Contemporary Reviews in Interventional Cardiology

Percutaneous Coronary Intervention With Stent Implantation Versus Coronary Artery Bypass Surgery for Treatment of Left Main Coronary Artery Disease

Is It Time to Change Guidelines?

Seung-Jung Park, MD, PhD; Duk-Woo Park, MD, PhD

Abstract—On the basis of clinical trials comparing coronary-artery bypass grafting (CABG) with medical therapy, current guideline recommend CABG as the treatment of choice for patients with asymptomatic ischemia, stable angina, or unstable angina/non-ST elevation myocardial infarction who have left main coronary artery disease. Percutaneous coronary intervention can be selectively performed in patients who are candidates for revascularization but who are ineligible for CABG. However, because of advances in periprocedural and postprocedural medical care in patients undergoing either CABG or percutaneous coronary intervention with stenting, new evaluation, and a review of current indications, may be required to determine the standard of care for patients with left main coronary artery disease. Current evidences indicate that stenting results in mortality and morbidity rates that compared favorably with those seen after CABG, suggesting that a current guideline (the Class III recommendation of percutaneous coronary intervention for unprotected left main coronary artery disease) may no longer be justified. Data from several extensive registries and a large clinical trial may have prompted many interventional cardiologists to select percutaneous coronary intervention with stenting as an alternative revascularization strategy for such patients. In addition, these data may inform future guidelines and support the need for well-designed, adequately powered, prospective, randomized trials comparing the 2 revascularization strategies. The cumulative evidence from ongoing and future clinical trials will change the current clinical practice of revascularization for unprotected left main coronary artery disease, which was introduced several decades ago and which has continued to date without major revision. (Circ Cardiovasc Intervent. 2009;2:59-68.)

Key Words: bypass surgery ■ stents ■ coronary disease

Significant left main coronary artery (LMCA) disease has been found in 3% to 5% of all patients who undergo coronary angiography and in 10% to 30% of patients who undergo bypass surgery. Critical LMCA stenosis puts patients at high risk of cardiovascular events because of the extent of jeopardized myocardium and concomitant multivessel coronary artery disease and, therefore, it has been considered as the most prognostically important coronary lesion.

Current practice guidelines recommend coronary artery bypass grafting (CABG) as the standard procedure for patients with unprotected LMCA disease, primarily because long-term outcomes of surgical revascularization are superior to those of medical treatment. However, because of anatomic accessibility and other characteristics, percutaneous coronary intervention (PCI) for LMCA disease was attractive to the interventional cardiologist, and data from several registries showed its feasibility and short- and mid-term effectiveness. Nevertheless, PCI for LMCA disease has been confined to surgically high-risk patients and those with protected LMCA disease, or has been used as bailout procedures in patients with angioplasty complications.

However, recent improvements in interventional techniques and adjunctive pharmacology have challenged the conventional wisdom that significant LMCA stenoses should be treated surgically. The introduction of coronary stenting has led to a reevaluation of the role of PCI as a viable treatment option for LMCA disease, and the widespread availability of drug-eluting stents (DES), together with improved stenting techniques, has lowered the threshold for use of PCI, instead of CABG, in patients with LMCA disease. The clinical experience with PCI for LMCA disease involves a broad spectrum of clinical and angiographic subsets of such patients. However, there has been little evaluation of the long-term safety and efficacy of PCI with stenting for unprotected LMCA disease, and no randomized trial has compared the 2 primary interventions (PCI versus CABG) in a large population. We have therefore reviewed recent advances and the current status of percutaneous versus surgical...
treatment for LMCA disease, focusing on whether PCI is an alternative to or a possible replacement for CABG in these patients.

**Anatomy and Pathophysiology of LMCA Disease**

The LMCA arises from the left aortic sinus just below the sinotubular junction of the aortic root. In approximately two thirds of patients, the LMCA bifurcates into the left anterior descending and left circumflex arteries; in one third of patients, the LMCA trifurcates into the left anterior descending, left circumflex, and ramus intermedius. The LMCA is responsible for supplying, on average, 75% of the left ventricular myocardium. Examination of 100 autopsy cases found that the LMCA had an average length of 10.8±5.2 mm (range 2 to 23 mm), an average diameter of 4.9±0.8 mm, and an average angle of the terminal branch division of 86.7±28.8° (range 40° to 165°), and that there was a positive correlation between LMCA length and the angles between the terminal branches.6

The anatomic portion of the LMCA stenosis is divided into 3 anatomic regions (the ostium, midshaft, and distal bifurcation). The atherosclerotic involvement has been found to vary with its histology and hemodynamic mechanics. Histologically, the ostial portion resembles the aorta, being rich in smooth muscle cells and elastic fibers. The distal bifurcation is the part of the LMCA most susceptible to the development of an atherosclerotic lesion because of low-shear flow disturbance.7 Especially in the bifurcation, the lateral wall (i.e., the wall opposite the flow divider) is the most frequent site of atherosclerotic plaque accumulation, whereas the flow divider (i.e., the bifurcation carina) is usually spared because of high shear stress. A previous intravascular ultrasound (IVUS) study evaluating the relationship between LMCA length and the morphology of atherosclerotic change showed that short LMCA (<10 mm) developed stenosis more frequently near the ostium than near the distal bifurcation (55% versus 38%); long LMCA developed stenosis more frequently near the distal bifurcation than near the ostium (77% versus 18%); and the midportion of the LMCA was infrequently stenosed (5% to 7% of patients).8 Ostial LMCA stenosis was more common in women (44% versus 20%) and was associated with larger lumen area, less calcification, and more negative remodeling than were midor distal-bifurcation LMCA stenosis. The plaque composition of the LMCA disease varies from pathological intimal thickening to thin-cap fibroatheroma with or without plaque rupture.9 In patients including those with minimal LMCA disease, the most frequent underlying plaque type was pathological intimal thickening (64%) followed by fibroatheroma with early or late core (17%). However, most lesions with significant LMCA stenosis (defined as >50% narrowing) showed more complex plaques, such as fibroatheromas with late core, thin-cap fibroatheroma, surface ruptures, fissures, and intraplaque hemorrhage.

**Management of LMCA Disease**

**Medical Treatment Versus Bypass Surgery**

Most studies on medically treated LMCA disease were conducted 3 decades ago in small numbers of patients (Table 1). Early observational studies demonstrated that long-term prognoses of patients with medically treated LMCA disease were poor, with 3-year survival rates of 50%.10–12

Controlled trials comparing CABG with medical therapy alone were initially performed in patients with stable angina and showed that surgical revascularization provided survival benefit to patients with >50% LMCA stenosis (Table 1). In the Veterans Administration Cooperative Study,13 113 patients with LMCA disease were randomly allocated to medical therapy (n=53) or bypass surgery (n=60); during follow-up (average, 30 months), the long-term mortality rate was significantly higher in the medical group than in the surgery group (36% versus 20%). Similar results were observed in the Coronary Artery Surgery Study and the European Coronary Surgery Study.4,14 In the Coronary Artery Surgery study, which included 1492 patients with LMCA disease, the 3-year survival rate was 91% for the surgical group and 69% for the medically-treated group. However, survival benefits were not observed in certain subgroups, including patients with mild-to-intermediate LMCA stenosis (<60%, normal left ventricular function or a nonstenotic (<70% diameter stenosis) right coronary artery; these patients had 3-year survival rate of ≈88%. In a meta-analysis of 7 randomized trials that assessed treatment effects on mortality of patients with stable coronary artery disease, the 5-year relative risk reduction for mortality provided by CABG over medical therapy was greater for LMCA disease.
than for 3-, 1-, or 2-vessel disease (odds ratios, 0.32, 0.58, and 0.77, respectively), and the absolute survival benefit time after CABG among patients with LMCA disease was 19.3 months.15

PCI With Stent Implantation

Bare-Metal Stents and DES

Clinical results of stenting in patients chosen for PCI, either because of prohibitive surgical risk or as bailout for angioplasty complications, depend mainly on baseline clinical characteristics, such as left ventricular function and coexisting conditions. The ULTIMA registry enrolled 279 patients with unprotected LMCA stenosis who were treated with bare-metal stents (BMS); of these, 46% were inoperable or at high surgical risk. Among these high-risk patients, the in-hospital mortality was 13.7%, and the 1-year incidence of all-cause mortality was 24.2%; whereas among the 32% patients at low risk (age <65 years, ejection fraction >30%), there were no periprocedural deaths and the 1-year mortality rate was only 3.4%.16 In a series of elective, low-risk patients, who were also not at increased risk for CABG, PCI with BMS for unprotected LMCA stenosis who were treated with bare-metal stents (BMS); of these, 46% were inoperable or at high surgical risk. 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With advances in stenting techniques, the availability of DES, and adjuvant pharmacotherapy such as clopidogrel, statins, and antiplatelet therapy, many experienced interventional cardiologists now perform PCI with stenting for patients with unprotected LMCA disease. Several observational studies, although limited by a nonrandomized nature, small number of patients, and short follow-up periods, have shown promising PCI outcomes using DES compared with BMS (Table 2).22-24 Most initial reports documented that DES afforded higher procedural success rates and lower rates of angiographic restenosis and target-vessel revascularization (TVR), with similar or lower rates of death and MI compared with BMS.

In a direct comparison, 103 patients with unprotected LMCA disease were randomly assigned to receive BMS (n=50) or DES (n=53) implantation and were followed for 6 months, at which time the DES group showed a statistically significant reduction in binary restenosis (6% versus 22%) and target-lesion revascularization (TLR) (2% versus 16%) and a significant reduction in the rate of major adverse cardiac events (death, MI, or TLR; 13% versus 30%), all of which were entirely attributable to reduction in repeat revascularization rate.25

Ostial and Midshaft Lesions

In some LMCA disease, atherosclerotic plaque is confined only to the ostium or midshaft of the LMCA, with differences in angiographic and clinical outcomes associated with lesion location. Park et al22 reported a lower restenosis rate after LMCA nonbifurcation intervention compared with bifurcation intervention (1.7 versus 10.9%). Similarly, the risk of TVR was significantly lower in nonbifurcation than in bifurcation stenoses (3% versus 13%).26 A multicenter observational study of 147 patients with unprotected nonbifurcation LMCA lesions demonstrated favorable long-term outcomes with DES.27 Procedural success was achieved in 99% of patients, and none experienced Q-wave MI or died during hospitalization. In the 106 patients who underwent angiographic follow-up at 4 to 6 months, mean late lumen loss was 0.01 mm and restenosis occurred in only 1 patient (0.9%). At a mean follow-up of 886 days, there were 5 deaths (3.4%...
cumulative mortality), 7 TVR (4.7%), and, of these, only 1 patient had a TLR.

**Bifurcation Lesions**

Bifurcations are prone to lesion development because of greater shear stress and more frequent turbulent blood flow.\(^7\)

The distal left main is involved in more than half of all patients (60% to 90%). Bifurcation LMCA lesions are bulky, and PCI is complicated by plaque shift in 4.5% to 26% of patients.

Currently available evidence suggest that results are less favorable when distal LMCA lesions are treated by a 2-stent approach compared with single-stent approach.\(^{28,29}\) The TLR rate is relatively low (<5%) with single stent approaches, even for distal LMCA lesions, and is nearly equivalent to results obtained with DES for ostial or mid-left main lesions.\(^{22–24}\) However, patients with distal LMCA lesions treated with 2-stent techniques showed a TLR rate as high as 25%, with restenosis confined mainly to the left circumflex ostium. A poorer outcome in distal LMCA disease was recently reported.\(^{30}\) In 50 patients (94% had distal bifurcation lesions treated with a double-stent technique) with unprotected LMCA stenting evaluated by 9-months routine angiography, in-lesion restenosis occurred in 21 patients (42%), was focal in 85%, and involved the branch ostia in 82%. TLR occurred in 19 patients (38%) at a mean follow-up of 276±57 days with 2 acute stent thromboses and 5 deaths at 1 year.

How should distal bifurcation LMCA disease be treated? For bifurcation lesions, a single-stent technique, in which a stent is placed across the side branch (usually the left circumflex), is preferred in patients with diminutive or normal-appearing side branches. However, if the operators decide on a single stent approach, it is almost always possible to place second stent on the side branch if stenting crossover does not yield an optimal result. A number of 2-stent techniques with various levels of complexities and indications, such as T-stenting, crush stenting, culotte stenting, and simultaneous kissing stenting or Y-stenting, are available. There is little consensus, and few data, on the optimal dual stent approach. Because restenosis or stent thrombosis can be catastrophic at LMCA locations, all measures for achieving optimal final result should be considered and IVUS assessment is advocated in most cases for stent optimization. In addition, because of the measurable risk of restenosis and revascularization after complex stenting, the use of dedicated LMCA bifurcation stents is currently being explored.\(^{31}\)

**Role of IVUS Guidance and Need for Routine Angiographic Surveillance During Follow-Up**

Because the conventional coronary angiogram is only a lumenogram providing information on lumen diameter but yielding little insight into lesion or plaque characteristics, exact evaluation of LMCA disease is sometimes difficult because of peculiar anatomic and hemodynamic factors such as large size, a short normal reference segment, overlapping of major vessels, aortic cusp opacification, streaming of contrast agent, and varied angulations. Therefore, the guidance afforded by IVUS during LMCA stenting has been very useful, compared with the use of IVUS in PCI treatment of other coronary lesions. IVUS evaluation before the stenting procedure cannot only measure the degree of stenosis, plaque involvement, and anatomic configuration (with delineation of major side branches), but can also select the appropriate diameter and length of the stent and the optimal stenting strategy. In addition, postprocedure IVUS interrogation is very helpful in detection of stent underexpansion, incomplete lesion coverage, large residual plaque, and stent inapposition. More data are needed to clarify the long-term impact of IVUS guidance on long-term clinical outcomes after unprotected LMCA stenting.

Whether routine angiography is needed during follow-up after LMCA stenting has not been well studied. In addition, although follow-up angiography was recommended at once after PCI, considering that patients with LMCA restenosis are at high risk for adverse events, little information is available on whether or not or timing for repetitive angiography. This issue warrants large studies comparing routine and repetitive follow-up angiography with noninvasive, functional follow-up evaluation after LMCA stenting. In addition, computed tomography coronary angiography with high negative predictive value needs to be evaluated for detection of LMCA restenosis, and utility in a supplementary follow-up role, in patients with LMCA stenting.

**Risk Stratification After PCI for LMCA Disease**

Although several “risk-stratification systems” have been suggested to predict early or long-term cardiovascular events after PCI treatment, little is known about useful clinical and angiographic indicators for risk prediction of adverse outcomes in patients with LMCA stenting. A previous study found that patients with a high EuroSCORE (≥6) were at greater risk of death or MI than those with a low EuroSCORE.\(^{32}\) Inflammatory biomarkers, such as C-reactive protein, have also been suggested as useful marker of the incidence of major cardiac events in patients undergoing LMCA stenting.\(^{33}\) Higher levels of C-reactive protein are associated with increased risk of death (19% versus 0%) and death/MI (31% versus 0%). Patients with high C-reactive protein levels may benefit from more aggressive pharmacological treatment (extended or high dose of clopidogrel or high-dose statin therapy).\(^{34}\)

However, limited data exist regarding uniform risk-indices without introducing bias against specific treatment. Because the widely used risk-scoring system (EuroSCORE and the Parsonnet score) for LMCA revascularization are based mainly on surgical risk parameters,\(^{35,36}\) fair risk-assessment and risk-prediction methods are currently lacking for PCI of unprotected LMCA disease. The SYNTAX score, currently under evaluation in patients undergoing revascularization for multivessel coronary artery disease, is related to coronary lesion complexity (number and location of lesions, LMCA involvement, 3-vessel disease, total occlusion, tortuosity, bifurcation, thrombus, calcification, and dominance), and therefore may be useful in guiding optimal revascularization strategies and in prediction of future cardiovascular events.\(^{37}\)

Further studies to develop a specific risk-scoring system that integrate clinical and anatomic characteristics in patients with LMCA disease are warranted.
Which DES Is Better? Sirolimus-Eluting Versus Paclitaxel-Eluting Stents

Several small observational studies have compared outcomes of the 2 types of DES for LMCA stenting. In a single-center, nonrandomized study comparing sirolimus-eluting (SES) and paclitaxel-eluting stents (PES) in 110 patients with LMCA disease, angiographic results (late loss in the main branch [0.32 versus 0.46 mm] and side branch [0.36 versus 0.52 mm]) and long-term clinical outcomes (death/MI [16% versus 18%] and TVR [9% versus 11%]) were comparable.38 A recent large randomized trial (the ISAR-LEFT MAIN trial) found that SES and PES were equally effective and safe in patients undergoing unprotected LMCA stenting.40 The study enrolled 607 patients (305 SES and 302 PES), at relatively high-risk (mean age, 69 years, 30% with diabetes, 40% with acute coronary syndrome, 50% with prior PCI, 63% with distal bifurcation stenosis, and 70% with multivessel disease). At 12 months of follow-up, the incidence of death (6.6% versus 5.0%), MI (4.6% versus 5.0%), stroke (1.0% versus 1.7%), and major cardiac events (death, MI, or revascularization; 15.8% versus 13.6%) were similar in the SES and PES group, as were angiographic restenosis rate at 6- to 9-months (19.4% versus 16.0%) and 2-year revascularization rates (7.8% versus 6.5%). The incidence of definite (0.3% versus 0.7%) and probable (0% versus 0.3%) stent thrombosis at 2 years was also similar in the 2 study arms.

Stent Thrombosis and Long-Term Clinical Outcomes With DES

Recently, concerns have been raised regarding the long-term safety of DES, with particular regard to late stent thrombosis and late mortality. Increasing concern over stent thrombosis, which may have more catastrophic consequences in patients undergoing unprotected LMCA stenting, and a lack of long-term clinical data, have hampered the widespread use of PCI with DES as an alternative to CABG.

However, recent data alleviate concerns about the safety of PCI with DES in the treatment of unprotected LMCA disease. A recent multicenter registry evaluated the occurrence of late and very late stent thrombosis in 731 patients undergoing elective LMCA stenting with DES. At 30 months, 4 patients had definite stent thrombosis (2 acute, 1 subacute, and 1 late) and 3 had probable thrombosis, for a combined incidence of definite or probable thrombosis of 0.95%. The cumulative rates of death, MI, and TVR were 6.2%, 1.5%, and 12.9%, respectively. Older age, lower ejection fraction, and EuroSCORE were identified as predictors of thrombotic events. A report from the DELFT registry, which included 358 patients undergoing LMCA stenting with a minimum of 3 years follow-up, noted that the incidence of definite, probable, and possible stent thrombosis were 0.6%, 1.1%, and 4.4%, respectively. Among the overall registry population, cardiac death occurred in 9.2% of patients, and MI, TLR, and TVR were noted in 8.6%, 5.8%, and 14.2% of patients, respectively. Compared with emergent PCI, elective PCI was associated with excellent 3-year rates of mortality (6.2% versus 21.4%), reinfarction (8.3% versus 10.0%), and TLR (2.8% versus 6.6%). In a recent clinical study, the ISAR-LEFT MAIN trial, in which 607 patients were treated with DES, the 2-year rate of definite or probable stent thrombosis was about 0.5 to 1.0%. In a large real-world observation (the MAIN-COMPARE registry), the incidence of definite thrombosis at 3 years was 0.6%. These results indicated that DES implantation in patients with unprotected LMCA disease results in relatively lower, or, at worst, similar rates of stent thrombosis and long-term mortality than seen when DES is used in subsets of patients with other coronary lesion.47

How long should dual antiplatelet therapy be continued after LMCA stenting with DES? Lifelong or limited therapy? Implantation of DES may delay protective endothelialization and may increase the risk of stent thrombosis, especially of late or very late thrombosis. Therefore, dual antiplatelet therapy is emphasized, and clopidogrel (75 mg daily) is recommended for at least 1 year in patients treated with DES who are not at increased risk of bleeding.48 The long-term benefits of clopidogrel use beyond 6 or 12 months are, however, unclear in such patients. Although the risk-benefit ratio of long-term clopidogrel therapy is not well-studied, many clinicians prolong dual antiplatelet therapy for up to several years or indefinitely after LMCA stenting with DES. Despite the various duration of applied clopidogrel treatment (at least 3 months, to life), the overall incidence of early and late stent thrombosis were very low, and similar among studies. Additional studies with large population and longer-term follow-up are warranted to evaluate the antithrombotic benefit versus major bleeding risk of long-term clopidogrel use, and to determine the optimal duration of clopidogrel therapy after DES placement in patients with LMCA disease.

Stents Versus Surgery

Patient Selection: Possible Indication or Contraindication for PCI or CABG

The choice of PCI or CABG for treatment of unprotected LMCA disease depends on several clinical and anatomic features, making optimal patient selection crucial for appropriate treatment of LMCA disease and achievement of favorable long-term outcomes. In patients with very complex anatomic features, which are not feasible for stenting, and concomitant diffuse multivessel disease, CABG is preferred so as to avoid procedural and future thrombotic risks and to provide more complete revascularization. However, in patients with relatively simple LMCA disease, such as ostial/shaft LMCA disease or isolated LMCA disease (with or without one or 2-vessel involvement), PCI is an alternative, and in some cases a preferred strategy to reduce surgical risks (eg, stroke and in-hospital events following major surgery). LMCA lesion characteristics (severe calcification, distal LMCA involvement with relation to major branches), the extent of extra-LMCA (concomitant multivessel disease, the status of distal run-off), and patient clinical characteristics (age, diabetes, ejection fraction, and other comorbidities) are important in patient selection. Patient/physician preference is also influential. Several clinical and angiographic factors generally considered for proper choice of patients for the PCI or CABG treatment are listed in Table 3. Briefly, selection of patients for PCI may be optimized as follows: (1) PCI with...
stenting is a reasonable option for patients with unprotected LMCA disease at high surgical risk or with protected LMCA disease; (2) patients presenting with acute coronary syndrome who have culprit LMCA occlusion and hemodynamic instability requiring emergent revascularization; and (3) isolated ostial or midshaft LMCA disease. For patients with anatomic and clinical characteristics suitable for both CABG and PCI, the benefits and risks of PCI versus CABG and patient/physician preference, need to be weighted.

Theoretical Advantages of CABG or PCI for Unprotected LMCA Disease

The potential benefit of bypass surgery over stenting in patients with multivessel or LMCA disease is that, in bypass surgery, a graft is placed on the midcoronary vessel well beyond the area of disease, whereas stents directly relieve the offending lesion. Thus, not only has the culprit lesion been directly treated, but also there are prophylactic benefits in the event that the patient develops new disease. If a patient receives a stent and develops new disease beyond the stented area, that patient is still at very high risk, but in patients who receive bypass grafting, the development of more proximal disease is irrelevant. However, although the benefits of bypass surgery are well known, the CABG procedure results in a large portion of the myocardium being supplied solely by the venous graft, which has limited patency, whereas successful LMCA stenting provides long-term patency and revascularization of the entire coronary arterial vasculature.

Current Evidence Supporting PCI or CABG for LMCA Disease

To date, a large body of data supports the feasibility, efficacy, and safety of stenting as compared with CABG for treatment of unprotected LMCA disease. We also expect that longer-term (5- and 10-year) data will soon be forthcoming.

Registry Data

Although several studies have reported on the midterm safety and feasibility of stenting in LMCA disease, long-term benefits of PCI compared with bypass surgery are less clear, in part because they have been evaluated less extensively. Several, small observational studies have compared PCI with stenting of unprotected LMCA to CABG (Table 4). The early clinical events of left main stenting are similar or

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Table 3. Clinical or Angiographic Characteristics Influencing the Choice Between Stenting and Surgery for Patients With Unprotected Left Main Coronary Artery Disease

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<tr>
<td>Serious comorbidity (high surgical risk): chronic lung disease, poor general performance status, advanced age such that major surgery cannot be tolerated, limited life expectancy, prior bypass surgery, unsuitable coronary anatomy for bypass grafting.</td>
<td>Patient refusal of surgery.</td>
</tr>
<tr>
<td>Patient refusal of stenting.</td>
<td>Patient refusal of stenting.</td>
</tr>
</tbody>
</table>

stenting is a reasonable option for patients with unprotected LMCA disease at high surgical risk or with protected LMCA disease; (2) patients presenting with acute coronary syndrome who have culprit LMCA occlusion and hemodynamic instability requiring emergent revascularization; and (3) isolated ostial or midshaft LMCA disease. For patients with anatomic and clinical characteristics suitable for both CABG and PCI, the benefits and risks of PCI versus CABG and patient/physician preference, need to be weighted.

Theoretical Advantages of CABG or PCI for Unprotected LMCA Disease

The potential benefit of bypass surgery over stenting in patients with multivessel or LMCA disease is that, in bypass surgery, a graft is placed on the midcoronary vessel well beyond the area of disease, whereas stents directly relieve the offending lesion. Thus, not only has the culprit lesion been directly treated, but also there are prophylactic benefits in the event that the patient develops new disease. If a patient receives a stent and develops new disease beyond the stented area, that patient is still at very high risk, but in patients who receive bypass grafting, the development of more proximal disease is irrelevant. However, although the benefits of bypass surgery are well known, the CABG procedure results in a large portion of the myocardium being supplied solely by the venous graft, which has limited patency, whereas successful LMCA stenting provides long-term patency and revascularization of the entire coronary arterial vasculature.

Current Evidence Supporting PCI or CABG for LMCA Disease

To date, a large body of data supports the feasibility, efficacy, and safety of stenting as compared with CABG for treatment of unprotected LMCA disease. We also expect that longer-term (5- and 10-year) data will soon be forthcoming.

Registry Data

Although several studies have reported on the midterm safety and feasibility of stenting in LMCA disease, long-term benefits of PCI compared with bypass surgery are less clear, in part because they have been evaluated less extensively. Several, small observational studies have compared PCI with stenting of unprotected LMCA to CABG (Table 4). The early clinical events of left main stenting are similar or
superior to those of bypass surgery because of significant increase in periprocedural MI\textsuperscript{53} or cerebrovascular events\textsuperscript{54} in the CABG patients. Long-term mortality up to approximately 1 year was similar in the PCI and the CABG groups. However, the risk of TVR was consistently higher with PCI than with CABG.

### Randomized Clinical Trials

The LeMANS trial was the first randomized comparison of PCI with stenting (52 patients) and CABG (53 patients) for treatment of unprotected LMCA stenosis, with or without multivessel coronary artery disease.\textsuperscript{57} DES were placed in 35% of PCI patients and left internal mammary artery grafts were used in 72% of CABG patients. At 1 year, the primary end-point of absolute change in left ventricular ejection fraction was significantly greater in the PCI than in the CABG group (3.3%±6.7% versus 0.5±0.8%; \(P=0.047\)), whereas the secondary endpoints, survival and major adverse cardiac and cerebrovascular events (MACCE), were comparable in the 2 groups. Although this was a prospective, randomized initial trial comparing outcomes of stenting versus CABG for LMCA disease, the results were limited by the small number of patients, and the nonspecific and inconclusive primary end-point was chosen to evaluate treatment effects.

As shown in the left main subsets (348 patients treated with CABG and 357 treated with PES) from the SYNTAX (SYNergy Between PCI With TAXUS and Cardiac Surgery) trial,\textsuperscript{37} PCI demonstrated 1-year clinical outcomes equivalent to those seen after standard bypass surgery (Table 5). In particular, PCI-treated patients showed a trend toward lower MACCE rates in cases with anatomically simple LMCA disease (LMCA only and LMCA plus single-vessel disease), compared with CABG-treated patients. The rate of revascularization was significantly higher in PCI-treated patients, whereas the stroke risk was significantly greater in CABG-treated patients. However, because of the exploratory, hypothesis-generating nature of subgroup analysis, results from more specific LMCA-targeted trial are needed. The ongoing PRECOMBAT (PREmiere of COMparison of By-pass Surgery and Angioplasty Using Sirolimus-Eluting Stents in Patients With Unprotected Left Main Coronary Artery Disease) trial, which is a prospective, multicenter, randomized study to compare the safety and efficacy of SES and CABG for treatment of unprotected LMCA disease with a primary study end-point of 1-year MACCE (death, MI, stroke, and TVR), is expected to provide a more definitive evaluation of the 2 primary interventions. However, because current results from randomized trial are relatively short term in nature (up to 1 year), longer-term data may also be needed to more strongly emphasize the long-term value of LMCA stenting compared with bypass surgery. If these studies provide long-term follow-up data supporting the clinical equivalence of PCI and CABG, PCI with stenting would be a viable strategy for treatment of LMCA disease. However, the choice of revascularization modality should still be made after thorough consideration of clinical and lesion characteristics.

### Meta-Analysis and Systemic Review

A recent meta-analysis, which considered results of 16 observational studies on 1278 patients undergoing PCI with DES for unprotected LMCA disease, showed a low in-hospital mortality rate of 2.3% and a low mid-term mortality rate of 5.5% at a median of 10 months follow-up, and adjusted odds ratios for MACCE (death, MI, TVR, or stroke) of 0.46 (0.24 to 0.90), favoring PCI with DES over CABG.\textsuperscript{58}

In contrast, another systemic review suggested that early (in-hospital, to 30 days) and longer-term (1 to 2 year) mortality rates were better after CABG (early, 2% to 4%, average 3%; late, 5% to 6%, average 5%) than PCI with BMS (early, 0% to 14%, average 6%; late, 3% to 31%, average 17%) or DES (early, 0% to 10%, average 2%; late, 0% to 14%, average 7%).\textsuperscript{59} However, these results should be interpreted with caution and regarded as only exploratory findings, given the limited number of patients, selection or publication bias in the literature reviewed, and caveats on internal validity of the included clinical studies.

### MAIN-COMPARE Registry

The MAIN-COMPARE registry is the first long-term study comparing PCI with stenting with bypass surgery for LMCA disease.\textsuperscript{66} This study evaluated 2240 patients with unprotected LMCA disease who underwent stenting (BMS=318 and DES=784) or CABG (1138) at 12 major cardiac centers in Korea, where left-main stenting is far more common than in Western countries. Outcome measures were compared during the first 3 years after treatment and included death; a composite outcome of death, Q-wave MI, or stroke; and TVR using propensity-score matching. The risks of death and the composite of death, Q-wave MI, or stroke were similar in the PCI and CABG groups and these results were consistent when either BMS or DES was compared with concurrent CABG (Figure). However, the rate of TVR was significantly lower in the CABG group than in the PCI group with hazard ratios varying by the type of stent. DES recipients were
almost 6-fold more likely, and BMS recipients almost 10-fold more likely, to require revascularization, compared with those who underwent surgery.

Conclusions

On the basis of clinical trials comparing CABG and medical therapy, current guideline recommend CABG as the treatment of choice for patients with asymptomatic ischemia, stable angina, or unstable angina/non-ST elevation MI who have LMCA disease. PCI can be selectively performed in patients who are candidates for revascularization but who are not suitable for CABG. However, because of advances in periprocedural and postprocedural medical care in patient undergoing either CABG or PCI with stenting, new evaluation, and a review of indications may be required to determine the standard of care for patients with LMCA disease.

Current evidences indicates that stenting yields mortality and morbidity rates that compare favorably with CABG, suggesting that a current guideline (class III recommendation of PCI for unprotected LMCA disease) may no longer be justified. A large clinical trial (the SYNTAX trial) showed that DES, compared with CABG, demonstrated acceptable outcomes in patients with LMCA disease. Also, data from large registries (the MAIN-COMPARE and the DELFT study) from routine clinical practice and from a DES clinical trial (the ISAR-LEFT MAIN trial) may have prompted many interventional cardiologists to choose PCI with stenting as a good treatment option for patients with LMCA disease. These results may inform future guidelines and support the current guideline for unprotected LMCA disease, which was introduced to date.


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