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Revascularization in Left Main Coronary Artery Disease

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Abstract

Purpose of review The goal of this review is to provide the reader with an up-to-date synopsis of the available literature surrounding the therapeutic options in the revascularization of significant left main (LM) coronary artery disease.
Recent findings Without revascularization, significant LM disease is associated with poor outcomes. Coronary artery bypass grafting (CABG) remains a mainstay of therapy in significant LM disease. More recently, long-term data from several studies suggests that percutaneous coronary intervention (PCI) is a reasonable alternative with comparable clinical outcomes in select patients. Recent study findings have helped to optimize PCI techniques to improve short- and long-term outcomes.
Summary CABG remains the cornerstone of therapy in significant LM disease. PCI is a reasonable alternative in select patients without highly complex disease. However, several technical considerations must be made to optimize outcomes after PCI.

Introduction

Depending on coronary dominance, the left main coronary artery supplies 75–100% of the left ventricular myocardium [1]. As such, atherosclerotic disease involving the left main conveys a high risk of adverse outcomes for patients. In the absence of revascularization, outcomes are poor, with early studies demonstrating mortality rates approaching 60% at 5 years for patients with a stenosis ≥ 50% [2]. The advent of landmark trials in the late 1970s and early 1980s established the clinical benefit of coronary artery

bypass grafting (CABG) over medical therapy [3, 4]. In contrast, outcomes for patients undergoing balloon angioplasty for left main disease were poor, with mortality rates of up to 64% at 3 years [5]. For this reason, CABG became the mainstay of revascularization for left main disease for nearly two decades.

More recently, a number of technological advancements have changed the landscape of percutaneous coronary intervention (PCI). The development of bare metal stents (BMS) and, subsequently, drug-eluting stents (DES) in addition to enhanced percutaneous techniques, use of intravascular imaging and novel medical therapy have led to marked improvement in patient outcomes [6]. A number of contemporaneous randomized, multicenter trials comparing CABG and PCI have delivered mixed but encouraging conclusions [7–11]. As a result, PCI for left main disease has increased 2- to fourfold in recent years [6, 12].

The importance of revascularization in left main disease in improving survival is emphasized by current guidelines. The 2021 American guidelines grant a class I recommendation for CABG for improving survival in patients with stable ischemic heart disease and significant left main disease [13••]. PCI is given a class 2a level of recommendation and is deemed reasonable for patients in whom PCI can achieve equivalent revascularization to CABG [13••].

This review aims to provide an overview of the current options in the revascularization of patients with left main disease. Particular focus will be made on contemporary literature comparing PCI with CABG as well as the latest techniques and evidence in PCI.

Treatment options

Invasive evaluation of left main disease

Angiography of the left main has the highest interobserver variability of any coronary segment [14]. Utilizing optimal fluoroscopic angles is vital. One study utilizing CT coronary angiography found that the average optimal viewing angle for the left main ostium was left anterior oblique (LAO) 37° and cranial (CRA) 22° (95% CI: LAO 33° to 40°, CRA 19° to 25°) [15]. The same study determined the average optimal viewing angle for the left main bifurcation to be LAO 0° and caudal (CAU) 49° (95% CI: right anterior oblique (RAO) 8° to LAO 8°, CAU 43° to 54°) [15]. However, even with optimized coronary angiography, further invasive assessment is often required in patients with ambiguous or equivocal left main disease on angiography. To this end, two methods are frequently employed: intravascular imaging, usually in the form of intravascular ultrasound or, IVUS; and invasive functional (such as fractional flow reserve (FFR)) assessments.

Discrepancies between angiographic and invasive left main assessments are common. In one study, 35% of left main lesions with an angiographic stenosis of ≥ 50% had an FFR of > 0.80 and 40% of patients with a stenosis of < 50% had an FFR of < 0.80 [16]. Deferring revascularization in patients with equivocal left main disease and a negative FFR has been demonstrated to have favourable clinical outcomes. In one prospective study of 213 patients with angiographically equivocal left main disease, 138 patients had an FFR of ≥ 0.80 and were managed with medical therapy alone. The remaining 75 patients with an FFR < 0.80 were referred for CABG. After 5 years, there was no significant difference in all-cause mortality or major adverse cardiovascular events between the two groups [17].

Of the two primary intracoronary imaging techniques, IVUS and optical coherence tomography (OCT), IVUS has the best available evidence in left

main interventions. IVUS has also been validated as a mean of determining the severity of left main disease. A minimum luminal area (MLA) of < 6 mm^2 strongly predicts the physiological significance of left main disease by FFR [18]. However, in Asian populations, smaller IVUS-derived MLA cutoffs of 4.5–4.8 mm^2 have been shown to correlate more closely with FFR [19, 20]. The 2011 LITRO (Spanish Working Group on Interventional Cardiology) study, which included 354 patients with an angiographically intermediate left main stenosis, demonstrated the clinical significance of an MLA of < 6 mm^2 [21]. In this study, revascularization was deferred in 90.5% of patients with an MLA ≥ 6 mm^2. Revascularization via CABG, PCI or CABG, and PCI was performed in 96% of patients with an MLA of < 6 mm^2. At 2-year follow-up, there was no difference in mortality between patients in whom revascularization was performed and those whom had revascularization deferred [21].

Pharmacologic treatment

Several randomized-controlled trials in the 1970s and 1980s established the efficacy of CABG over medical therapy for significant left main disease (3, 4). A subsequent meta-analysis of these trials demonstrated a reduction in 5- and 10-year all-cause mortality [22]. Since this time, revascularization has been the mainstay therapy for those with left main disease. However, medical therapy in these early trials was limited, with around two-thirds of patients taking beta-blockers and only one-fifth taking aspirin [22]. Furthermore, as a consequence of the robust results of these early studies, subsequent large RCTs comparing medical therapy with revascularization in stable coronary artery disease excluded patients with significant left main disease [23, 24]. Therefore, the effect of contemporary guideline-directed medical therapy, including more potent statins and antiplatelets, on morbidity and mortality in left main disease is unclear.

CABG vs PCI

After the publication of the seminal trials establishing the benefit of CABG in left main disease, CABG remained the revascularization modality of choice for over two decades. However, advancements in stent technology and PCI techniques at the beginning of the new millennium prompted several randomized studies to evaluate PCI as an alternative revascularization strategy (see Table 1). Several underpowered, but hypothesis-generating studies, were published—the LE MANS registry study (2008), a substudy of the SYNTAX trial (2010) and the PRECOMBAT trial (2011) [9–11].

The SYNTAX trial was the largest, and arguably the most important, of these three early trials. Of the 1800 patients recruited, it included a prespecified subgroup of 705 patients with a left main stenosis ≥ 50%. Patients were deemed by a multidisciplinary "Heart Team" to be suitable for either CABG or PCI with first-generation paclitaxel-eluting stents [10]. Based on the anatomical complexity of their disease, patients were also divided into terciles using the study's newly developed SYNTAX score. At the conclusion

Table 1. Randomized trials in CABG vs. PCI

	SYNTAX substudy (2010) (10)	PRECOMBAT (2011) (9)	EXCEL (2016) (8)	NOBLE (2016) (7)
Trial design	Subgroup analysis of multicenter RCT	Multicenter RCT, non-inferiority	Multicenter RCT, non-inferiority	Multicenter RCT, noninferiority
Follow-up	1 year	1 year	3 years	Median 3.1 years
n	705	600	1905	1201
Primary endpoint	Composite: all-cause death, stroke, myocardial infarction, or repeat revascularization	Composite: all-cause death, stroke, MI, ischemia-driven TVR	Composite: all-cause death, stroke MI	Composite: all-cause death, stroke, MI, repeat revascularization
Result	No significant difference—13.7% CABG vs 15.8% PCI ($p=0.44$) Repeat revascularization significantly higher with PCI (11.8% vs. 6.5%, p 0.02) Stroke significantly higher with CABG (2.7% vs 0.3%, $p=0.03$)	6.7% CABG vs 8.7% PCI ($p=0.01$ for non-inferiority)	14.7% CABG vs. 15.4% PCI ($p=0.02$ for non-inferiority)	28% for PCI vs 18% for CABG (HR1.51 [95% CI 1.13–2.00]) – exceeded the limit for non-inferiority
Conclusion	Substudy only—hypothesis-generating	Rates of primary endpoint similar but study underpowered due to low event rate – hypothesis-generating	PCI non-inferior to CABG	PCI inferior to CABG
Longest r eported follow-up data	10 years (25)	10 years (54)	5 years (28)	5 years (30)
Results	No difference in all-cause mortality between PCI and CABG – 27% vs 28% (HR 0.92 [95% CI 0.69–1.22])	No significant difference in primary outcome—29.8% for PCI vs 24.7% for CABG (HR 1.25 [95% CI 0.93–1.69] Ischemia-driven TVR more frequent with PCI – 16.1% vs 8.0% (HR 1.98 [95% CI 1.21–3.21])	No significant difference in primary outcome – 22.0% for PCI vs 19.2% for CABG ($p=0.13$)	28% PCI vs 19% CABG (HR 1.58 [95% CI 1.24–2.01], $p=0.0002$) HR exceeded limit for non-inferiority for PCI

of the initial 1-year follow-up period, there was no overall difference in major adverse cardiovascular and cerebrovascular events (MACCE) between CABG and PCI (13.7% versus 15.8% [95% confidence interval − 3.2 to 7.4%]; $p = 0.44$) [10]. However, rates of stroke were significantly higher in the CABG arm (2.7% versus 0.3% [95% confidence interval − 4.2 to − 0.1%]; $p = 0.009$]) and repeat revascularization was significantly higher in the PCI arm (6.5% versus 11.8%; Δ5.3% [95% confidence interval 1.0 to 9.6%]; $p = 0.02$) [10]. Importantly, in the subgroup of patients in the highest tercile of anatomical complexity (SYNTAX score ≥ 33), MACCE was significantly higher in the PCI cohort.

Extended 10-year follow-up data from the SYNTAX trial was subsequently published [25–27] and provided insight into long-term mortality outcomes. In patients revascularized for left main disease, there was no significant difference in all-cause death, occurring in 27% of patients in the PCI subgroup and 28% of patients in the CABG subgroup (HR 0.92 [95% CI 0.69–1.22]) [25]. This result for left main disease stood in contrast to patients who were treated for three-vessel disease, with CABG demonstrating a mortality benefit over PCI (HR 1.42 [95% CI 1.11–1.81]) [25].

The publication of these initial hypothesis-generating studies spurred the development of two large dedicated randomized-controlled trials comparing CABG and PCI for left main revascularization—the EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and the NOBLE (Nordic-Baltic-British Left Main Revascularization) trials [7, 8]. These studies were notable as the first large-scale trials to utilize second-generation drug-eluting stents for left main revascularization. The EXCEL trial included patients with unprotected left main disease with a stenosis of ≥ 70% or a stenosis of 50–69% with evidence of hemodynamic significance by non-invasive or invasive resting. Of importance, as a result of the outcomes of the SYNTAX study, patients were required to have a SYNTAX score of 32 or lower. One thousand nine hundred five patients were randomly assigned to undergo PCI with everolimus-eluting stents or CABG. Though patients with high anatomical complexity were excluded at a site level, 24.2% of patients were noted to have a SYNTAX score ≥ 33 when angiograms were assessed by a core laboratory [8]. At 3 years, there was no significant difference in the composite primary endpoint of all-cause death, stroke, or myocardial infarction between the PCI and CABG groups (15.4% vs 14.7%, HR 1.00 [95% CI 0.79–1.26], p for non-inferiority = 0.02) [8]. However, ischemia-driven revascularization was noted to be significantly more frequent in the PCI group (12.6% vs 7.5%, HR 1.72 [95% CI 1.27–2.33], $p < 0.001$).

Five-year outcomes for the EXCEL trial were published in 2019 [28]. With regard to the primary composite endpoint of all-cause death, stroke, or myocardial infarction, there continued to be no significant difference between PCI and CABG (22% vs 19.2%, OR 1.19 [95% CI 0.95–1.50], $p = 0.13$) [28]. Revascularization continued to be more frequent in the PCI cohort (17.2% vs 10.5%, OR 1.79 [95% CI 1.36–2.36]). However, there was a significantly higher rate of all-cause mortality in the PCI cohort which was inexplicably driven by non-cardiac causes, such as malignancy and infection in the late follow-up period (13.0% vs 9.9% OR 1.38 [95% CI 1.03–1.95]).

Notable controversy arose after the publication of the EXCEL trial. The study did not utilize the third Universal Definition of Myocardial Infarction (UDMI) to define periprocedural events. The third UDMI was widely adopted at the time of publication of the EXCEL trial results but was only published during early recruitment. Investigators instead used a modified version of the Society for Cardiovascular Angiography and Interventions (SCAI) definition and included these events as part of the primary endpoint. Using the protocol definition, rates of periprocedural MI were significantly lower with PCI than with CABG (3.6% vs 6.1%, $p = 0.015$). However, when the third UDMI was applied, rates were significantly higher with PCI than with CABG (4.0% vs 2.2%, $p = 0.025$) [29]. As a result, some have questioned the validity of the EXCEL trial results. However, the EXCEL investigators have argued that the third UDMI has been strongly associated with mortality after CABG but not PCI. Conversely, the protocol definition was associated with subsequent cardiovascular and all-cause death during 5-year follow-up, with similar hazard after PCI and CABG and is, therefore, a more appropriate outcome measure [29].

The NOBLE trial randomized 1201 patients to receive either CABG or PCI for symptomatic patients with a left main stenosis ≥ 50% or an FFR ≤ 0.80 [7]. Unlike the EXCEL trial, the SYNTAX score was not utilized as an exclusion criterion. Instead, patients were required to have no more than three additional non-complex lesions to be included in the study. Of the patients who underwent PCI, 11% received first-generation sirolimus-eluting stents and 89% received biodegradable umirolimus-eluting stents [7]. The primary endpoint was a composite of all-cause mortality, stroke, non-procedural myocardial infarction, and repeat revascularization. This is also in contrast to the EXCEL trial, which included periprocedural myocardial infarction but did not include repeat revascularization as a component of the primary composite outcome. At a median follow-up of 3.1 years, CABG was found to superior to PCI with 28% of patients in the PCI group experiencing a primary endpoint compared with 18% in the CABG cohort (HR 1.51 [95% CI 1.13–2.00), $p = 0.004$) [7]. Like the EXCEL trial, rates of repeat revascularization were noted to be significantly higher in the PCI cohort (15% vs 10%, HR 1.50 [95% CI 1.04–2.17] $p = 0.0304$) and similar to the rates observed in the 5-year results of the EXCEL trial [7, 8]. Updated 5-year follow-up data of the NOBLE trial was published in 2020. Similar rates of the primary endpoint were reported with 28.4% of the PCI cohort experiencing a primary endpoint compared with 19.0% in the CABG cohort (HR 1.58 [95% CI 1.24–2.01], $p = 0.0002$) [30]. Importantly, the higher all-cause mortality observed in the EXCEL trial was not reproduced in the NOBLE trial.

A meta-analysis published in 2021 included 5-year individual patient data from the EXCEL, NOBLE, SYNTAX, and PRECOMBAT trials [31••]. Four thousand three hundred ninety-four patients with mostly low-to-intermediate SYNTAX scores (median 25.0, IQR 18.0–31.0) were included in the analysis. There was no significant difference in all-cause death between PCI and CABG (11.2% vs 10.2%, HR 1.10, 95% CI 0.91–1.32, $p = 0.33$) [31••]. Bayesian analyses showed that there was an 85.7% probability that death at 5 years was greater with PCI. However, this difference was likely < 1.0% (< 0.2%/year). Spontaneous myocardial infarction was found to be more common with PCI than with CABG (HR 2.35, 95% CI 1.81–3.23, $p < 0.0001$) and repeat revascularization

was also significantly more frequent with PCI (HR 1.78, 95% CI 1.51–2.10, $p < 0.0001$). Although there was no overall difference in the risk of stroke, the risk was significantly lower with PCI in the first year after randomization (HR 0.37, 95% CI 0.19–0.69, $p = 0.0019$) [31••].

Perioperative major adverse events are more common after CABG than PCI [32]. A recent analysis of the EXCEL trial also suggests that these events are strongly associated with mortality after revascularization [32]. In this study, a perioperative major adverse event even was defined as the occurrence within 30 days of death, MI, thrombolysis in myocardial infarction (TIMI) major or minor bleeding, blood product transfusion ≥ 2 U, unplanned repeat coronary revascularization procedures, unplanned surgery or therapeutic radiological procedures, renal failure, prolonged intubation (> 48 h), sternal wound dehiscence, post-pericardiotomy syndrome, major arrhythmias, infection requiring antibiotics, or sepsis. In the EXCEL trial, non-fatal major adverse events were significantly more common after CABG than PCI (11.9% vs 45.4%; OR 0.16; 95% CI 0.14–0.21; $p < 0.0001$) [32]. Importantly, these events were strongly associated with 5-year mortality after both PCI (adjusted OR 4.61; 95% 2.71–7.82) and CABG (adjusted OR 3.25; 95% CI 1.95–5.41) [32].

Current revascularization guidelines grant a class 1 level of recommendation for CABG to improve survival in patients with significant left main stenosis [13••]. PCI is granted a class 2a ("reasonable") for patients who do not have highly complex disease and in whom equivalent revascularization to that possible with CABG can be achieved [13••].

The role of PCI is also vital in the revascularization of patients who are declined CABG due to unacceptable procedural risks or in patients who refuse surgery due to personal preference. This patient cohort is typically excluded from clinical trials but may still stand to benefit significantly from revascularization. One observational study of 726 patients with complex coronary artery deemed ineligible for CABG demonstrated that PCI can be performed with significantly lower risk than surgeon estimates with significant improvements in health status [33]. Importantly, this cohort included approximately 40% of patients who underwent PCI to the left main [33]. This study also demonstrated that mortality after PCI in this patient cohort was approximately the same as that predicted by the Society for Thoracic Surgeons (STS) and the EuroSCORE II surgical risk score but were significantly underestimated by the NCDR CathPCI score [33]. Therefore, it has been suggested that the STS score and EuroSCORE II can be calculated and used as part of the informed consent process in PCI patients deemed ineligible for surgery [34].

Considerations in left main PCI

If a decision has been made to perform PCI for left main disease, several technical considerations must be made in order to reduce procedural complications and optimize long-term outcomes. IVUS to help plan and guide left main PCI carries a class 2a recommendation in current guidelines [13••]. IVUS should be performed pre-PCI to assess plaque distribution, plaque

composition, the need for more extensive plaque modification techniques such as rotational atherectomy and intravascular lithotripsy, and for stent sizing. Following PCI, IVUS can assist in ensuring adequate stent expansion and apposition, and lesion coverage, as well as absence of edge dissections and plaque prolapse into the stent.

Current evidence indicates that IVUS improves long-term outcomes in patients undergoing left main PCI. Ten-year outcome data from the MAIN-COMPARE (The Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry was published in late 2021 and included 975 patients who underwent PCI for significant unprotected left main disease [35•]. The 10-year incidence rate of death was significantly lower in the IVUS-guided group (756 patients) compared with patients who underwent PCI with angiography alone (219 patients) (16.4% vs 31.0%, $p<0.001$). After adjusting for potential confounders, IVUS was still associated with a lower incidence of mortality, but this did not reach statistical significance (HR = 0.79 [95% CI 0.59–1.02]; $p=0.07$) [35•]. A substudy of the NOBLE trial, which included 603 patients and was published in 2020, demonstrated a non-statistically significant reduction in major adverse cardiac events at 5 years in patients undergoing IVUS guidance (18.9% vs 25.0%, $p=0.45$ after adjustment) [36]. However, left main target lesion revascularization was significantly reduced by IVUS guidance (5.1% vs 11.6%, $p=0.01$) [36].

OCT also has a role in left main PCI. Its spatial resolution and axial resolution are superior to that of IVUS and is, therefore, of particular utility when assessing lesion morphology, and optimizing PCI results. However, imaging depth is comparatively lower than IVUS and blood clearance with contrast is required to obtain images [13••]. Therefore, its use is limited in assessing the left main ostium and can be diminished in patients with a large-diameter left main. However, its utility in guiding distal and left main shaft PCI has been demonstrated in some studies. A single center retrospective study of 331 patients undergoing provisional left main bifurcation PCI followed by routine kissing balloon inflation in the jailed side branch compared the outcomes of patients undergoing OCT-guided PCI ($n=58$) compared with IVUS-guided PCI ($n=273$). There was no significant difference in the primary composite endpoint of cardiac death, myocardial infarction, and target lesion revascularization at 1 year (7.0% vs. 7.4%, $p=0.98$) [37]. The ROCK II study is a retrospective, multicenter study which included 730 patients and compared the outcomes of patients undergoing distal left main PCI with guidance by IVUS ($n=215$), OCT ($n=162$), or angiography alone ($n=353$) [38]. At 1 year, the rate of target lesion failure was significantly lower in patients who underwent intravascular imaging than those who underwent angiography alone (12.7% vs 21.2%, $p=0.039$). Importantly, there was no significant difference between patients whose PCI was guided by IVUS or OCT ($p=0.26$) [38].

The left main bifurcation is involved in over 60% of left main lesions [26]. When performing left main bifurcation PCI, the decision between a provisional or two-stent strategy is a crucial one. In essence, most bifurcation lesions can be treated with a provisional approach. The EBC Main study included 467 patients undergoing PCI for Medina 1,1,1 or Medina 0,1,1 left main bifurcation disease [39]. Patients were randomized to undergo either

provisional stenting or an upfront two-stent strategy with either a culotte, DK-minicrush, T-stent, or T-and-protrude (TAP) technique. The primary composite endpoint of death, myocardial infarction, or target vessel revascularization at 12 months was numerically lower in the provisional group but did not reach statistical significance (14.7% vs 17.7%, hazard ratio 0.8; 95% CI 0.5–1.3; $p = 0.34$) [39]. The provisional approach was also associated with significantly lower procedure times, radiation doses, and consumable use [39].

In contrast, complex bifurcation lesions have been demonstrated to have better outcomes with an upfront two-stent strategy. Complex bifurcation lesions can be defined according to the DEFINITION criteria—a set of major and minor angiographic criteria that predict major adverse events post-PCI [40]. The DEFINITION II study was a prospective study that randomly assigned patients who met these criteria to undergo either a provisional or a two-stent strategy (41). Of the 653 patients included in the study, 28.7% underwent PCI for left main bifurcation disease. At 1 year, the composite primary endpoint of cardiac death, target vessel MI, and clinically driven target lesion revascularization was significantly lower in the two-stent group (6.1% vs 11.4%, HR 0.52 [95% CI 0.30–0.90]; $p = 0.019$) [41•].

When performing up-front two-stent PCI of the left main bifurcation, the double kissing (DK) crush technique has the most evidence available to support its use. In Medina 1,1,1 or 0,1,1 left main bifurcation disease, the prospective randomized DK Crush V study demonstrated the superiority of this technique compared with provisional stenting with a reduced primary composite endpoint of cardiac death, target vessel MI or clinically driven target vessel revascularization at up to 3-year follow-up [42]. The DK Crush III study also demonstrated significantly reduced major adverse cardiovascular events when compared with the culotte technique at up to 3 years of follow-up [43].

Given the large degree of myocardium at risk, unprotected left main PCI is often considered a "high-risk" procedure. The use of hemodynamic devices, such as Impella left ventricular-assist device (Abiomed, Danvers, MA, USA) and intra-aortic balloon pumps (IABP), have been proposed for high-risk PCI, but have not demonstrated any benefit with routine use [44, 45]. Therefore, current guidelines have granted the elective use of these devices a class 2b level of recommendation for selected high-risk patients [13••]. Further studies dedicated to left main PCI are still needed to demonstrate which subgroup of patients may benefit from their use.

The optimal duration of dual antiplatelet therapy (DAPT) after left main PCI is currently a topic of debate. As a large-diameter and relatively short vessel, the left main has relatively low rates of restenosis and stent thrombosis after PCI [46]. However, this must be balanced against the fact that stent complications may result in significant morbidity or mortality due to the large amount of myocardium supplied by this vessel. Current guidelines grant a class I recommendation to 6 months of dual antiplatelet therapy after PCI with a drug-eluting stent for stable coronary artery disease and 12 months for an acute coronary syndrome [13••]. The decision to extend or truncate dual antiplatelet therapy is often a very nuanced decision that takes into account many procedural and patient-specific factors and balances the risk of future ischemic and bleeding events. Prolonged DAPT after left

main PCI is supported by a recent prospective observational study of 3865 patients which demonstrated reduced major adverse cardiovascular events in patients with > 12 months of DAPT compared with those with ≤ 12 months of DAPT with no significant increase in bleeding risk [47]. On the other hand, a post hoc analysis of the EXCEL trial did not demonstrate any difference in composite endpoint of death, stroke, or MI between patients who continued ceased DAPT at 12 months and those who continued for 3 years [48]. The recent IDEAL-LM randomized, prospective trial compared left main PCI with a biodegradable polymer platinum-chromium everolimus-eluting stent followed by 4 months of DAPT with a durable polymer cobalt-chromium everolimus-eluting stent followed by 12 months of DAPT [49]. At the conclusion of the two-year follow-up period, there was no significant difference in the combined endpoint of all-cause death, MI, or ischemia-driven target vessel revascularization (14.6% vs. 11.4%; $p = 0.04$ for non-inferiority) [49]. However, counterintuitively and inexplicably, bleeding events occurred significantly more frequently in the shortened DAPT/biodegradable polymer stent group compared with more prolonged DAPT/durable polymer stent group (2.7% vs. 0.5%; $p = 0.02$) [49].

The Heart Team

The "Heart Team" forms an integral part on the management of patients with significant left main disease. This is particularly true for patients in whom the optimal revascularization strategy is unclear. The concept of the "Heart Team" was first introduced into the clinical arena by the SYNTAX trial and was originally designed to confirm the suitability of patients for both PCI and CABG in a trial context [50]. A modern heart team should include representatives from interventional cardiology, cardiac surgery, and non-invasive cardiology, but may also include any additional health professional that may provide specific input into a given patient's care [13••]. When deciding the optimal treatment strategy for a patient, a number of factors should be considered including surgical risk scores, such as the Society of Thoracic Surgeons (STS) score, and a multitude of other anatomical and clinical factors [13••, 51]. Small observational studies that included patients with significant left main disease have demonstrated good clinical outcomes with the use of a heart team [52, 53]. Current guidelines grant the heart team a class Ia indication in patients for whom the optimal treatment strategy is unclear [13••].

Conclusion

Revascularization is a key pillar in the management of patients with significant left main disease. Given the high interobserver variability of angiographic assessments, additional information obtained by IVUS or invasive ischemia assessment may provide great value in patients with angiographically ambiguous disease. CABG remains a mainstay of treatment, but recent literature

suggests that PCI may offer a reasonable alternative in select patients without highly complex disease. To select the most appropriate revascularization strategy, a "Heart Team" approach, which considers a patient's individual clinical and anatomic factors in addition to their preferences, is strongly recommended. When left main PCI is performed, the routine use of IVUS is of vital importance to enhance short- and long-term outcomes. Similarly, the appropriate selection of patients for provisional or two-stent strategies is critical. If a two-stent strategy is selected, current evidence suggests that the DK Crush technique is associated with better long-term outcomes.

Declarations

Conflict of Interest
Dr. Maffey reports personal fees from AstraZeneca, outside the submitted work. Dr. Ybarra has nothing to disclose.
Human and Animal Rights and Informed Consent Statement.
The article does not contain any studies with human or animal subjects performed by any of the authors.

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• Of importance
•• Of major importance

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