Left Main Percutaneous Coronary Intervention

Paul S. Teirstein, MD, Matthew J. Price, MD

La Jolla, California

The introduction of drug-eluting stents and advances in catheter techniques have led to increasing acceptance of percutaneous coronary intervention (PCI) as a viable alternative to coronary artery bypass graft (CABG) for unprotected left main disease. Current guidelines state that it is reasonable to consider unprotected left main PCI in patients with low to intermediate anatomic complexity who are at increased surgical risk. Data from randomized trials involving patients who are candidates for either treatment strategy provide novel insight into the relative safety and efficacy of PCI for this lesion subset. Herein, we review the current data comparing PCI with CABG for left main disease, summarize recent guideline recommendations, and provide an update on technical considerations that may optimize clinical outcomes in left main PCI. (J Am Coll Cardiol 2012;60:1605–13) © 2012 by the American College of Cardiology Foundation

More than 30 years have passed since the first—and failed—attempt at left main percutaneous coronary intervention (PCI) by Andreas Gruentzig. Given the low prevalence of this lesion subset, robust data from dedicated randomized controlled trials (RCTs) comparing PCI with coronary artery bypass graft (CABG) are lacking, and CABG remains the traditional standard for the treatment of left main obstruction according to society guidelines (1). The introduction of drug-eluting stents (DES), combined with a culture within interventional cardiology that promotes shared experience through prompt dissemination of new techniques and outcomes, has led to a rapid evolution in the percutaneous approach to left main disease and broad clinical adoption of PCI that outpaces current guidelines. Herein, we summarize these guidelines, review the current state of observational and RCT data that pertain to left main intervention, and provide an update on technical considerations that may optimize clinical outcomes in left main PCI.

RCTs of Left Main PCI Disease Compared With CABG

To date, 4 RCTs have compared the efficacy of PCI with CABG for the treatment of left main disease, 1 using surrogate endpoints and 3 having a noninferiority design (Table 1). The LE MANS (Study of Unprotected Left Main Stenting Versus Bypass Surgery) enrolled 105 patients with >50% left main narrowing, with or without multivessel coronary artery disease, who were equally suitable for PCI or CABG (2). The primary endpoint was the change in left ventricular ejection fraction according to echocardiography at 12 months; clinical outcomes were key secondary endpoints. At 1-year follow-up, the mean ejection fraction increased with PCI compared with CABG (3.3 ± 6.7% vs. 0.5 ± 0.8%, p = 0.047), resulting in a greater ejection fraction in the PCI group (58.0 ± 6.8% vs. 54.1 ± 8.9%, p = 0.01). The risk of major adverse cardiac and cardiovascular events (MACCE) at 30 days was lower with PCI (2% vs. 13%; relative risk: 0.88 [95% confidence interval (CI): 0.79 to 0.99]; p = 0.03), whereas the risk of MACCE at 1 year was similar (31% vs. 25%; relative risk: 1.09 [95% CI: 0.85 to 1.38]), primarily due to the need for repeat revascularization in the PCI group. Left main restenosis occurred in 5 patients (9.6%), 4 of whom had received bare-metal stents (BMS). At a longer-term follow-up of 28.0 ± 9.9 months, there was a trend toward better survival after PCI (p = 0.08).

The SYNTAX (Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) trial provides the largest randomized dataset from which to assess the early and longer-term safety and efficacy of PCI for left main disease (3,4). A total of 1,800 patients with 3-vessel and/or left main disease (angiographic stenosis ≥50%) were randomly assigned to PCI with paclitaxel-eluting stents or to CABG; randomization was stratified according to the presence or absence of left main disease. The primary endpoint was MACCE at 1 year, and PCI would be deemed noninferior to CABG if the upper bound of the 95% CI for the absolute risk difference between the 2 strategies was <6.6%. The prespecified statistical analysis
plan was to first compare the overall population, with the left main subgroup compared subsequently only if noninferiority was concluded for the overall comparison. PCI was not noninferior to CABG for the prevention of MACCE in the overall trial (17.8% vs. 12.4%) (3), and therefore the findings within the left main cohort must be interpreted as observational and hypothesis-generating only. The trial used a novel method to calculate angiographic complexity, called the SYNTAX score, which incorporates the number of lesions, lesion location, lesion length, the presence of chronic total occlusions, bifurcations or trifurcations, aorto-ostial stenoses, vessel tortuosity, calcification, thrombus, and diffuse disease. A higher SYNTAX score reflects greater anatomic complexity. Among the 750 patients in the unprotected left main cohort, the mean EuroSCORE (a measure of surgical risk) was 3.9, the mean SYNTAX score was 30, and slightly more than one-third of the patients had 3-vessel disease in addition to left main obstruction. The 1-year MACCE rates were similar for PCI and CABG (15.8% vs. 13.7%, p = 0.48), with significantly lower rates of repeat revascularization in the patients randomly assigned to CABG (11.8% vs. 6.5%, p = 0.02) at the cost of more strokes (0.3% vs. 2.7%, p = 0.009). In patients with low and intermediate SYNTAX scores (0 to 22 and 23 to 32), 1-year MACCE rates were numerically lower with PCI (7% vs. 13% [p = 0.19]; 12.6% vs. 15.5% [p = 0.54]), whereas in those with SYNTAX scores >32, MACCE rates after CABG were significantly better (25.3% vs. 12.9%, p = 0.008). At the 3-year follow-up, there continued to be no significant difference within the overall left main cohort in the rate of MACCE between treatment strategies (26.8% vs. 22.3%, p = 0.20); repeat revascularization was still more frequent with PCI (20.0% vs. 11.7%, p = 0.004), whereas the risk of stroke after PCI remained lower (1.2% vs. 4.0%, p = 0.02) (Fig. 1) (5). Consistent with the 1-year results, patients with the greatest anatomic complexity (SYNTAX score >32) had inferior outcomes when treated with PCI at 3 years (MACCE rates: 37.3% vs. 21.2%; p = 0.003). With regard to safety, patients randomized to PCI had a numerically lower but not significantly different rate of the composite endpoint of death, myocardial infarction (MI), or stroke (13.0% vs. 14.3%, p = 0.60) and of all-cause death (7.3% vs. 8.4%, p = 0.64). Therefore, within SYNTAX, with the exception of the highest-risk anatomy (SYNTAX score >32), unprotected left main PCI seemed to be as safe as CABG at 3 years, and PCI outcomes were most favorable in the patients with low to intermediate anatomic complexity. Although there are many limitations to the SYNTAX trial, it currently remains the largest RCT comparing PCI with CABG in a prespecified left main subgroup.

Although the SYNTAX trial stratified randomization according to the presence of left main disease and prespecified the left main subgroup as a secondary analysis, Boudriot et al. (6) performed a small, multicenter, randomized trial dedicated to patients with significant (>50%) left main disease. The goal of the trial was to assess whether PCI with sirolimus-eluting stents would be noninferior to CABG with respect to the rate of the combined endpoint of death, MI, and repeat revascularization. Patients who had chronic

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Completed and Planned RCTs of PCI Compared With CABG for the Treatment of Unprotected Left Main CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Name</td>
<td>n</td>
</tr>
<tr>
<td>LE MANS</td>
<td>105</td>
</tr>
<tr>
<td>Boudriot et al. (6)</td>
<td>201</td>
</tr>
<tr>
<td>PRECOMATIC</td>
<td>600</td>
</tr>
<tr>
<td>SYNTAX</td>
<td>705</td>
</tr>
<tr>
<td>EXCEL</td>
<td>2,634</td>
</tr>
<tr>
<td>MILESTONE</td>
<td>1,000</td>
</tr>
</tbody>
</table>

*Noninferiority comparison.

CABG = coronary artery bypass graft; CAD = coronary artery disease; CVA = cerebrovascular event; EXCEL = Evaluation of XIENCE PRIME Everolimus Eluting Stent System (EECSS) or XIENCE V EECSS Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization; LE MANS = Study of Unprotected Left Main Stenting Versus Bypass Surgery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MILESTONE = Revascularization Strategy (PCI With DES Implantation vs CABG) in Patients With Non ST Elevation Acute Coronary Syndrome With Multivessel and/or Unprotected Left Main Coronary Disease; NA = not applicable; PCI = percutaneous coronary intervention; PRECOMATIC = Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease; RCT = randomized clinical trial; ST = stent thrombosis; SYNTAX = Synergy between Percutaneous Coronary Intervention with Taus and Cardiac Surgery; TVR = target vessel revascularization.
total occlusions, lesions >30 mm, and “extreme” left-dominant coronary systems were excluded. A total of 201 patients were enrolled, providing 80% power assuming a 15% event rate in the surgical group and an allowable relative risk difference of 10% between groups. Enrolled patients had lower anatomic and surgical risk compared with those in the SYNTAX trial: the mean SYNTAX score was 23.5, the mean logistic EuroSCORE was 2.5, and 14% had concomitant 3-vessel disease. A median of 2 sirolimus-eluting stents per patient were implanted in the PCI group, and 65% of the CABG group received total arterial revascularization. Compared with PCI, significant periprocedural adverse events occurred more frequently after CABG (4% vs. 30%, p < 0.001). At 12-month follow-up, the combined endpoint of death, MI, and repeat revascularization occurred in 19% of patients after PCI and in 13.9% of patients after CABG, and therefore PCI did not satisfy the statistical criteria for noninferiority (p = 0.19). The difference between groups was driven by increased repeat revascularization in the patients undergoing PCI (14.0% vs. 5.9%). PCI was noninferior to CABG with respect to the secondary endpoints of death (2% vs. 5%; 95% CI for differences: −9.4 to 2.7; p < 0.001) and death or MI (5% vs. 7.9%; 95% CI for differences: −10.6 to 4.4; p < 0.001), although these observations must be considered hypothesis-generating given that the trial did not achieve its primary endpoint. The rate of death and MI remained similar between groups at an average of 3 years of follow-up. Therefore, the results of this small trial are consistent with those of SYNTAX and suggest that compared with a surgical cohort treated with optimal arterial revascularization, left main PCI with sirolimus-eluting stents in patients at relatively low surgical risk and without highly complex anatomy provides a similar longer-term rate of death and MI at the cost of more repeat procedures.

Uniquely, this trial prospectively assessed the morbidity of the 2 treatment strategies and demonstrated that any differences in “hard endpoints” must be interpreted in the context of a greater risk of periprocedural events with CABG, including atrial fibrillation, major infection, and stroke.

The PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial is the largest dedicated unprotected left main RCT to compare DES with CABG to date (7). The primary endpoint was the composite of death, MI, ischemia-driven target vessel revascularization, and stroke at 1-year follow-up. A total of 600 patients suitable for either treatment approach were enrolled, which provided 80% power to show noninferiority assuming a 13% event rate in the CABG group and an absolute risk difference <7%. The enrolled population was at low surgical risk, with a mean EuroSCORE of 2.7, and the coronary anatomy was less complex than SYNTAX (mean SYNTAX score: 25). According to the criteria used in the trial, the 1-year rate of the primary endpoint after PCI was noninferior to CABG (8.7% vs. 6.7%; absolute risk difference: 2.0% [95% CI: −1.6 to 5.6]; p = 0.01). At 2 years, the rate of death, MI, and stroke was numerically lower with PCI and did not differ between the groups (4.4% vs. 4.7%; hazard ratio [HR]: 0.92 [95% CI: 0.43 to 1.96]; p = 0.83), although repeat revascularization was significantly higher after PCI (9.0% vs. 4.2%; HR: 2.18 [95% CI: 1.10 to 4.32]; p = 0.02). This increased rate of repeat revascularization was restricted to the patients who had concomitant 3-vessel disease. The findings of PRECOMBAT have substantial limitations. The study was underpowered given the lower-than-expected rates of the primary endpoint in the CABG group, and the margin for noninferiority was set so wide.
that PCI was deemed noninferior despite possibly resulting in nearly twice the MACCE as CABG. However, the apparent safety of PCI compared with CABG at 2 years is consistent with that observed in SYNTAX.

**Meta-analyses and registries.** Several meta-analyses of observational and randomized studies comparing the safety and efficacy of PCI with CABG have been conducted. Among 2,905 patients from 8 studies comparing DES with CABG, there were no differences in the risk of death, MI, or stroke at 1 year (odds ratio [OR]: 1.25 [95% CI: 0.86 to 1.82]) or the risk of death alone (OR: 1.12 [95% CI: 0.80 to 1.56]), whereas repeat revascularization was significantly reduced with CABG (OR: 0.44 [95% CI: 0.32 to 0.59]) (8).

Similarly, in 10 studies involving 3,773 patients with unprotected left main stenosis treated with PCI using DES or BMS or with CABG, the risk of death, MI, or stroke was similar at 3 years (OR: 1.16 [95% CI: 0.68 to 1.98]) as was mortality alone (OR: 1.11 [95% CI: 0.66 to 1.86]), whereas the risk of repeat revascularization was greater with PCI (OR: 3.30 [95% CI: 0.96 to 11.33]) (9). At 5-year follow-up in the MAIN-COMPARE registry, there was no significant difference between PCI with DES or CABG in the adjusted risk of death (HR: 0.83 [95% CI: 0.34 to 2.07]) or in the risk of the composite of death, Q-wave MI, or stroke (HR: 0.91 [95% CI: 0.45 to 1.83]); the risk of the primary efficacy endpoint, target vessel revascularization, was significantly higher with DES (HR: 6.22 [95% CI: 2.26 to 17.14]) (10). Recent registry data also support a significant, negative interaction between anatomical complexity and outcome after PCI compared with CABG (11). In 1,146 patients with unprotected left main disease who received either DES or CABG, the adjusted risk of mortality at 5 years favored PCI in patients with low SYNTAX scores (<23) (HR: 0.52 [95% CI: 0.21 to 1.28]; p = 0.15) but favored CABG in patients with high SYNTAX scores (≥32) (HR: 1.46 [95% CI: 0.92 to 2.30]; p = 0.11, p interaction = 0.047) (12).

Several tentative conclusions regarding left main PCI can be drawn from the current evidence base of trial data, which involve a total of >1,600 randomized patients. First, PCI may provide at least equivalent results to CABG in the setting of less complex anatomy, as the rates of death and the combined endpoint of death, MI, and stroke are similar between PCI with "first-generation" DES and CABG up to 3 years of follow-up, with a numerical advantage favoring PCI across the trials. Several meta-analyses of observational and randomized comparisons of PCI and CABG similarly demonstrate no differences in mortality up to the 3-year follow-up (8,9,13). These findings must be interpreted with caution because these studies were underpowered, and the left main disease data from SYNTAX are based on a subgroup analysis of a negative trial (3,4). The durability of PCI, especially in patients who have intermediate SYNTAX scores, must be confirmed with continued follow-up. Second, PCI seems to be inferior to CABG with respect to the composite of death, MI, and stroke, as well as death alone, in patients with greater anatomic complexity (SYNTAX scores >32) or when considering the endpoint of repeat revascularization. “Next-generation” DES with better safety and clinical outcomes and more objective approaches to revascularization may further optimize PCI outcomes. This hypothesis is being tested in the EXCEL (Evaluation of XIENCE PRIME Everolimus Eluting Stent System [EES] vs XIENCE V EES Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial (NCT01205776), which will examine the safety and efficacy of PCI with everolimus-eluting stents compared with CABG in approximately 2,600 patients with unprotected left main disease who are eligible for either treatment strategy and have SYNTAX scores <32. The primary endpoint is the composite of death, MI, or stroke at 3 years, and the trial is powered for sequential noninferiority and superiority testing. The rate of repeat revascularization, which in previous clinical trials has favored CABG, will be considered a secondary endpoint, and therefore the overall clinical efficacy of PCI within the trial will need to be interpreted within this context.

**Acute coronary syndrome and left main PCI.** Left main disease is rare in patients presenting with acute coronary syndrome. In the GRACE (Global Registry of Acute Coronary Events) registry, the incidence of significant unprotected left main obstruction was approximately 4% (14). Data regarding clinical outcomes in this patient cohort are limited to small observational studies that suffer from substantial confounding. Patients with acute MI and a left main culprit lesion are more frequently in cardiogenic shock and are more likely to have suffered cardiac arrest before intervention compared with patients with culprit lesions in other parts of the coronary tree (15,16). Among PCI registries, in-hospital mortality is high (21% to 58%) and is related to the prevalence of cardiogenic shock within the cohort studied, but patients surviving hospitalization seem to have an excellent long-term prognosis (16). In the GRACE registry, left main revascularization by PCI or CABG was associated with improved survival after discharge compared with no revascularization. PCI patients had greater unadjusted rates of in-hospital mortality (11% vs. 5.4%) and 6-month out-of-hospital mortality (5.4% vs. 1.6%) with fewer strokes (0.4% vs. 2.1%), although CABG-treated patients were at substantially lower clinical risk (14). Because left main PCI has the advantage of providing more rapid reperfusion compared with CABG with acceptable short- and longer-term outcomes, and is associated with a lower risk of stroke, some have opined that PCI should be considered for the treatment of patients presenting with acute MI and a left main culprit lesion, particularly those who experience cardiogenic shock, persistent ventricular arrhythmias, slow flow, and significant comorbidities (17). Current guidelines recommend PCI in patients presenting with acute coronary syndrome who are not suitable candidates for CABG (Class IIa, Level of Evidence: B) or in patients with ST-segment elevation MI due to a left main
culprit lesion with reduced Thrombolysis In Myocardial Infarction flow and in whom PCI can be performed more quickly and safely than CABG (Class IIa, Level of Evidence: C) (Table 2).

Society guidelines. The 2011 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Society of Cardiovascular Angiography and Interventions (SCAI) Guidelines for PCI provide detailed recommendations regarding left main revascularization that have been revised substantially from prior versions (Table 2) (1). First, the guidelines state that a heart team approach should be used in the management of these patients (Class I, Level of Evidence: C), which is consistent with the protocols of several of the recent left main PCI studies, including SYNTAX. Second, anatomic risk stratification according to the SYNTAX score and surgical risk stratification according to the Society of Thoracic Surgeons' score are recommended (Class IIa, Level of Evidence: B). The guidelines incorporate the relation between coronary anatomy and adverse outcomes after left main PCI that was observed in randomized studies: consideration for PCI rather than CABG is based on the degree of anatomic complexity (for SYNTAX score <22 or ostial/branch disease, Class IIa; for SYNTAX score <33 or distal bifurcation disease, Class IIb). The guidelines restrict the recommendation to consider PCI only in those patients at increased surgical risk, although the RCTs of left main PCI included patients who were candidates for either treatment approach.

The European Society of Cardiology and the European Association for Cardio-Thoracic Surgery Guidelines on myocardial revascularization address the indications for CABG compared with left main PCI in stable patients with lesions suitable for both procedures and low predicted surgical mortality (18). These guidelines provide a Class IIa (Level of Evidence: B) recommendation for PCI of left main ostial or shaft disease when it exists in isolation or in combination with 1-vessel disease; a Class IIb (Level of Evidence: B) recommendation for left main distal bifurcation disease when it exists in isolation or in combination with 1-vessel disease; a class IIb recommendation for any left main disease with concomitant 2- or 3-vessel disease and a SYNTAX score ≤32; and a Class III recommendation for left main disease with concomitant 2- or 3-vessel disease and a SYNTAX score ≥33. CABG is the favored approach for all of these scenarios (Class I, Level of Evidence: A).

### Procedural Considerations

Assessing the severity of left main obstruction. Due to the short length of the left main and the diffuse nature of the disease, angiographic determination of the severity of left main disease is notoriously less reliable compared with other locations in the coronary tree (Fig. 2) (19). Further invasive evaluation should be strongly considered in the setting of a lesion of indeterminate severity or discordance between angiographic views. When performing intravascular ultrasound (IVUS), it is important to image the left main beginning in the daughter vessel with the least angulated access, usually the left anterior descending artery, especially when assessing disease of the distal left main. A minimal luminal area (MLA) <6 mm² has been proposed as the criteria for a significant left main obstruction according to Murray’s law, based on an MLA threshold of <4 mm² for

---

**Table 2**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Level of Evidence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
<td>A heart team approach to revascularization is recommended in patients who have unprotected left main disease or complex CAD</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>Calculation of the STS and SYNTAX scores is reasonable in patients who have unprotected left main and complex CAD</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>IVUS is reasonable for the assessment of angiographically indeterminate left main CAD</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
<td>IVUS may be considered for guidance of coronary stent implantation, particularly in cases of left main coronary artery stenting</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>PCI to improve survival is reasonable as an alternative to CABG in selected patients whose disease is stable with significant unprotected left main CAD with: 1) anatomic conditions associated with a low risk of PCI procedural complications and a high likelihood of a good long-term outcome (e.g., a low SYNTAX score &lt;22), ostial trunk or left main CAD; and 2) clinical characteristics that predict a significantly increased risk of adverse surgical outcomes (e.g., STS-predicted risk of operative mortality ≥5%)</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>PCI to improve survival is reasonable in patients who have UA/NSTEMI when an unprotected left main coronary artery is the culprit lesion and the patient is not a candidate for CABG</td>
</tr>
<tr>
<td>IIa</td>
<td>C</td>
<td>PCI to improve survival is reasonable in patients who have acute STEMI when an unprotected left main coronary artery is the culprit lesion, distal coronary flow is TIMI flow grade &lt;3, and PCI can be performed more rapidly and safely than CABG</td>
</tr>
<tr>
<td>IIb</td>
<td>B</td>
<td>PCI to improve survival may be reasonable as an alternative to CABG in selected stable patients who have significant unprotected left main CAD with: 1) anatomic conditions associated with a low to intermediate risk of PCI procedural complications and an intermediate to high likelihood of good long-term outcome (e.g., low-intermediate SYNTAX score of &lt;33, bifurcation left main CAD); and 2) clinical characteristics that predict an increased risk of adverse surgical outcomes</td>
</tr>
<tr>
<td>III (harm)</td>
<td>B</td>
<td>PCI to improve survival should not be performed in stable patients with significant unprotected left main CAD who have unfavorable anatomy for PCI and who are good candidates for CABG</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; CAD = coronary artery disease; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention; STS = Society of Thoracic Surgeons; SYNTAX = Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; TIMI = Thrombolysis In Myocardial Infarction; UA/NSTEMI = unstable angina/non-ST-segment elevation myocardial infarction.
the left anterior descending and left circumflex arteries. This cutoff has been shown to have a high sensitivity and specificity to predict a fractional flow reserve (FFR) <0.75 (20). Recently, in a single-center study of 55 patients with isolated, de novo left main disease of indeterminate severity, an MLA = 4.8 mm² provided 89% sensitivity and 83% specificity to predict an FFR <0.80 (21). A prospective, multicenter trial involving 354 patients who had intermediate unprotected left main lesions demonstrated that deferring revascularization for lesions with an MLA ≥6 mm² was safe, resulting in a 2-year cardiac death–free survival rate of 97.7% (22). The 2011 ACCF/AHA/SCAI guidelines for PCI state that IVUS is reasonable for the assessment of angiographically indeterminate left main coronary artery disease (class IIa, Level of Evidence: B) (1).

An FFR <0.80 has also been validated for the diagnosis of left main obstruction, and an FFR-guided strategy between medical therapy or CABG provides favorable long-term outcomes (23). In the setting of concomitant lesions of the left anterior descending and/or left circumflex arteries, FFR may be challenging to interpret. Unlike FFR, IVUS provides plaque morphologic and anatomic data that can help guide and optimize PCI (24,25). Optical coherence tomography imaging can also provide detailed plaque morphology and anatomy (Fig. 1), although ostial left main lesions cannot be assessed with this technology because intubation of the left main with the coronary guiding catheter and contrast injection is required to provide a blood-free lumen.

**Stenting approach. BMS OR DES.** A meta-analysis of observational studies and RCTs involving 10,342 patients demonstrated lower crude event rates for DES than BMS for mortality, repeat revascularization, and major adverse cardiovascular events (MACE) at 6 to 12 months, 2 years, and 3 years (26). Adjusted analyses of 5,081 patients demonstrated a significantly lower risk of mortality with DES at the 2-year (OR: 0.42 [95% CI: 0.28 to 0.62]; p < 0.001) and 3-year (OR: 0.70 [95% CI: 0.53 to 0.92]; p = 0.01) follow-up. Although these analyses are prone to confounding and do not consider differences in the duration of dual antiplatelet therapy, these data support a default strategy of DES for left main PCI except in cases in which it is not anatomically feasible (e.g., very large reference vessel diameter) or in which long-term dual antiplatelet therapy is contraindicated.

**Provisional versus dedicated 2-stent approach for the distal left main.** The distal bifurcation is the most common site of left main obstruction, and it represented 54% of the target lesions in the left main cohort of the SYNTAX trial (4). In observational studies, PCI of the left main ostium and/or shaft, which is technically less challenging, seems to be associated with lower rates of MACE compared with PCI of the bifurcation (27–29). Small randomized trials of PCI with DES for bifurcation lesions have demonstrated that a provisional stenting strategy of the distal bifurcation (stent the main vessel only, with optional stenting of the side branch) is associated with reduced periprocedural MI, less contrast use, and decreased procedural and fluoroscopy times compared with a systematic 2-stent approach (both main vessel and side branch) (30). A pooled analysis found that a provisional approach provided similarly beneficial outcomes even for more anatomically complex lesions (31). However, the target lesion involved the left main bifurcation in only 2% of the enrolled patients.
in these studies, and side branch compromise may have more profound acute and longer-term clinical impact in the setting of the left main. In an observational study of 773 patients with distal left main disease, a single stent technique was associated with a reduced propensity-adjusted risk of 2-year MACE as well as cardiac mortality and MI compared with a 2-stent technique; final kissing balloon dilation, regardless of stent approach, was also a predictor of improved outcomes (32). Because stent technique is usually dictated by plaque burden and coronary anatomy, the observed differences in outcomes between 1- and 2-stent approaches may depend on differences in the complexity of the treated lesions. The current data support provisional stenting as the primary strategy for approaching the left main bifurcation, although there are several scenarios in which a dedicated 2-stent approach for left main PCI is reasonable and may be preferred. Some examples of anatomy favoring a 2-stent approach include: left circumflex disease extending >5 mm from the carina, threatened closure of the left circumflex, or when re-access to the left circumflex would be particularly challenging (33).

2-STENT APPROACHES. An operator can select from a plethora of 2-stent techniques, including but not limited to crush, culotte, T-stenting, T-and-protrusion, and simultaneous kissing stents. The Nordic Stent Technique study randomly assigned 424 patients who had a bifurcation lesion to crush or culotte stenting; the left main was the target lesion in 10% of cases. At 6 months, there were no differences in clinical outcomes between the 2 groups, although there was significantly less angiographic restenosis in patients treated with culotte stenting (4.5% vs. 10.5%, p = 0.046). A registry of unprotected left main PCI showed no difference in outcomes between the different 2-stent techniques (32), but the technique selection was not randomized, and the study was underpowered to see differences in clinical outcomes. Simultaneous kissing stents are associated with an unacceptably high rate of target lesion revascularization (34), and when restenosis occurs, percutaneous reintervention is challenging. However, it can be useful when speed and simplicity, rather than longer-term outcomes, are the priority. The optimal 2-stent approach should be dictated by operator comfort and coronary anatomy (e.g., similar diameters of the circumflex and left anterior descending arteries favor culotte, dissimilar diameters favor crush, and a very steep angle of the bifurcation may favor a T- or T-and-protrusion technique).

INTRAVASCULAR IMAGING AND FUNCTIONAL ASSESSMENT TO OPTIMIZE TECHNICAL RESULTS. Randomized trials in the BMS era did not show a clinical benefit of routine IVUS to guide PCI. However, because the true luminal diameter of the left main is difficult to determine angiographically, and bifurcation stent techniques can result in substantial stent distortion (35), many operators advocate the use of intravascular imaging with IVUS or optical coherence tomography to help guide the left main PCI procedure and to confirm the technical adequacy of the stent result (Fig. 3). After PCI for non–left main lesions, edge dissections, stent underexpansion, and malapposition have been associated with stent thrombosis; a smaller, final minimal stented area has been associated with the need for target lesion revascularization; and early malapposition may diminish the antirestenotic effect of DES (36,37). The clinical sequelae of these phenomena are potentially greater within the left main. A final minimal stent area >9.6 mm² has been associated with a very low rate of repeat revascularization after left main PCI (38), and IVUS guidance led to a lower 3-year mortality rate compared with angiographic guidance alone in 145 matched pairs of patients who underwent left main PCI with DES (25). Narrowing of the left circumflex ostium is not uncommon after crossover stenting into the left anterior descending artery, and recent studies using intravascular imaging have demonstrated that the mechanism of this phenomenon is frequently carina shift, rather than plaque shift, especially when the angle between the left anterior descending and left circumflex arteries is narrow (39). The degree of angiographic stenosis of the jailed left circumflex ostium after crossover stenting is frequently discordant with functional severity according to FFR (40), and therefore FFR may help the operator decide whether to provisionally stent a “pinched” left circumflex. Such a physiology-guided strategy to provisional stenting of the distal left main seems reasonable, although its clinical safety and efficacy have not been assessed.

ANGIOGRAPHIC FOLLOW-UP. A rationale for routine surveillance angiography after left main PCI arose from the findings of the ULMTR (Unprotected Left Main Trunk Intervention Multicenter Assessment) registry, in which there seemed to be an early hazard for mortality after BMS implantation in the first 6 months after discharge (41). However, the SYNTAX trial demonstrated the excellent safety profile of left main PCI with DES in the absence of such routine angiography, and angiographic follow-up is not mandated in the EXCEL trial protocol. A previous Class IIa recommendation for angiographic follow-up was removed from the 2011 ACCF/AHA/SCAI PCI guidelines.

Conclusions

Evidence from RCTs involving more than 1,600 patients with left main disease who are suitable candidates for either CABG or PCI suggests that PCI may provide at least equivalent results to CABG in the setting of less complex coronary anatomy. However, these individual trials were underpowered to detect differences in this endpoint, and, in the case of the SYNTAX trial, this finding must be considered hypothesis-generating given that the PCI did not achieve the primary endpoint in the overall trial. The durability of outcomes must also be confirmed with longer-term follow-up. Intravascular imaging and/or functional assessment before and after intervention and a provisional stent approach to left main bifurcation lesions may optimize
technical and possibly clinical outcomes, although robust data supporting these approaches are lacking. Clinical outcomes after PCI appear worse in patients with more complex coronary anatomy, in particular those with SYNTAX scores >32. The current ACCF/AHA/SCAI guidelines state that left main PCI is a reasonable alternative to CABG in patients who have anatomic conditions associated with good procedural and longer-term outcomes and who are at increased risk for surgery. The EXCEL trial will provide more definitive data regarding the safety and efficacy of left main PCI compared with CABG in patients suitable for either treatment strategy.

Reprint requests and correspondence: Dr. Matthew J. Price, 10666 North Torrey Pines Road, Maildrop S1056, La Jolla, California 92037. E-mail: price.matthew@scrippshealth.org.

REFERENCES

1. Levine GN, Bates ER, Blankenship JC, et al., American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines for PCI state IVUS may be considered for guidance of coronary stent implantation particularly in cases of left main coronary artery stenting (Class IIb, Level of Evidence: B).


---

Figure 3  Intravascular Imaging Guidance of Complex Left Main Coronary Stent PCI

(A) Baseline left coronary angiography demonstrating severe left main bifurcation disease (arrow). (B) Initial angiographic result after 2 drug-eluting stents using the culotte technique and final kissing balloon dilation. (C) Intravascular ultrasound (IVUS) of distal left main demonstrates stent underexpansion and malapposition (arrows). (D) IVUS after repeat kissing dilation with larger diameter noncompliant balloons demonstrates improved expansion and apposition. IVUS assessment during left main percutaneous coronary intervention (PCI) with drug-eluting stents may identify technical complications including but not limited to stent malapposition, stent underexpansion, lack of lesion coverage, and edge dissection, which could affect clinical outcomes (25). Current American College of Cardiology Foundation/American Heart Association/Society of Cardiovascular Angiography and Interventions guidelines for PCI state IVUS may be considered for guidance of coronary stent implantation particularly in cases of left main coronary artery stenting.


Key Words: left main • percutaneous coronary intervention • stent.