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REVIEW

Frontiers in cardiovascular medicine

Current management of left main coronary artery disease

Jean Fajadet[1]* and Alaide Chieffo[2]

[1]Clinique Pasteur, Toulouse, France; and [2]San Raffaele Scientific Institute, Milan, Italy

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Coronary artery bypass surgery is considered as the gold standard treatment of unprotected left main coronary artery (ULMCA) disease. Over the last 20 years, improvement in stent technology and operators experience explained the increased number of reports on the results of percutaneous coronary interventions (PCIs) for the treatment of left main (LM) coronary artery lesion. The recent data comparing efficacy and safety of PCIs using drug-eluting stent and coronary artery bypass surgery showed comparable results in terms of safety and a lower need for repeat revascularization for coronary artery bypass surgery. Patient selection for both techniques is fundamental and directly impacts the clinical outcome. Further randomized trials must be conducted to precise the indications of both techniques of revascularization in the treatment of LM disease.

Keywords Left main coronary artery disease • Bifurcation lesions • Coronary bypass grafting • Percutaneous coronary interventions

Introduction

Significant unprotected left main coronary artery (ULMCA) disease occurs in 5–7% of patients undergoing coronary angiography[1,2] and patients with ULMCA disease treated medically have a 3-year mortality rate of 50%.[3,4] Several studies have shown a significant benefit following the treatment of left main (LM) stenosis with coronary bypass grafting (CABG) compared with medical treatment.[5–8] Until recently, CABG has been the gold standard therapy for LM disease. However, advances in percutaneous intervention techniques and stent technology have allowed evaluation of the role of percutaneous coronary intervention (PCI) for LM disease. Recent studies have focused on the safety and efficacy of stenting the LMCA to determine whether it does provide a true alternative to CABG. So should we stent the LM?

Why left main lesion is particular?

The LMCA refers to the proximal segment of the left coronary artery that arises from the left aortic sinus just below the sinotubular junction to its bifurcation into the left anterior descending (LAD) and left circumflex (LCx) arteries. The LMCA is responsible for supplying ~75% of the left ventricular (LV) cardiac mass in patients with right dominant type or balanced type and 100% in the case of left dominant type, and as a result, severe LMCA disease will reduce flow to a large portion of the myocardium, placing the patient at high risk for life-threatening events of LV dysfunction and arrhythmias.[9]

The LMCA is generally divided into three anatomic regions: the ostium or origin of the LMCA from the aorta, a mid-portion, and the distal portion.[10] The LMCA differs from the other coronary arteries by its relatively greater elastic tissue content which can explain elastic recoil and high restenosis rate following balloon angioplasty.[11] The segment of the LMCA which extends beyond the aorta displays the same layered architecture as that of the other coronary arteries.

Most of the time, there is a continuous involvement of atheroma from the distal LMCA into the proximal LAD.[12]

Atherosclerotic lesions tend to form at specific regions of the coronary vasculature where flow is disturbed, particularly in area of low shear stress.[13] In the LMCA bifurcation, intimal atherosclerosis is accelerated primarily in area of low shear stress in the lateral wall close to the LAD and LCx bifurcation (*Figure 1*). Thus, the carena is frequently free of disease and this can explain the reason why single-stent strategy (provisional stenting) can be successfully performed in patients with no or moderate disease by angiography.

* Corresponding author. Tel: +33 562211699, Fax: +33 562211637, Email: fajadet@interv-cardio-toul.com

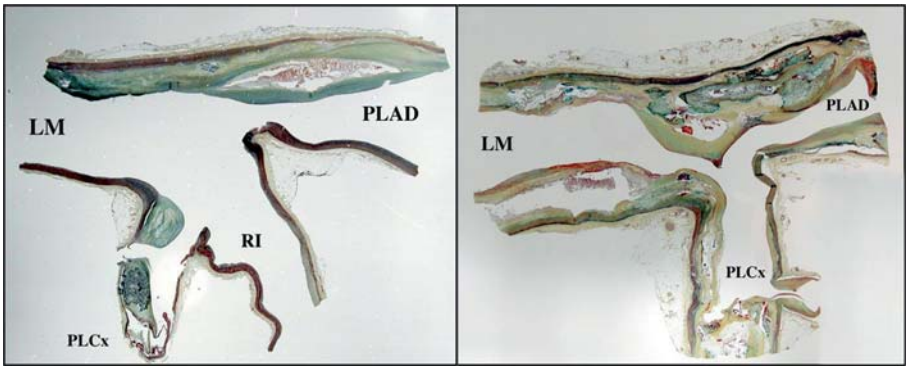

Figure 1 Longitudinal section of bifurcation of the left main coronary artery showing distribution of the atherosclerotic plaque. Note plaque is located in the lateral wall (area of low shear stress) while sparing the flow divider region (high shear). PLAD, proximal left anterior descending artery; PLCx, proximal left circumflex artery; RI, ramus intermedius.

Data from the literature

Results of surgery

Coronary artery bypass surgery is a well-established technique, with excellent proven results for the treatment of coronary artery disease, dating back to the early 1970s.[3]

A recent review by Taggart *et al.*[14] published in 2008 reported on a series of studies, all of which had an in-hospital mortality of between 2 and 3% after CABG for LM stenosis, and although there was a less data on long-term follow-up, those studies which did report on long-term outcomes had results showing 5–6% mortality at 5 years (*Table 1*).

In their review of the Cleveland Clinic experience of CABG for patients with LM stenosis, Sabik *et al.*[15] report a 20-year follow-up of all patients operated on between 1971 and 1998. They have shown that for the 3803 patients with LM stenosis, 30-day survival is 97.6%, with 93.6% at 1 year and 83% at 5 years. Ten year survival rate is 64%. Importantly, rates of freedom from coronary reintervention are 99.7% at 30 days, 98.9% at 1 year, and 89% at 5 years. At 10 years, 76% of surviving patients remain free from reintervention and 61% at 20 years.

These studies represent the benchmark against which other treatments of the LM stem must be compared.

Results of percutaneous coronary intervention with bare-metal stents in left main stenosis

The first reported balloon angioplasty of the LMCA was performed in 1979 by Gruntzig as one of five angioplasties that he performed.[16] After the first series of 129 patients, reported by Hartzler and O'Keefe in 1989,[17] showed a 10% in-hospital mortality and 64% 3-year mortality, the practice was quickly abandoned due to poor outcomes and better surgical results.

However, the development of stenting techniques and dual antiplatelet regimes allowed LM stenting to be again considered as a treatment by the mid-1990s.

Stenting of the LM with bare-metal stents (BMS) was characterized by high procedural success rates, a 17–20% target lesion revascularization (TLR), and a 10–20% mortality rate at 1 year.[18–23]

Results of percutaneous coronary intervention with drug-eluting stent in left main stenosis

The availability of drug-eluting stent (DES) for the treatment of ULMCA stenosis led to a significant reduction in restenosis and TLR when compared with prior experiences with BMS limited by higher rates of restenosis and in some series sudden deaths.[24–43]

Table 1 In-hospital and long-term mortality after coronary bypass grafting for left main coronary artery disease (adapted from Taggart *et al.*[14])

Author (ref. #) (year)	Year of surgery	*n*	Mortality (%)			
			Hospital	30 days	1 year	2 years
Jonsson *et al.* (31) (2006)	1970–99	1888	2.7	—	—	—
Lu *et al.* (30) (2006) (2005)	1997–2003	1197	2.8	3	5	6
Keogh and Kinsman (16) (2003)	2003	5003	3	—	—	—
Dewey *et al.* (29) (2006) (2001)	1998–99	728	—	4.2	—	—
Yeatman *et al.* (28) (2006) (2001)	1996–2000	387	2.4	—	—	5
Eilis *et al.* (27) (2006) (1998)	1990–95	1585	2.3	—	—	—
Weighted average	—	10 788	2.8	—	—	—

Three single-centre studies[25–27] showed high procedural success rates, low procedural complication rates, and encouraging long-term outcome with an 11.5–20.3% major adverse cardiac event (MACE) rate at 2- to 3-year follow-up.

Those results were confirmed by the FRIEND registry[28] results with a major adverse cardiac and cerebrovascular event (MACCE) rate of 10.6% at 450 days.

In a systematic review and meta-analysis of 1278 patients, Biondi-Zoccai *et al.*[29] have shown that treating ULMCA lesions with drug-eluting stents is associated with a 5.5% (3.3–7.7%) risk of death, a 16.5% (11.7–21.3%) MACE rate, and a TLR rate of 6.5% (3.7–9.2%). Distal LM disease is a predictor of MACE and TLR; however, it is the presence of high-risk features that predicts death. The review also shows that most series have reported low rates of stent thrombosis (ST) (0–2%) apart from the Price *et al.*[30] group (4%).

Drug-eluting stent in LMCA PCI has been evaluated in several observational single- and multicentre registries showing a good efficacy and safety profile.[24–26,30,33–43]

Moreover, several observational, non-randomized registries have shown no difference in the occurrence of MACCE between patients treated with DES compared with the ones treated with CABG in this subset of patients up to 5 years of clinical follow-up[44–53] (*Table 2*).

Different anatomic lesion complexity: ostial/shaft and simple bifurcation/ complex bifurcations

Non-distal lesions treatment is associated with favourable clinical and angiographic outcomes.[25–27,54–56]

A meta-analysis of 17 trials involving PCI for ULMCA identified distal lesion as the most significant predictor of repeated revascularization and overall MACE.[29]

Some reports suggest that results in the case of 'simple' bifurcation lesions treated with a one-stent approach are more favourable when compared with 'complex' bifurcation lesions treated with a two-stent approach.[43,57] The TLR rate is relatively low (<5%) with a one-stent approach resulting nearly equivalent to results obtained with DES for ostial or mid-ULMCA lesions.[25,26,58]

Conversely, because of the extensive plaque burden, patients with distal ULMCA disease approached with two-stent techniques showed a TLR rate as high as 25% with restenosis.[59,60] There is little consensus on the optimal two-stent strategy (i.e. crush, culotte, V- or T-stenting) to approach a distal ULMCA lesion mostly driven by the preference of the operator but so far never investigated in a randomized comparison. In addition, the use of dedicated stent ULMCA dedicated stents is currently under investigation.[61]

Complex calcified LM lesions can be prepared with rotational atherectomy (rotablator) or cutting balloon before stent deployment. However, no strong data can be found in the literature.

Drug-eluting stent choices in treating left main coronary artery

Several small observational studies have compared outcomes following 'first generation' DES implantation.[26,62]

In the 'Intracoronary Stenting and Angiographic Results: Drug-eluting Stents for Unprotected LM Lesions' (ISAR-LM) randomized trial,[59] comparing PCI with sirolimus-eluting stent (SES) vs. paclitaxel-eluting stent (PES), no significant differences were

Table 2 Clinical outcome after left main stenting with drug-eluting stents

Author	Park *et al.*[52]	Buszman *et al.*[51]	Chieffo *et al.*[53]	Palmerini *et al.*[48]	Lee *et al.*[45]	Sanmartin *et al.*[41]
Treatment	DES/BMS/CABG	DES/BMS/CABG	DES/CABG	DES vs. CABG	DES/CABG	DES/CABG
Patients, *n*	1102/1138	52/53	107/142	157/154	50/123	96 vs. 245
Study design	Registry	Randomized	Registry	Registry	Registry	Registry
Age (mean, years)	62/64	61/61	64/68	73/69	72/70	66/66
Diabetes (%)	29.7/34.7	19/17	18.7/23.2	26.1/25.3	36/31	19/32
Distal lesion (%)	49.5/53.8	56/60	81.3/NA	80.3/82.5	60/NA	62/NA
EuroSCORE (mean)	NA	3.3/3.5	4.4/4.3	6/5	NA	27/25.3[b]
SYNTAX score (mean)	NA	25/24	28/29	NA	NA	NA
Follow-up time (years)	5	1	5	1	1	1
Cardiac death (%)	9.9[a]	NA	7.5/11.9		2/1.6	NA
MI (%)	1[a]	1.9/5.6	0.9/7.7	8/5	NA	0/1.3
TLR (%)	NA	NA	18.7/8.4****	25.5/2.6****	NA	NA
TVR (%)	9.7***	28.8/9.4*	28/8.4	NA	7/1	5.2/0.8**
CVA (%)	1.8[a]	0/3.7	0.9/4.2	NA	NA	0/0.8
ST/symptomatic graft occlusion	NA	NA	0.93/2.8	NA	NA	NA
MACCE (%)	NA	30.7/24.5	32.4/38.3	NA	17/25	10.4/11.4

MI, myocardial infarction; TLR, target lesion revascularization; CVA, cerebrovascular accidents; ST, ARC definite/probable stent thrombosis; MACCE, major adverse cerebrovascular events; NA, not available.
[a]Cumulative for overall study population.
[b]Euroscore >6
*$P = 0.01$, **$P = 0.02$, ***$P = 0.001$, ****$P = 0.0001$.

reported in the composite outcome of death, myocardial infarction (MI), and TLR [13.6% PES vs. 15.8% SES, relative risk: 0.85; 95% confidence interval (CI): 0.56–1.29] at 12-month follow-up. No difference was reported also in restenosis (16% PES vs. 19.4% SES, $P = 0.30$) and 2-year LM-specific revascularization (9.2% PES vs. 10.7% SES, $P = 0.47$). The incidence of definite (0.7% PES vs. 0.3% SES) and probable (0.3% PES vs. 0% SES) ST was also similar at 2-year follow-up.

Few data are available regarding the safety and efficacy of 'new generation' DES in ULMCA PCI. In the LEMAX non-randomized registry, 173 patients with ULMCA disease treated with everolimus-eluting stent (EES) were compared with a historical cohort of 291 patients treated with PES for ULMCA stenosis. At 12-month clinical follow-up, EES was associated with lower target lesion failure (a composite of cardiac death, target vessel MI, and TLR) and ST when compared with PES.[57] The ongoing ISAR-LM 2 randomized trial, which evaluates the safety and efficacy of EES vs. zotarolimus-eluting stent, will provide more information about the performance of new-generation DES platforms in this complex subset of lesions.

Intravascular ultrasound and optimal coherence tomography

Intravascular ultrasound (IVUS) guidance is helpful in assessing vessel size, adequate stent expansion, and absence of stent malapposition. A subgroup analysis from the MAIN-COMPARE registry reported that IVUS guidance was associated with improved 3-year mortality compared with a conventional angiography-guided procedure after adjustment with propensity-score matching [6.3% IVUS vs. 13.6% angiography, log-rank $P = 0.063$, hazard ratio (HR): 0.54; 95% CI, 0.28–1.03].[63] In particular, for patients receiving DES, IVUS-guided PCI was associated with a significantly lower 3-year incidence of mortality compared with angio-guided PCI (4.7% IVUS vs. 16% angiography, log-rank $P = 0.048$, HR: 0.39; 95% CI: 0.15–1.02).[63,64]

Optimal coherence tomography has been recently reported to assess vascular response to LMCA stenting.[65]

Dual anti-platelet therapy

The current guidelines support long-term aspirin administration and at least 6- to 12-month dual anti-platelet therapy (DAT) in patients receiving a DES (Class: I, Level of Evidence: B); however, this is not specific for ULMCA stenting.[66,67] Although the risk–benefit ratio of long-term DAT is not well defined, many clinicians prolong DAT long-term after ULMCA stenting with DES. Migliorini *et al.*[68] reported the outcomes of 215 patients treated with DES for ULMCA who had prospective platelet reactivity assessment by light transmittance aggregometry after a loading dose of 600 mg of clopidogrel. The incidence of high residual platelet reactivity (HRPR) after clopidogrel loading was 18.6%. The 3-year cardiac mortality and ST rate were significantly reduced in the low residual platelet reactivity group compared with the HRPR group. HRPR after clopidogrel loading was the only independent predictor of cardiac death and ST. Additional studies are strongly required in order to resolve these issues and to determine the optimal duration of DAT administration after DES placement in ULMCA disease.

The new anti-platelet agents (prasugrel and ticagrelor) have been evaluated in acute coronary syndromes but not yet in LM PCI. They could be used in ST elevation MI (STEMI) or high-risk acute coronary syndromes and might have an interest in complex LM intervention, but this needs to be evaluated.

Drug-eluting stent versus coronary bypass grafting

The 'Revascularization for Unprotected LM Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty vs. Surgical Revascularization' (MAIN-COMPARE) Registry[42] was the first large multicentre non-randomized study comparing long-term outcome following PCI with stenting vs. CABG for ULMCA disease. This registry involved 2240 patients with ULMCA stenosis who underwent stenting (DES = 784; BMS = 318) or CABG ($n = 1138$). Patients in the PCI cohort were less likely to have diabetes or multivessel coronary artery disease; however, after adjustment with propensity scoring model, in the matched cohort, no significant difference was observed between the two revascularization strategies in terms of risk of death and risk of the composite outcome of death, MI, and cerebrovascular events (CVE). The rate of target vessel revascularization (TVR) was significantly higher in the group that received stents than in the group that underwent CABG. The follow-up at 5 years confirmed those results.[52]

Consistently with this finding, Chieffo *et al.*[47,53] showed in a non-randomized comparison from a single-centre no difference between PCI with DES implantation and CABG in the occurrence of cardiac death, whereas CABG was correlated with lower TVR and no difference was detected in the occurrence of MACCE at 5-year clinical follow-up.

Recently, encouraging results were reported from the 'Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery' (SYNTAX) trial for patients stratified according to the presence of ULMCA disease were randomized to CABG ($n = 348$) or PCI ($n = 357$).[69] In the ULMCA subgroup, the primary endpoint of non-inferiority in 12-month rate of MACCE was met in the PCI group (13.7 vs. 15.8%, $P = 0.44$).[57] Moreover, although the rate of repeat revascularization among patients with ULMCA disease was significantly higher in the PCI group (11.8 vs. 6.5%; $P = 0.02$), this result was offset by a significantly higher rate of stroke in the CABG subgroup (2.7 vs. 0.3%; $P = 0.01$). Recently, 3-year results of the ULMCA subgroup from the SYNTAX trial were presented at Transcatheter Cardiovascular Therapeutics 2010.[70] Percutaneous coronary intervention with PES implantation resulted in equivalent 3-year overall MACCE compared with CABG (22.3% CABG vs. 26.8% PCI, $P = 0.20$). Notably, the MACCE rate was similar between the groups for patients with low (23% CABG vs. 18% PCI, $P = 0.33$) and intermediate (23.4% CABG/23.4% PCI, $P = 0.90$) SYNTAX score whereas resulted significantly higher for PCI in the high score group (21.2% CABG vs. 37.3%. PCI, $P = 0.003$). Even the overall safety outcomes (death/CVE/MI) resulted similar between the groups (14.3% CABG vs. 13% PCI, $P =$ NS). As reported at 1-year follow-up, there was a higher revascularization rate in the PCI group (11.7% CABG vs. 20% PCI, $P = 0.01$) and a higher rate of CVE in the CABG group (4% CABG vs. 1.2% PCI) even at 3-year follow-up (*Table 3*). Because of the hypothesis-generating nature of subgroup analysis, results from adequately powered trials for patients with ULMCA disease are needed.

Table 3 SYNTAX trial: results from the left main subgroup analysis

	PCI ($n = 358$)	CABG ($n = 357$)	*P*-value
1-year clinical outcomes			
Death (%)	4.2	4.4	0.88
Stroke (%)	0.3	2.7	0.0009
MI (%)	4.3	4.1	0.97
Revascularization (%)	12	6.7	0.02
ST or graft occlusion (%)	2.7	3.7	0.49
Overall MACCE (%)	15.8	13.6	0.44
MACCE low SYNTAX score (0–17)	7.7	13	0.19
MACCE intermediate SYNTAX score (23–32)	12.6	15.5	0.54
MACCE high SYNTAX score (≥33)	25.3	12.9	0.008
3-year clinical outcomes			
Death (%)	7.3	8.4	0.64
Stroke (%)	1.2	4	0.02
MI (%)	6.9	4.1	0.14
Revascularization (%)	20	11.7	0.004
ST or graft occlusion (%)	4.1	3.7	0.80
Overall MACCE (%)	26.8	22.3	0.20
MACCE low SYNTAX score (0–17)	18	23	0.33
MACCE intermediate SYNTAX score (23–32)	23.4	23.4	0.90
MACCE high SYNTAX score (≥33)	37.3	21.2	0.003

MI, myocardial infarction; ST, ARC definite/probable stent thrombosis; MACCE, major adverse cardiac and cerebrovascular events.

More recently, the randomized PRECOMBAT trial that compared patients with ULMCA stenosis to undergo CABG (300 patients) or PCI with SESs (300 patients) showed non-inferiority of PCI to CABG for the primary composite endpoint of major adverse cardiac or cerebrovascular events (death from any cause, MI, stroke, or ischaemia-driven TVR) at 1 year. However, the non-inferiority margin was wide, and the results cannot be considered clinically directive. By 2 years, no significant difference was found for the primary endpoint, respectively, between PCI and CABG (cumulative event rate, 12.2 vs. 8.1%; $P = 0.12$) and for the composite rate of death, MI, and stroke (4.4 vs. 4.7%; $P = 0.83$). Ischaemia-driven revascularization was lower in the CABG group (4.2 vs. 9%; $P = 0.02$).[71]

Stratification of the risk for procedural and long-term outcomes

Most of the clinical risk-scoring system used for ULMCA has been extrapolated from patients treated with CABG.

Recently, the application of a coronary anatomical risk score based on lesion severity and extent (SYNTAX score)[72] has provided insight into both patient selection. In the LM subgroup of the SYNTAX trial, it is interesting to point out that the patients

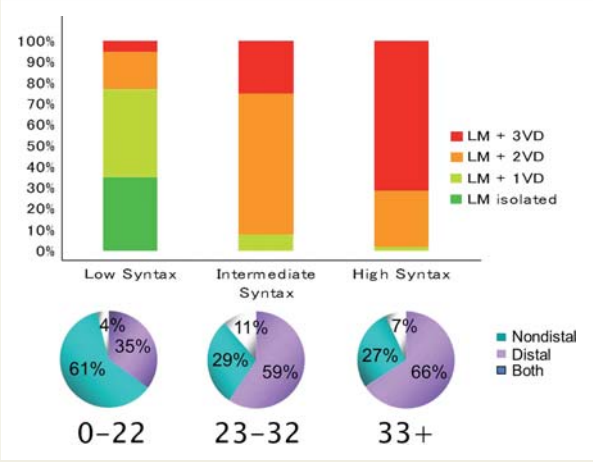

Figure 2 Vessel distribution in left main population according to SYNTAX score terciles.

with a low SYNTAX score have a higher rate of non-distal LM lesions with a majority of isolated LM disease or LM disease associated with single-vessel disease. On the opposite, the group of patients with a high SYNTAX score has a higher rate of distal LM lesions and a majority of LM disease lesions associated with two or three vessels diseased (*Figure 2*).

In this study, the increasing number of additional vessels treated was identified as the single independent procedural determinant of 1-year MACCE.[57,69] A recent study demonstrated that combining the SYNTAX and the EuroSCORE into a common risk model (Global Risk Classification) was correlated with a significant improvement in predicting cardiac mortality in patients undergoing PCI for ULMCA.[73] Another novel score, the NERS (New Risk Stratification Score) score, consisting of 54 variables (17 clinical, 4 procedural, and 33 angiographic) showed a higher sensitivity and specificity to predict clinical outcome.[74]

Impact of diabetes on the clinical outcome

Subgroup analysis of the SYNTAX trial at 1 year suggest the following key findings.[75]

(i) In patients with LM and/or three-vessel disease, MACCE rates were significantly higher in the PES arm compared with the CABG arm in diabetic patients and directionally higher (but non-significant) in non-diabetic patients. Although there was no statistically powered pre-specified primary endpoint of this subgroup analysis, this result suggests that MACCE after PES treatment might be inferior to CABG treatment for diabetic patients with LM and/or three-vessel disease.

(ii) There were no significant differences in composite death/cerebrovascular accident/MI or in the individual components of death or MI between the CABG and PES groups, regardless of diabetic status or lesion complexity. Compared with non-diabetic patients, patients with diabetes had increased mortality in both the CABG and PES groups.

(iii) In both diabetic and non-diabetic patients with the greatest anatomical complexity (SYNTAX scores ≥33), mortality was significantly increased with PES treatment compared with CABG.

(iv) Repeat revascularization was higher with PES compared with CABG in both diabetic and non-diabetic patients.
(v) Patients with diabetes had significantly increased repeat revascularization rates compared with non-diabetic patients when treated with PES, but not when treated with CABG.
(vi) Repeat revascularization rates after PES treatment (and hence the relative difference between the PES and CABG groups) tended to increase with increasing lesion complexity (i.e. higher SYNTAX score), particularly in patients with diabetes; in non-diabetic patients with low lesion complexity, repeat revascularization rates were similar between treatment arms.

Primary percutaneous coronary intervention of unprotected left main coronary artery for patients with stent thrombosis elevation myocardial infarction

Limited data are available on patients who undergo primary PCI of ULMCA in STEMI. In the AMIS (Acute Myocardial Infarction in Switzerland) Plus Registry Experience, Pedrazzini *et al.*[76] reported results of 348 patients who underwent LM primary PCI, either isolated ($n = 208$) or concomitant to PCI for other vessel segments ($n = 140$). They were compared with 6318 patients undergoing PCI of non-LM vessel segments only. The LM patients with higher rates of cardiogenic shock (12.2 vs. 3.5%; $P < 0.001$), had a remarkably high (89%) in-hospital survival and concurrent LM and non-LM PCI had worse outcomes than isolated LM PCI.

Different strategies and techniques for percutaneous coronary intervention of left main lesions

Left main disease is often associated with lesions in the other coronary arteries, giving a pattern of complex multivessel disease (MVD). The treatment of these lesions needs to be considered when deciding on the treatment strategy of the LM and the feasibility of a complete revascularization approach (*Figure 3*).

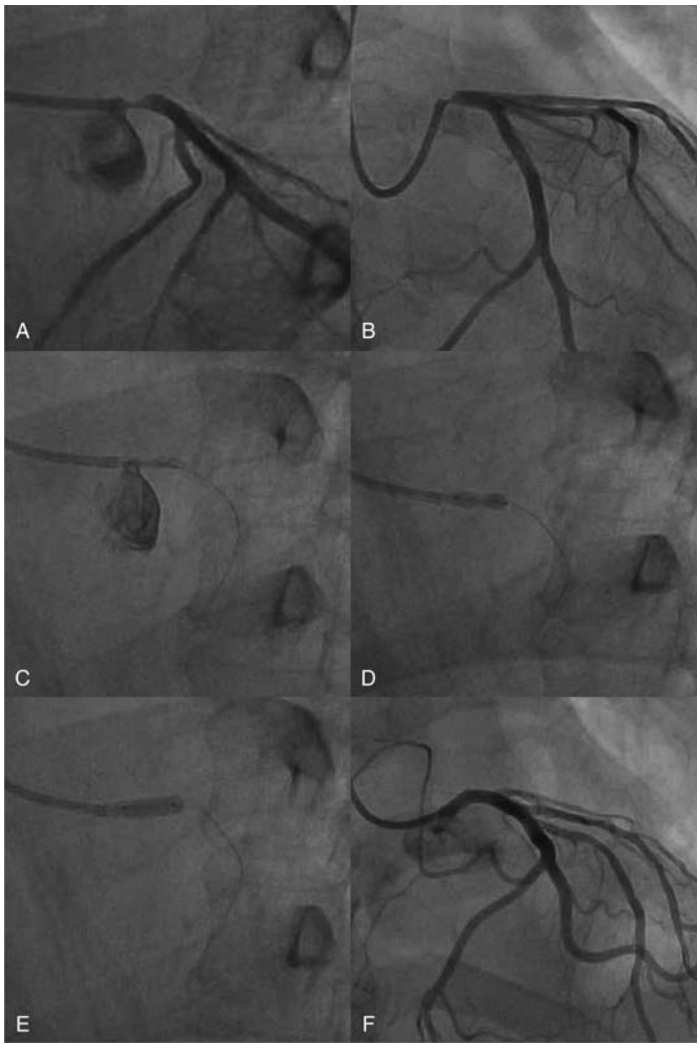

Figure 3 Stenting of isolated ostial left main stenosis. (*A* and *B*) Initial appearance. (*C*) Positioning stent with guide disengaged. (*D*) Stent deployment with proximal stent protruding into the aorta. (*E*) High pressure post-dilatation. (*F*) Final appearance.

Ostial and mid vessel lesions

These lesions can essentially be treated as in any other vessel and be stented with a single-stent strategy (*Figures 3* and *4*).

Distal left main lesions

Distal LM lesions are in most cases treated as true bifurcation lesions.

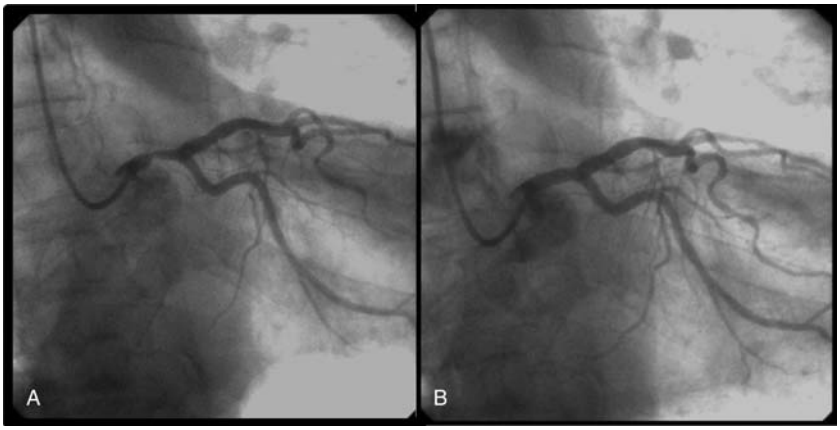

Figure 4 Direct stenting of isolated mid-shaft left main stenosis. (*A*) Baseline angiography: short, non-calcified lesion of mid-left main treated by direct stenting. (*B*) Final angiographic result.

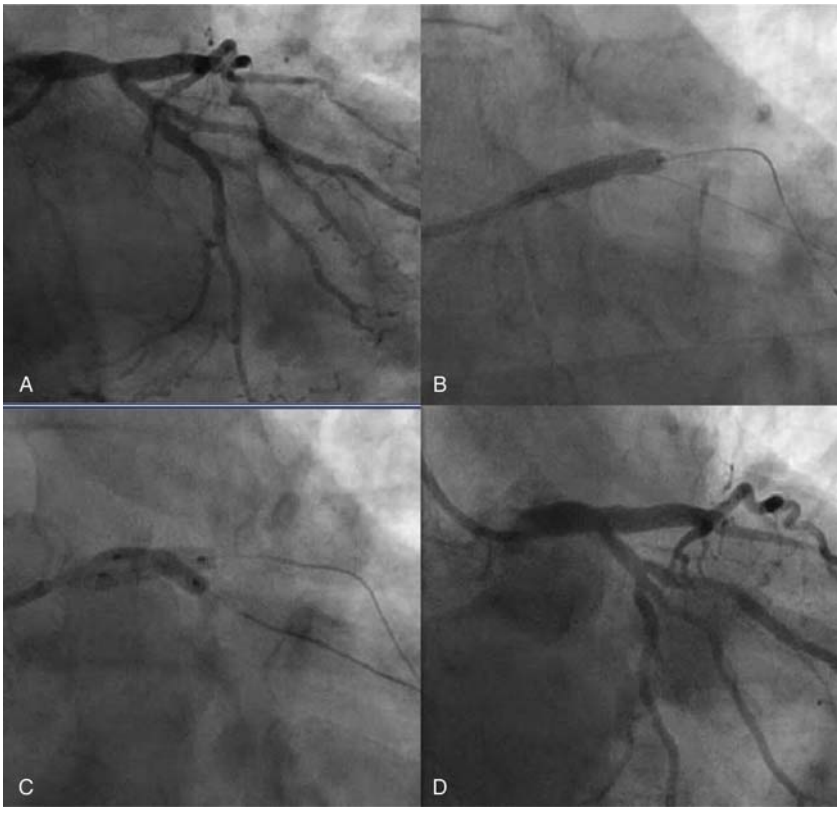

Figure 5 Provisional stenting. (*A*) Initial appearance. (*B*) Stent to left main-left anterior descending. (*C*) Kissing balloon post-stent deployment. (*D*) Final result.

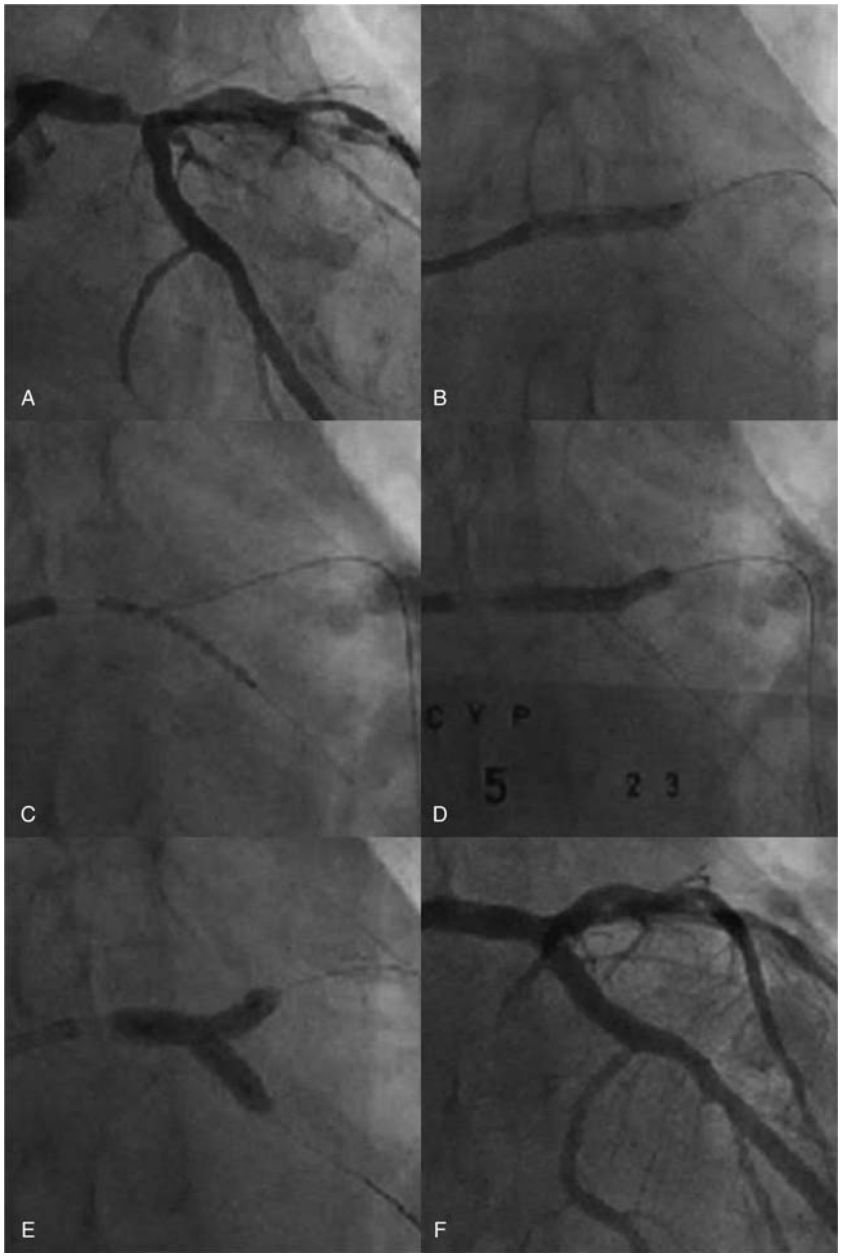

Figure 6 Culotte stenting. (*A*) Initial appearance. (*B*) Pre-dilatation of the left anterior descending. (*C*) First stent deployed in the left circumflex. (*D*) Second stent deployed in the left anterior descending after recrossing with wire and pre-dilatation. (*E*). Kissing balloon post-dilatation. (*F*) Final result.

True distal bifurcation lesions may be treated by either a single-stent or by a two-stent strategy. Choice of strategy is based on vessel and lesion characteristics (plaque distribution, the diameter of the branches and the angle between them, anatomy of the side branch) but also on operator experience and expertise. The provisional stenting is a single-stent strategy, although it allows the placement of a second stent if required [T, T and protrusion (TAP), culotte techniques]. More complex lesions may require double-stent strategy (T stenting, TAP, crush, culotte, V stenting).

Single-stent strategy

The provisional stenting

This is a single-stent strategy but allows the positioning of a second stent if required. The main vessel (almost always the LAD) is wired. A second wire is usually placed in the side branch. The stent is deployed in the LM-LAD and post-dilated as required.

The LCx may be left untouched or treated by a kissing balloon inflation. If necessary, a second stent may be deployed into the ostial LCx using the 'T' technique. A kissing inflation completes the procedure if two stents have been used (provisional T stenting; *Figure 5*).

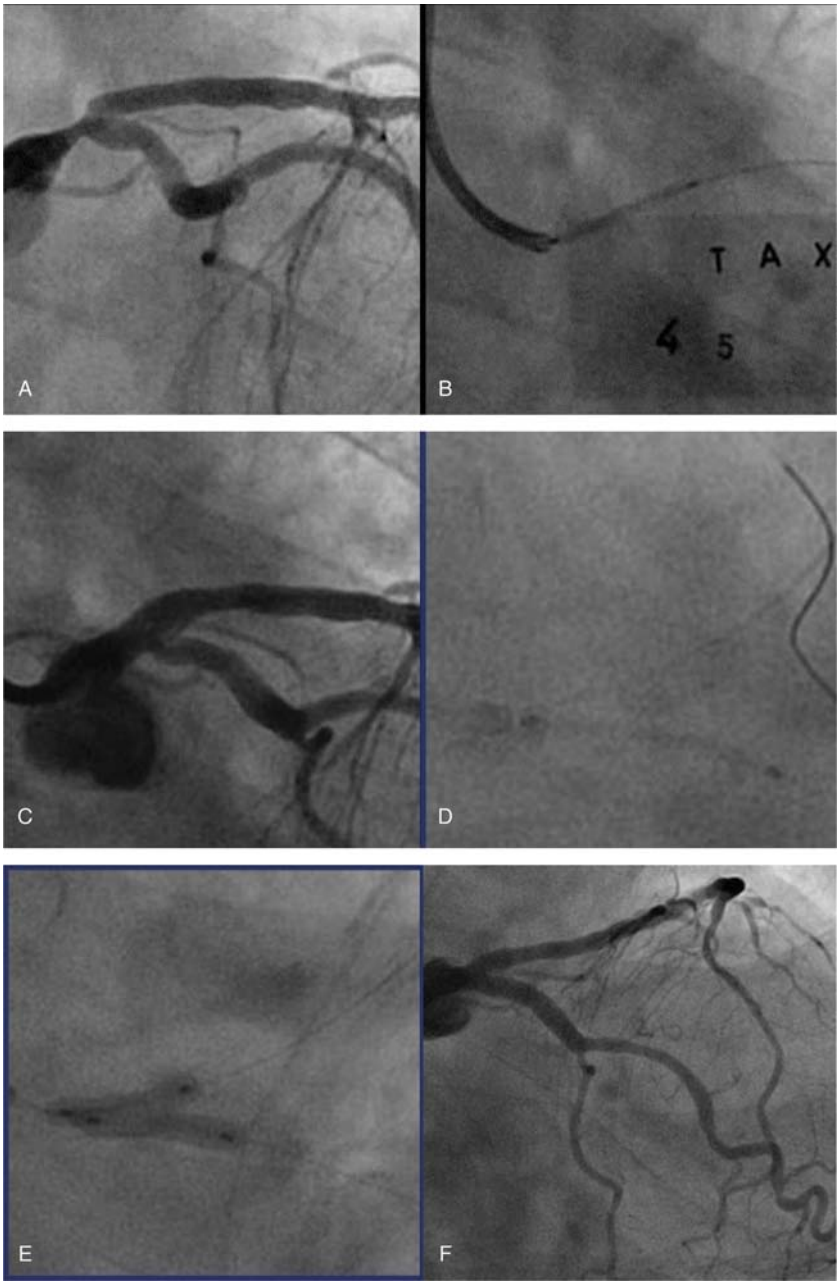

Figure 7 T stenting. (*A*) Initial appearance. (*B*) Stent to left main-left anterior descending. (*C*) Dissection of ostial left circumflex. (*D*) Advancement of the stent into left circumflex. (*E*) Kissing balloons. (*F*) Final result.

Double-stent strategies

The culotte stenting

This is a strategy suitable for lesions where the ostium of the LCx is diseased, the angulation between the vessels is $<60^{\circ}$ (higher risk of plaque shift), and the two vessels are of similar diameter. The main vessel, usually the LM-LAD, is stented. A second stent is then passed through the struts of the first into the side vessel, leaving an overlap of both stents in the LM. The LM-LCx stent is deployed. The procedure is completed with a 'kissing balloon' inflation.

This technique provides an optimal reconstruction of distal LM bifurcation but with a significant area of stent overlap. The use of new generation of stents with open cells facilitates this technique (*Figure 6*).

The T stenting

The T stent is used when a two-stent strategy is required but the angulation between the two vessels approached 90°. A stent is deployed in the side vessel, making sure to cover the ostium with only minimal protrusion into the LAD. The LM-LAD lesion is then stented followed by a 'kissing balloon' inflation.

This technique provides a good reconstruction of T shape distal LM bifurcation but with the risk of leaving the side branch ostium

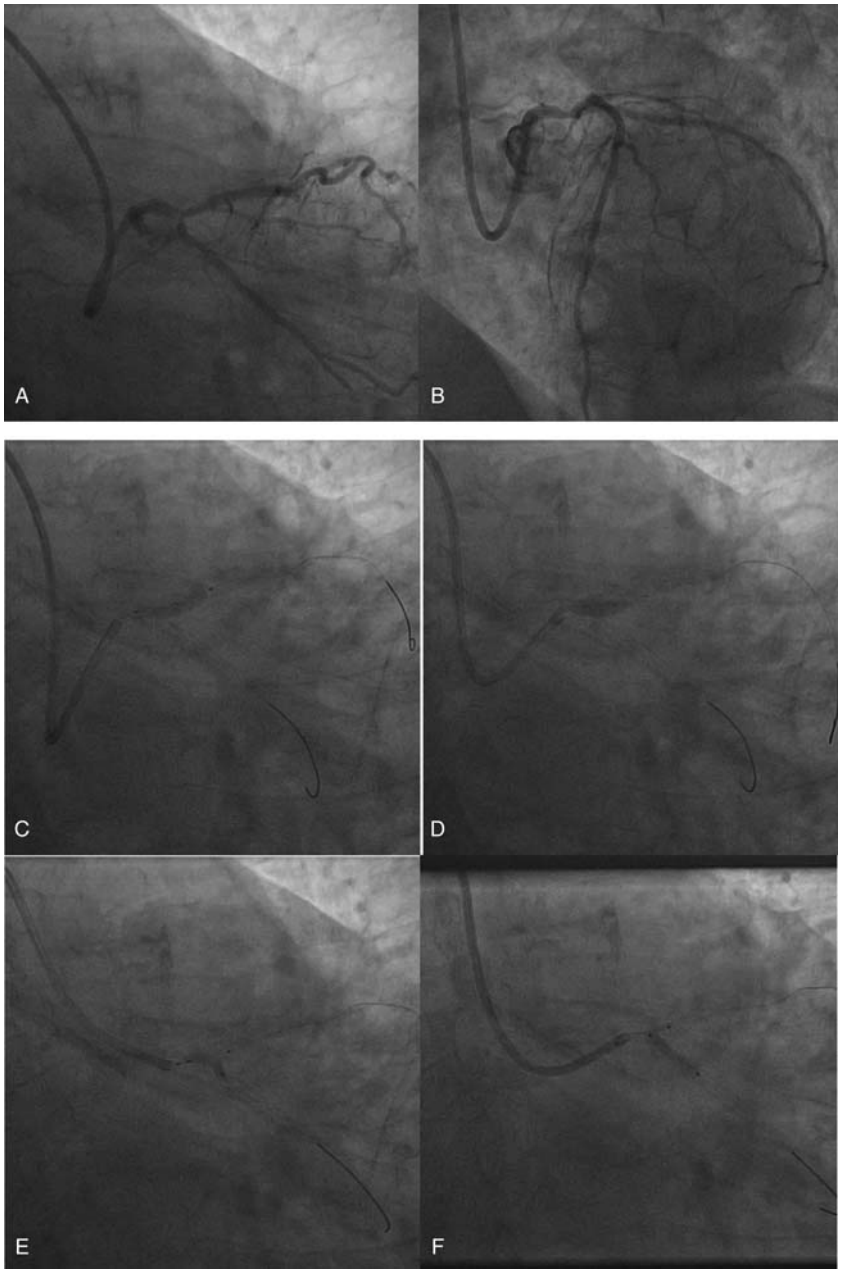

Figure 8 T and protrusion technique. (*A* and *B*) Baseline angiography: severe eccentric distal left main stenosis. (*C* and *D*) 3.5 × 18 mm DES implanted in left main-left anterior descending. Post-dilatation with a 4.0 mm balloon. (*E*) 2.5 mm balloon inflated in left main-left circumflex through the stent struts. (*F*) 3.5 × 18 mm drug-eluting stents placed in left circumflex with proximal edge inside the left main and a deflated 3.5 mm balloon in the left main. (*G*) Final kissing balloon. (*H* and *I*) Final angiographic result.

uncovered (side branch stent to distal) or of placing the side branch stent to proximal protruding in the LM stent.

The 'T' technique can be performed by placing the first stent in the main vessel and the second stent in the side branch as described above with the provisional T stenting (*Figure 7*).

The T and protrusion (TAP) technique

This technique can be used in the majority of the bifurcation lesions.

It can provide a good reconstruction of distal LM bifurcation with minimal stent overlap.

The main vessel (LM-LAD) is stented. Then, a stent is placed at the ostium of the side branch (LCx) with a balloon left in the main stent. After positioning the proximal edge of the side branch stent 1–2 mm inside the main stent, the side branch stent is delivered at high pressure while a deflated balloon is left in the main stent. Then, a final kissing balloon is performed in order to reshape the carena (*Figure 8*).

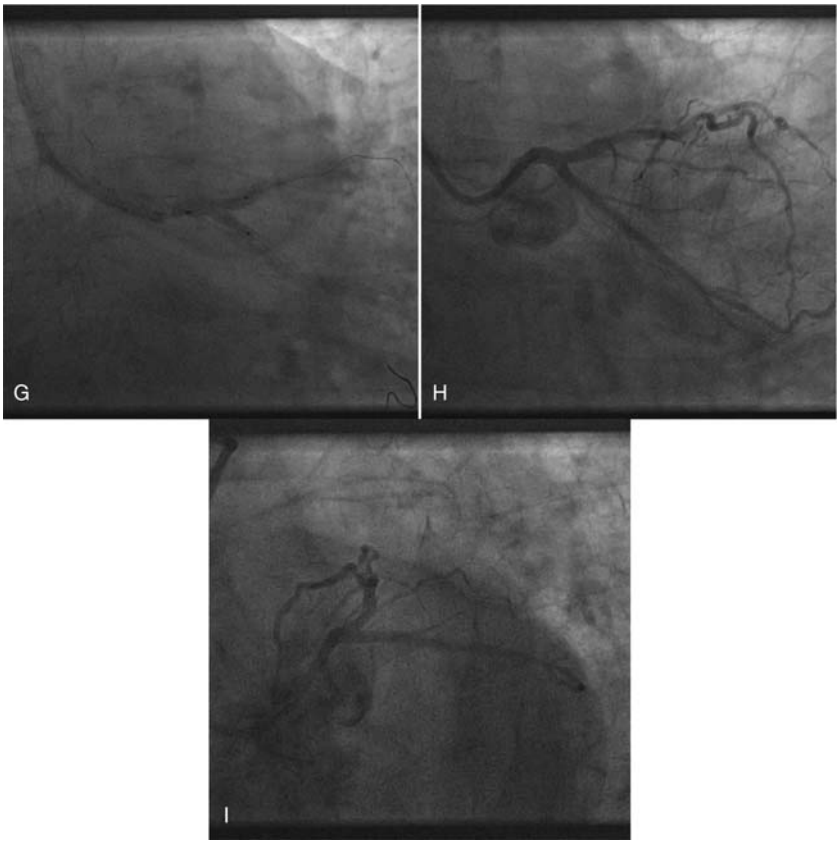

Figure 8 Continued

The crush stenting

The crush technique can be used when the diameter of the main vessel is greater than the side branch and the angulation is favourable (approximately ≤60%). The side branch is stented first, positioning the stent to allow 1–2 mm (minicrush) to protrude into the LM. The main vessel is then stented. Deployment of the main vessel stent crushes the proximal side branch stent against the LM wall. It is necessary to rewire the LCx, through the stent struts of both the LAD and crushed LCx stent to perform a final post-dilatation of the side branch ostium and a final 'kissing balloon' inflation (*Figure 9*).

The V stenting

The V stent technique (or 'kissing stent' technique) is mainly used in Medina 0,1,1 lesions that can be treated with a minimal and very short neo-carena. The two stents are placed into the LM and respective arteries and deployed by simultaneous inflation (*Figure 10*).

Indications for percutaneous coronary intervention

Basics for decision-making

The first step in safely performing PCI to the LM stem is careful patient selection. There are four important areas to consider when selecting patients for LMCA PCI:

- The knowledge: data from literature and guidelines
- The global appraisal of the patient:
  - clinical presentation: stable, functional class, ACS, STEMI, shock
  - clinical characteristics: age, diabetes, renal function, cognitive status, valvular disease, carotid disease, previous cardiac intervention, other co-morbidities, EuroSCORE
  - angiographic characteristics: LV function (LVEF), LM anatomy (distal/non-distal lesion, calcification, bifurcation angle, diseased LCx ostium, trifurcation), MVD, number of lesions, diffuse disease, complexity of additional lesions (length, calcifications, bifurcations, chronic total occlusion [particularly right coronary artery (RCA) total occlusion], diffuse calcified and porcelain aorta, possibility of complete or incomplete revascularization, number of stents needed, overlapping, SYNTAX score
- The local experience of the centre
- The evolution of techniques and technology for PCI and CABG

Indications for percutaneous coronary intervention

Favourable for stenting

Low-risk patients, with good LV function, non-distal and non-calcified LM stenosis, ostial LM lesions and mid-shaft LM lesions, and very

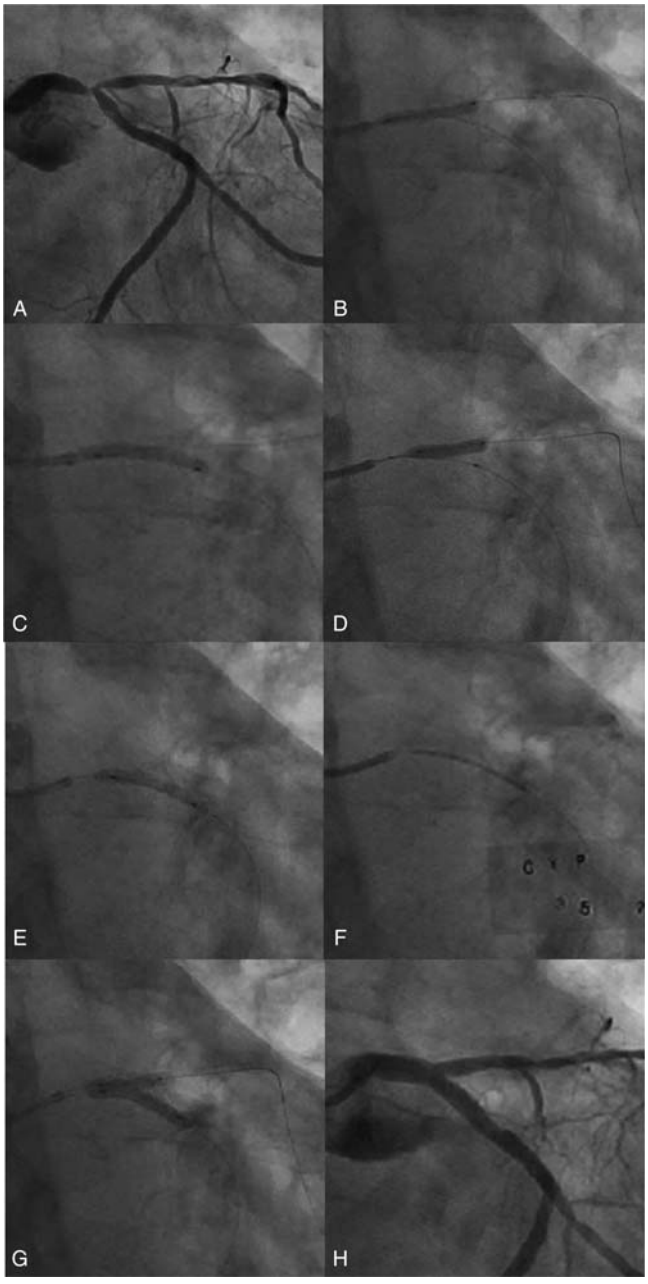

Figure 9 Crush technique. (*A*) Initial appearance. (*B*) Pre-dilatation of left anterior descending. (*C*) Pre-dilatation of left circumflex. (*D*) Stent to left anterior descending ('side branch' due to large dominant left circumflex). (*E*) Remove side branch wire and balloon to dilate main vessel (left circumflex) and 'crush' side vessel stent. (*F*) Deploy main vessel. (*G*) Rewire side branch and 'kissing balloon' post-dilate. (*H*) Final appearance.

few additional lesions on the other coronary vessel (low or intermediate SYNTAX score). These patients have been shown to have excellent outcomes following LM stenting.

Patients with STEMI, LM acute occlusion during catheterization, and shock. In these cases, PCI is a fast way to recanalize the LM but clinical outcome is poorer compared with stable patients.

Technically more difficult and debatable

Patients with preserved LV function and non-calcified distal LM bifurcation lesion involving the ostium of LAD and LCx.

Percutaneous coronary intervention could be considered in

- elderly patients (octogenarians)
- patients with small left circumflex artery
- patients without any complex additional lesions (low or intermediate SYNTAX score)
- non-diabetic patients
- poor surgical candidates:
  - distal coronary disease unfavourable to CABG
  - high surgical risk (high EuroSCORE)

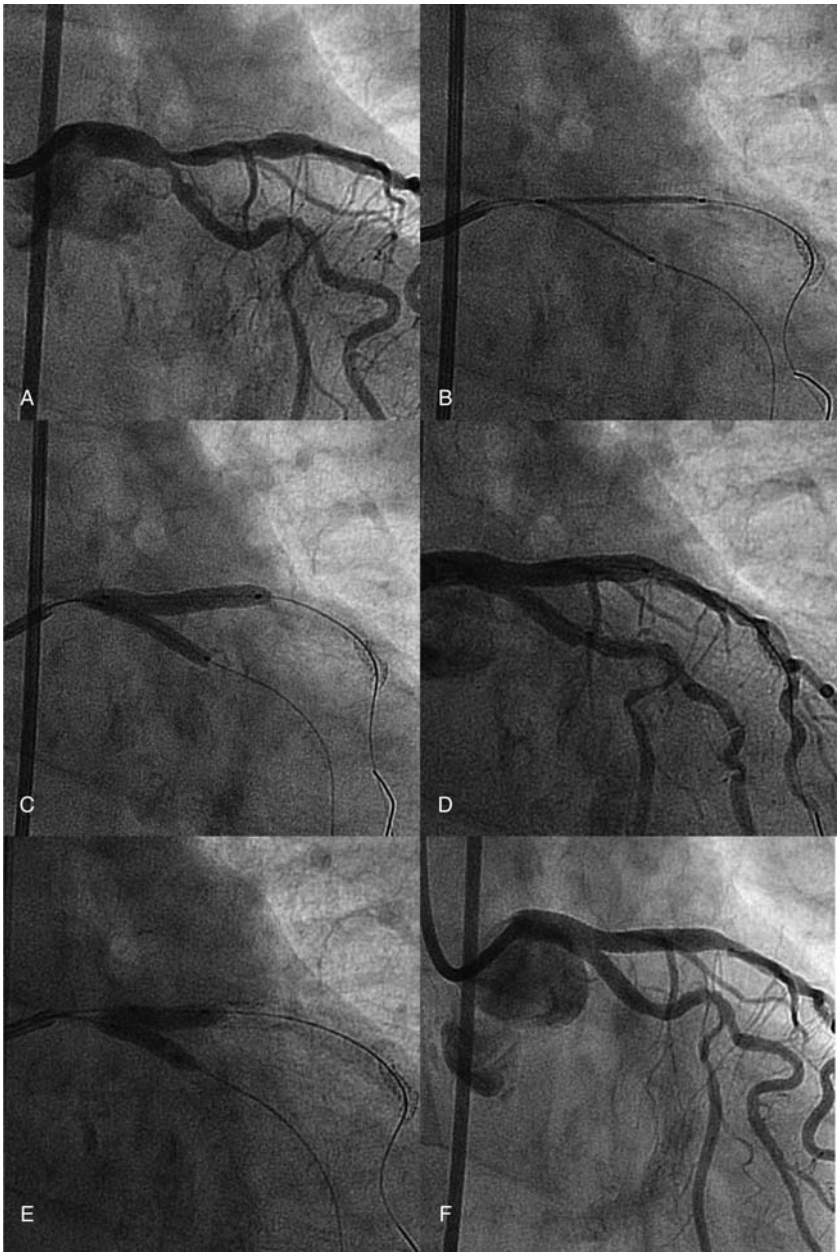

Figure 10 V stenting. (*A*) Initial appearance (Medina 0,1,1). (*B* and *C*) Two drug-eluting stents implanted in left anterior descending and left circumflex. (*D*) Intermediate result. (*E*) Post-dilatation (kissing). (*F*) Final angiographic result.

- co-morbidity (chronic obstructive lung disease)
- emergency clinical situation, i.e. acute LM occlusion.

Surgery

Surgery should be preferred in

- patients with heavy calcified LM disease
- reduced LV function
- diabetic patients particularly with insulin-dependent diabetes
- MVD suitable for CABG (particularly with low EuroSCORE)
- distal LM bifurcation lesion with reduced LV function or with occluded RCA or with additional complex lesions on the other coronary vessels (high SYNTAX score).

What do the joint ESC–EACTS guidelines on myocardial revascularization tell us about left main coronary artery stenosis?

'Significant LM stenosis and significant proximal LAD disease, especially in the presence of multivessel CAD, are strong indications for

Table 4 Indications for revascularization in stable angina or silent ischaemia

	Subset of CAD by anatomy	Class	Level
For prognosis	Left main > 50%*	I	A
	Any proximal LAD > 50%*	I	A
	2VD or 3VD with impaired LV function*	I	B
	Proven large area of ischaemia (>10% LV)	I	B
	Single remaining patent vessel > 50% stenosis*	I	C
	1VD without proximal LAD and without > 10% ischaemia	III	A

	Subset of CAD by anatomy	Class	Level
For symptoms	Any stenosis >50% with limiting angina or angina equivalent, unresponsive to OMT	I	A
	Dyspnoea/CHF and >10% LV ischaemia/viability supplied by >50% stenotic artery	IIa	B
	No limiting symptoms with OMT	III	C

* With documented ischaemia or Fractional Flow Reserve (FFR) < 0.80 for angiographic diameter stenosis 50–90%.

Table 5 Indications for coronary bypass grafting vs. PCI in patients with lesions suitable for both procedures and low predicted surgical mortality

Classes of Recommendations	Definition
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

	Favours CABG	Favours PCI
Left main (isolated or 1VD, ostium/shaft)	I A	IIa B
Left main (isolated or 1VD, distal bifurcation)	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≤ 32	I A	IIb B
Left main + 2VD or 3VD, SYNTAX score ≥ 33	I A	III B

revascularization. In the most severe patterns of CAD, CABG appears to offer a survival advantage as well as a marked reduction in the need for repeat revascularization, albeit at a higher risk of CVA, especially in LM disease'.

Tables 4 and *5* should form the basis of recommendations by the Heart Team in informing patients and guiding the approach to informed consent.

The current European Society of Cardiology guidelines consider the presence of an ostial and/or shaft lesion as a Class IIa indication for PCI level of evidence B.[71]

Distal isolated LM lesion or associated with single-vessel disease is considered as a Class IIb indication.

Left main lesion associated with two- or three-vessel disease and a low or intermediate (<32) SYNTAX score is considered as a Class IIb indication.

Left main lesion associated with two- or three-vessel disease and a high (>32) SYNTAX score is considered as a Class III indication.

The future

New generation of DES, dedicated bifurcation stents, and improvement of procedural techniques will probably improve the clinical outcome.

The new anti-platelet agents (prasugrel and ticagrelor) could improve the safety of PCI in complex LM lesions, but they need to be evaluated in this particular setting.

The future EXCEL trial (evaluation of Xience Prime or Xience V-eluting stent vs. CABG for effectiveness of LM revascularization) will evaluate the safety and efficacy of PCI with Xience Prime or Xience V EES vs. CABG in patients with ULMCA disease with a low or intermediate SYNTAX score (<33). The composite measure of all-cause mortality, MI, or stroke at an anticipated median follow-up duration of 3 years will be the primary endpoint. The need for repeat revascularization will be considered as a secondary endpoint. The results of the trial might impact the current guidelines.

Conclusion

Stenting of ULMCA stenosis can be performed with good results in carefully selected patients.

Patient selection is crucial and must be based on medical–surgical consultation (Heart Team concept) and ethics of information.

Stenting of non-distal LM can be achieved without major technical difficulties and with good immediate- and long-term results.

Stenting of distal LM lesion is a true technical challenge.

From the results of SYNTAX LM study, we can better define the subgroups of patients for whom PCI is a good alternative to surgery and those for whom surgical revascularization is definitely a better treatment option.

The objective of the next EXCEL trial will be to demonstrate that PCI with new generation of DES will compete with CABG as regards safety endpoint.

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