMCA-related MI (18.9% vs. 4.6%, p=0.0005) and LMCA-related ischaemia-driven revascularisation (19.6% vs. 7.7%, p=0.02) were greater in lesions with versus without deformation even though there was only a trend towards a smaller MSA in lesions with deformation (8.6 [7.1, 10.9] vs. 10.0 [8.3, 11.5] mm^2, p=0.06).

Supplementary Table 1. Measurements of a normal or minimally diseased LMCA and the corresponding proximal LAD and LCx.

	Kim [6]		**Montreff [4]**	**Fassa [7]**	**PROSPECT [8]**
#	141 men	116 women	28 (23 men)	122	175 (lowest tertile plaque burden)
LMCA					
Vessel CSA, mm^2	20.6±4.9	17.2±4.0	24.9±5.4	21.0±6.5	25.3 (IQR: 21.1-29.1)
Lumen CSA, mm^2	16.7±4.0	14.0±3.2	18.1±3.9	16.3±4.3 (range 8.3-28.5)	18.9 (IQR: 15.5-21.9)
Derived lumen diameter, mm			4.8±0.5		
Maximum lumen diameter, mm				4.8±0.7	
Minimum lumen diameter, mm	4.3±0.6	3.9±0.5		4.2±0.6	
Plaque burden, %			27.0±6.9	26.3±8.3	26.5 (IQR: 21.3-30.0)
LAD					
Lumen CSA, mm^2			10.7±2.5		
Derived lumen diameter, mm			3.7±0.4		
Plaque burden, %			34.0±6.8		
LCx					
Lumen CSA, mm^2			10.2±3.4		
Derived lumen diameter, mm			3.6±0.6		
Plaque burden, %			31.0±6.8		

CSA: cross-sectional area; LAD: left anterior descending; LCx: left circumflex; LMCA: left main coronary artery