Is surgery or percutaneous revascularization the preferred strategy for patients with significant left main coronary stenosis?

Percutaneous Revascularization Is the Preferred Strategy for Patients With Significant Left Main Coronary Stenosis

Paul S. Teirstein, MD

In the early 1970s, coronary artery bypass graft (CABG) was found to improve late survival in comparison to medical therapy in patients with significant left main stenosis.1–3 Once CABG became the standard of care for left main disease, a distinction between “protected”—by at least 1 patent bypass graft to the left coronary artery—and “unprotected left main (UPLM)”—no patent bypass graft to the left coronary artery—was made. In the 1980s, early attempts at balloon angioplasty of UPLM stenoses were associated with poor early outcomes because of coronary dissection, abrupt closure, and restenosis. Mortality rates as high as 30% at 1 year were reported.4–6 In the 1990s, bare metal stents were introduced and soon used to treat UPLM disease. Several small registries found a low rate of procedural complications, but repeat revascularization rates of 20% to 30% because of restenosis were considered unacceptable.7–12 Early bare metal stent registries for UPLM also found high mortality rates, particularly in high-risk patients, such as patients with acute coronary syndromes and poor left ventricular function. Importantly, high-risk subgroups often presented with late sudden death after stenting.11,13 In the early 2000s, the introduction of drug-eluting stents (DES), with the promise of vastly reduced rates of restenosis,14–17 raised the possibility of improved late outcomes in this challenging patient group.

Current Data Supporting DES for UPLM Disease

Clinical outcomes after treatment of UPLM disease with either the sirolimus-eluting stent or the paclitaxel-eluting stent from >20 small registries have been published. Results reported in these registries vary widely.18–40 As depicted in Table 1, cardiac mortality between 6 and 12 months after the procedure ranges from 0% to 11%. Target lesion revascularization (TLR) or target vessel revascularization (TVR) rates range from 2% to 38%. This wide variation in clinical outcome appears largely because of variation in both patient selection and procedural technique.

Although results after UPLM stenting are usually reported as a single, homogeneous subgroup of coronary artery disease, in reality, UPLM encompasses a wide spectrum of disease states. Outcomes are particularly dependent on lesion location. Left main disease can be confined solely to the left main ostium or to the mid-shaft, regions technically not difficult to treat with a single stent, where excellent outcomes can be expected. A recent multicenter registry of 147 patients undergoing UPLM stenting of ostial or mid-shaft lesions with sirolimus-eluting stent (n=107) or paclitaxel-eluting stent (n=40) found excellent results at mid-term...
clinical follow-up (886±308 days). In this registry, cardiac mortality was 0 in hospital and 2.7% at follow-up. At follow-up, cardiac mortality was 0 in 87 patients judged low risk because of a EuroSCORE ≤0 and/or Parsonnet score ≤1341,42 but was 6.7% in 60 patients with high-risk scores. With >2-year mean follow-up in the entire group, TVR was only 4.7%. Thus, patients with ostial and mid-shaft UPLM lesions appear to have excellent outcomes after DES. These outcomes are likely to compare favorably with surgical outcomes.

In contradistinction to patients with left main ostial or mid-shaft lesions, patients with distal UPLM bifurcation lesions involving the ostium of the left anterior descending (LAD) and/or circumflex arteries are technically more demanding to treat. These bifurcation lesions often require double stenting, with less favorable long-term outcomes. The initial Scripps Clinic UPLM experience included patients with predominantly distal bifurcation disease. In this small, 50-patient registry in which sirolimus-eluting stent for UPLM was used, 94% of patients had disease at the distal left main location. Instead of a single stent treating the left main and/or ostium of the LAD or circumflex artery, multiple stents were used in 84% of patients.32 This registry found a 9-month cardiac mortality rate of only 2% but a TLR rate of 38%. Interestingly, the high TLR rate was also driven by an extremely high rate of angiographic follow-up. Fully 98% of patients had a follow-up angiogram at 3 and/or 9 months. With the use of an “ischemic-driven TLR” definition (patient has signs or symptoms of coronary ischemia), TLR was observed in only 14% of patients. This emphasizes the confounding impact of the oculostenotic reflex when results of UPLM stenting studies are interpreted. Patients undergoing stenting of UPLM are often compliant with protocol-mandated surveillance angiography, and interventionalists are likely to have a low threshold to intervene when clinically silent restenosis is found in the left main or the ostium of the circumflex or LAD artery because of the large quantity of myocardial territory perceived at risk.

Additional anatomic and clinical factors are worthy of consideration. The diseased left main can be large in diameter and free of calcium, which is associated with better outcomes, or small in diameter and contain significant quantities of calcium, creating a technically demanding procedure that results in less favorable short- and long-term outcomes. Another important differentiating patient characteristic is the additional presence of significant distal disease in the LAD and/or circumflex arteries, requiring multilevel intervention. The presence of multiple downstream lesions and especially 1 or more total occlusions and/or disease of the right coronary artery will increase procedural complexity and also increase the need for subsequent repeat revascularization. Finally, any study of UPLM must take patient comorbidity into consideration. Often, patients are refused CABG for UPLM disease because of serious comorbidities (ie, stenting in the setting of acute myocardial infarction, advanced age, poor left ventricular function, coexisting malignancy, renal failure, and porcelain aorta), many of which will also affect long-term outcome after coronary stenting. Thus, published studies of UPLM stenting must be viewed in the context of the clinical, angiographic, and procedural (especially number of stents needed) characteristics of the patients enrolled in each specific study.

Interestingly, a universal finding of the many DES UPLM registries is that when restenosis occurs, it usually is found at the ostium of the left circumflex artery, especially in patients initially presenting with distal bifurcation disease and treated with 2 stents. The cause of this restenosis predilection for the ostium of the circumflex is unknown but may be due to the sharp bend often taken by the circumflex in this location, which could result in lack of stent and drug apposition to the vessel wall or perhaps even stent collapse or fracture.

From the available registry data, it appears that restenosis and repeat revascularization rates are profoundly lower if only 1 stent is used when the distal left main bifurcation is treated.18-40 Provided that the risk of closing the branch vessel is low, the currently favored technique is the “provisional” approach of stenting across the distal bifurcation (the “crossover” technique), usually into the LAD.45 The circumflex ostium is then treated with balloon angioplasty. Provisional stent deployment at the circumflex ostium is only undertaken if the angiographic results are suboptimal. Unfortunately, it must be appreciated that even when the operator rigorously attempts a strategy of single-stent treatment, deployment of 2 stents will often be required. Planned deploy-

### Table 1. DES for the UPLM in Several Published Registries

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>Distal lesion location, %</th>
<th>Cardiac mortality (6–12 mo), %</th>
<th>Angiographic follow-up, %</th>
<th>Angiographic restenosis, %</th>
<th>TLR or TVR, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al32</td>
<td>102</td>
<td>71</td>
<td>0</td>
<td>84.3</td>
<td>2*</td>
</tr>
<tr>
<td>Chieffo et al19</td>
<td>85</td>
<td>81</td>
<td>3.5</td>
<td>Not reported</td>
<td>18.8†</td>
</tr>
<tr>
<td>Valgimigli et al37</td>
<td>95</td>
<td>65</td>
<td>11</td>
<td>Not reported</td>
<td>6.3†</td>
</tr>
<tr>
<td>Lee et al38</td>
<td>50</td>
<td>60</td>
<td>4</td>
<td>Not reported</td>
<td>13†</td>
</tr>
<tr>
<td>Price et al32</td>
<td>50</td>
<td>94</td>
<td>2</td>
<td>Not reported</td>
<td>13†</td>
</tr>
<tr>
<td>Migliorini et al30</td>
<td>101</td>
<td>94</td>
<td>11</td>
<td>42</td>
<td>38*</td>
</tr>
<tr>
<td>Erglis et al38</td>
<td>53</td>
<td>87</td>
<td>2</td>
<td>98</td>
<td>14†</td>
</tr>
</tbody>
</table>

Expanded from Baim et al.39 The reports of Valgimigli et al and Migliorini et al included patients with acute myocardial infarction.

*TLR.†TVR.
ment of 2 stents in the distal left main should be undertaken only when the operator strongly believes that the probability of acute closure of 1 of the branches is very high. Faced with this situation, any 1 of the well-described double stent techniques, ie, a “double barrel,” “crush,” “T-stent,” or “modified T-stenting with intentional protrusion of the side-branch stent within the main vessel stent—TAP stenting,” can be used.\textsuperscript{44–56} The importance of intravascular ultrasound guidance during UPLM stenting should be emphasized.

Figure 1 demonstrates a “relatively” favorable UPLM distal bifurcation lesion. This 54-year-old patient with unstable angina has a lesion involving the distal left main (arrow), but very little involvement of the ostium of the circumflex artery (left). A single stent was deployed from the distal left main into the LAD (arrow) crossing over the circumflex artery (the crossover technique). Mild plaque shift into the circumflex was treated with a final kissing balloon inflation, providing an excellent angiographic result (right).

Figure 1. A 54-year-old man with favorable UPLM distal bifurcation lesion. The lesion involves the distal left main (arrow), but very little involvement of the ostium of the circumflex artery (left). A single stent was deployed from the distal left main into the LAD (arrow) crossing over the circumflex artery (the crossover technique). Mild plaque shift into the circumflex was treated with a final kissing balloon inflation, providing an excellent angiographic result (right).

is at higher risk for restenosis, especially at the circumflex ostium.

There have been several small, published registries comparing UPLM DES with CABG. Chieffo et al\textsuperscript{22} compared 107 DES with 142 CABG patients in a nonrandomized registry. At 1 year, death trended higher in CABG patients (6.4% versus 2.8%), and TVR trended similarly higher in DES patients (19.6% versus 3.6%). Lee et al\textsuperscript{28} compared 173 consecutive patients at a single institution undergoing both procedures. The authors found a nonsignificantly higher mortality rate at 6 months with CABG compared with DES (11% versus 4%). Conversely, the rate of TVR was nonsignificantly higher in DES patients (7% versus 1%). This registry was more recently updated to include 343 patients with longer follow-up.\textsuperscript{57} After statistical adjustment, no difference was found in late mortality, although a trend existed toward improved survival in higher-risk patients treated with CABG. Palmerini et al\textsuperscript{58} reported a registry of 259 patients aged >75 years with unprotected left main coronary artery disease: 161 treated with CAGB and 98 with DES. Mortality at 2 years was similar, at 17% in CABG compared with 18% in DES patients ($P=0.71$). However, TLR was higher in DES patients (25% versus 3%; $P<0.0001$). Finally, in the largest UPLM registry to date, Seung et al\textsuperscript{59} compared 1102 patients who underwent stenting with 1138 patients who underwent CABG. The authors found no significant difference in the risk of death (hazard ratio for stenting, 1.18); however, TLR was higher in the stent group (hazard ratio for stenting, 4.76).

Recently, results from the first, albeit small, randomized trial of stents versus CABG for UPLM disease was reported.\textsuperscript{60} In the prospective, multicenter Study of Unprotected Left Main Stenting versus Bypass Surgery (LE MANS) trial, Buszman et al\textsuperscript{60} randomized 105 patients with UPLM disease to stents (n=52) or CABG (n=53) (Table 2). In the stent arm, 35% of patients were treated with DES, and 65% received bare metal stents (bare metal stents were chosen if the left main diameter was $\geq3.8$ mm). At 1-year follow-up, improvement in left ventricular ejection fraction (the primary study end point) was greater in patients receiving stents compared with bypass surgery ($3.3\pm6.7\%$ after percutaneous coronary
intervention [PCI] versus 0.5 after CABG; \( P = 0.047 \). Mortality trended lower for stent compared with CABG patients (1.9% versus 7.5%; \( P = 0.37 \)). Angina status was similar between the 2 groups (\( P = 0.11 \)). In-stent restenosis of the left main occurred in 9.6% of stented patients. Whereas TVR (of the left main artery) rates were similar between stent and CABG patients (9.6% versus 9.4%; \( P = \text{NS} \), repeat revascularization of any vessel (ie, including non–left main lesions) occurred in 28.8% of stent patients compared with 9.4% of CABG patients (\( P = 0.01 \)). The trend toward improved survival in the stent group observed at 1 year continued at 28.9 months of follow-up (5.8% versus 13.2%; \( P = 0.08 \)). Although this randomized study is supportive of stenting for UPLM disease, the limitation of its small size and the relatively high complication rate in the CABG arm must be recognized.

The first large-scale randomized comparison of CABG versus DES for UPLM was the SYNTAX (The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery) trial. This large trial contained a prespecified subgroup of 705 randomized UPLM patients.\(^6^1\) At 1-year follow-up, the combined safety end point of death, myocardial infarction, and stroke was nonsignificantly higher in CABG patients (7% versus 9.2%; \( P = 0.29 \)). Although the repeat revascularization rate was statistically worse in stent patients (12% versus 6.7%; \( P = 0.002 \)), these differences were modest.

A meta-analysis of 1278 patients from 17 published studies undergoing DES for UPLM disease was recently reported.\(^4^0\) Wide variation among trials was found with respect to baseline patient and angiographic characteristics. Some trials even included patients with UPLM receiving primary DES for acute myocardial infarction. The importance of varying baseline characteristics is illustrated by a recent report by Taggart et al\(^6^2\) critical of UPLM stenting. The authors emphasized double-digit early mortality rates within some UPLM stent registries, but this is misleading because the registries quoted with high mortality included patients presenting with acute infarction and patients who died of noncardiac comorbid conditions. In the meta-analysis, the overall mid-term results (median follow-up was 10 months, ranging from 6 to 19 months) were encouraging, with a pooled mortality rate of 5.5% and TVR rate of 6.5% (Figures 3 and 4).

Although coronary stent thrombosis has received a great deal of recent attention, the aforementioned studies have not identified thrombosis as a major problem after UPLM stenting, likely because of the large diameter of the left main artery. However, we must continue to evaluate this important end point with ongoing patient follow-up. Of equal signifi-
UPLM stent patients are usually prescribed dual antiplatelet therapy for a minimum of 1 year, preferably indefinitely. The challenges of prolonged antiplatelet therapy are substantial and represent a significant hurdle for UPLM stenting.

To summarize, many early registries, 1 small randomized trial, and 1 subgroup of a larger randomized trial comparing stents with CABG for UPLM are favorable for DES, with similar or improved mortality at early follow-up and an expected increase in repeat revascularization in stent patients. Although these results are encouraging, it must be emphasized that substantial variation in outcome exists among trials. The 5.5% pooled risk of late mortality for stent patients reported in the meta-analysis may not apply to a specific patient in whom treatment options are being considered.

Obtaining Patient Consent for PCI of UPLM Disease

Although numerous patients throughout the world are currently undergoing DES for UPLM disease, it should be emphasized that the current American College of Cardiology/American Heart Association/Society for Cardiac Angiography and Interventions Practice Guidelines for percutaneous coronary interventions clearly categorize UPLM stenting as a class III indication (meaning it should not be undertaken) unless the patient is not a candidate for bypass surgery. However, the level of evidence provided is C (ie, only consensus opinion of experts, case studies, or standard of care). In patients not eligible for CABG, UPLM stenting carries a IIa indication (meaning weight of evidence/opinion is in favor). Informed consent is essential when patients are considered for UPLM stenting. Patients who are not candidates for surgery because of comorbidities or poor distal targets are the least controversial to treat. These patients should be informed that although stenting may be their best option, the long-term outcome after DES is at present, poorly characterized. It is extremely challenging to obtain consent from patients who are acceptable candidates for CABG. Usually these patients request stenting instead of bypass surgery, with varying degrees of conviction. It is important to spend considerable time with this patient group, reviewing the DES procedure and its potential risks and benefits in comparison to CABG. Ad hoc UPLM stenting, wherein the patient is asked for consent while remaining on the catheterization table after a diagnostic examination, should be avoided. The importance of the UPLM artery should be described graphically to the patient. It is helpful to use an analogy, such as “the trunk of the tree,” to visually emphasize the importance of the location of this lesion. It is critical to make it very clear to the patient that UPLM stenting is not currently considered the standard of care by practice society guidelines and that the data set we have on mid-term and long-term outcomes is limited. It is often helpful to have a cardiovascular surgeon speak independently with the patient, as well as another cardiologist who is not an interventionalist. However, having multiple physicians provide multiple opinions can also confuse some patients, upsetting them and making the decision process more difficult. The requirement for routine follow-up surveillance angiography must be explained and agreed to by the patient. Although some physicians do not believe that routine surveillance angiography is warranted after UPLM stenting, I strongly believe that...
follow-up angiography at 3 to 9 months is important, particularly in light of the limited data we have on late outcomes. Surveillance angiography after UPLM stenting is currently an American College of Cardiology/American Heart Association/Society for Cardiac Angiography Practice Guideline class IIa (meaning it is favored) recommendation.64

The Argument Against CABG for UPLM Disease

CABG is a medical marvel that has extended and improved the quality of life for millions of patients. It is difficult to dispute the clinical benefit and durability of a left internal mammary artery (LIMA) bypass of the LAD artery.66 Indeed, if a minimally invasive method of implanting a LIMA existed, associated with negligible morbidity and pain, it would be hard to argue for an alternative. The case for CABG of UPLM disease would also be considerably strengthened if other commonly used conduits had track records that were similar to the LIMA graft. Sadly, CABG, as practiced in most centers today, is a major invasive procedure, associated with considerable pain and morbidity, and usually involves the placement of several saphenous vein grafts (SVGs) that are much less effective at late follow-up compared with the LIMA.67,68 The debate surrounding CABG versus PCI is usually centered on differences in mortality and the need for repeat revascularization procedures. I believe that this discussion is often misdirected because it ignores the critically important problems of procedural morbidity and the long-term untoward impact of SVGs and other non-LIMA conduits.

The Case Against the SVG Bypass

I often hear clinicians use the phrase, “He’ll get 2 good grafts” when referring a patient for bypass surgery. The overwhelming majority of patients, however, only receive 1 “good” (ie, arterial) graft. Although the surgical literature often emphasizes the benefits of bilateral mammary implantation,69,70 of the 156 128 patients receiving isolated CABG reported in the 2006 Society of Thoracic Surgeons database,71 the LIMA was used in 88.2%, both internal mammary arteries were used in only 4.4%, and the radial artery was used in only 7.7% (personal communication, Data Analysis of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database, Society of Thoracic Surgeons, fall 2006). Similarly, in the run-in survey of centers participating in the SYNTAX trial, total arterial revascularization was used in only 12% of CABG patients.72 Presently, the most frequently implanted surgical graft worldwide is the SVG. The SVG is a suboptimal conduit for 2 major reasons. First, and rarely discussed, is the profound acceleration of upstream native coronary artery disease that occurs after CABG with the use of a SVG. After implantation of a SVG, the diseased native vessel proximal to the anastomosis is subjected to increased shear stress, eddies, vortices, flow separations, and bidirectional flow73 (Figure 5) that lead to acceleration of bypassed stenoses. Interestingly, this clinically important phenomenon is almost never entertained by practicing physicians when deciding between PCI and CABG for their patients. Reports describing proximal native disease progression after SVG implantation first appeared in the very early CABG literature of 1970 to the 1980s.74,75 In a recent report, 35% of native coronary arteries bypassed by a vein graft progressed to a total occlusion by 5-month angiography.76 Although the finding of severe, diffuse underlying proximal native coronary disease is common in the postsurgical patient with vein grafts, one wonders whether physicians fully appreciate how much of this native vessel disease is iatrogenic. It is not unusual for a clinician to view an angiogram of a completely graft-dependent patient and comment, “It’s a good thing his grafts are open,” completely missing the point that before surgery, the patient’s native coronaries were stenotic yet patent, but his native disease profoundly accelerated to total occlusions as a result of the bypass procedure. Interestingly, native disease progression is more common after SVG compared with LIMA implantation, likely because of increased competitive flow rates provided by the larger-diameter SVG.

Native coronary artery disease progression would not be so clinically devastating if vein grafts were durable, but this is not the case. Although the long-term patency of the SVG has improved with advanced medical therapies, it is still suboptimal. In a recent series from the Cleveland Clinic, by 5 years, vein graft patency (defined as <70% stenosis) was <40%. Patency was even worse for the radial artery conduit and not much better for the right internal mammary artery77 (Figure 6).

Perhaps the most contemporary study of the SVG comes from the recent Project of Ex Vivo Vein Graft Engineering via Transfection IV (PREVENT IV) trial, wherein 3014 patients were randomized to an E2F transcription factor decoy versus placebo in the hope of preventing vein graft failure.78 This was a contemporary study enrolling patients from 2002 to 2003. Statins and aspirin were used in 73% and
90% of patients, respectively. Follow-up angiography at 12 to 18 months was obtained in 1829 patients. The study drug did not improve vein graft patency compared with placebo, and by just 12 to 18 months, fully 25% of the SVGs were occluded. More than 40% of patients had at least 1 occluded SVG, and this was just after 1 year. Furthermore, in PREVENT IV, vein graft failure profoundly increased death, infarction, and repeat revascularization. Another recent trial, PRAGUE-4, randomized 400 consecutive patients to on-pump (n=192) or off-pump (n=208) surgery.79 By 1 year, fully 41% of on-pump and 51% of off-pump SVGs had completely occluded. The results of these studies are particularly alarming given the brief, 12- to 18-month, period of follow-up. Over 5 to 10 years, SVG patency has been reported to be only 40% to 50% in most studies.68,77,80 – 83 Even the most favorable recent data available on SVG patency from the Radial Artery Patency and Clinical Outcomes (RAPCO) study found 5-year SVG patency rates of only 83% and 7-year patency of ~75%.84 Although I agree that some interventionalists can be appropriately faulted for not giving objective informed consent, I also believe that the same can be said for some surgeons. How many surgeons and cardiologists adequately inform their patients that the non-LIMA conduits they receive during their surgery will have a high likelihood of failure during the ensuing 5 to 10 years?

Future Revascularization in the Post-CABG Patient
Most interventional cardiologists are all too familiar with the “double hit” of native vessel disease acceleration caused by a SVG bypass, followed by failure of the SVG. This process typically manifests several years after CABG in a patient with a patent LIMA supplying the LAD, who is now symptomatic because of an occluded or highly stenotic SVG anastomosed to the right and/or circumflex coronary artery. The underlying native vessel disease, which was often a good target for PCI before the CABG procedure, has now progressed to either total occlusion or a fibrotic and calcified lesion requiring advanced and more challenging interventional techniques. Indeed, for many post-CABG patients, native disease progression plus SVG failure means losing the opportunity for PCI forever. This is another point often overlooked when physicians evaluate trials comparing PCI versus CABG. Repeat revascularization rates are usually lower after CABG compared with PCI, but how much of this difference is due to the post-CABG patient’s relative ineligibility for another revascularization procedure? Both the native vessel and SVG often progress to a total occlusion or diffuse disease, resulting in limited options for PCI. Given the high threshold for repeat bypass surgery (particularly in the presence of a patent LIMA graft), many patients are not offered repeat revascularization, not because they don’t need reintervention but because the risks are prohibitive and the likelihood of success is small. Thus, some of the relative increase in repeat revascularization after PCI observed in clinical trials is misleading because the post-PCI patient, in contradistinction to the post-CABG patient, remains a good candidate for further revascularization.

The Morbidity of CABG
Many current comparisons of CABG versus PCI focus on randomized trial data. In patients with multivessel disease, most randomized trials demonstrate no mortality differences85 but a significant reduction in the need for repeat revascularization86 after CABG. One wonders, however, if these results are clinically meaningful. Although controversial, one might even argue that CABG and PCI are inherently not comparable. The procedures are so different that to compare them as one would compare 2 hypertensive drugs ignores enormous differences in patient impact. Ironically, CABG is given the label of “conservative” therapy from the first definition of the word, ie, “to conserve the traditional approach,” when the second definition of conservative, ie, “moderate, cautious, restrained in style” is much better suited to PCI, which is clearly the less aggressive procedure. In a recent registry from Cedars-Sinai comparing CABG with...
DES, Lee et al
 did not find differences in procedural mortality. However, CABG patients sustained more stroke, serious arrhythmia, need for permanent pacemaker, renal failure, repeat surgery for bleeding, and cardiac tamponade. One or more of these morbid complications occurred in 53% of CABG patients compared with only 1% of DES patients.87 In-hospital length of stay was 8.4±6.3 days for the CABG patients compared with 3.0±4.8 days (P<0.001) for DES patients. These differences were observed despite the PCI group having significantly more comorbidities. In the recent LE MANS randomized study of CABG versus PCI for UPLM disease,80 rates of major morbid events at 30 days were also higher in CABG patients (28% versus 8%; P=0.006), and the authors made the point that “treatment of peri-procedural atrial fibrillation or infection needs time and resource-consuming therapy, not less than repeat angioplasty for restenotic lesions.” Similar rates of untoward events were noted in the 3014 patient PREVENT IV trial.88 Indeed, in a recent meta-analysis of 15 PCI versus CABG randomized trials,89 the risk of stroke was doubled after CABG (1.2% versus 0.6%; P=0.002), and these differences were even more profound in the SYNTAX trial.61 Even in the absence of stroke, neurocognitive deterioration after CABG is well documented.89 In 1 recent study from the Duke Medical Center, cognitive decline was observed in 53% of CABG patients at discharge and persisted in 42% of patients at 5 years.90 These very real differences in morbidity should be given considerable weight when physicians recommend treatment options to patients.

Interestingly, differences in the emotional impact of CABG versus PCI are almost never discussed by practicing physicians. PCI is a relatively painless procedure, whereas CABG entails significant suffering. PCI patients can drive an automobile the day after the procedure, whereas CABG patients must wait 2 to 4 weeks. The typical PCI patient is back to work in 1 to 3 days compared with 4 to 6 weeks after CABG. I find it particularly ironic to hear some physicians extol the virtues of CABG when, as a group, doctors are such ardent workaholics, often equating work with life itself. In my experience, when physicians undergo PCI, they usually request that the procedure be done on a Friday afternoon so they can make rounds on the morning of the procedure and be back at work the first thing on Monday. Imagine how it feels to be the passionate worker who is told to take a month off after CABG surgery. Have our randomized trials adequately explored these differences?

**When Is a Significant P Value Not Significant?**

Most CABG versus PCI debates acknowledge the lack of mortality differences in randomized trials but emphasize significant probability values for mortality in some diabetic subgroups and some comparative registries.91,92 Typically, at this point in the discussion, the listener is admonished to await the late outcome results of ongoing randomized trials that include DES. Most relevant to the UPLM debate is the prespecified UPLM subgroup of the SYNTAX trial.61 I take the somewhat controversial position that late outcome results of SYNTAX and other upcoming randomized controlled trial results are unlikely to influence my practice unless enormous differences in mortality (ie, >35% differences in mortality) are observed. To illustrate this point, I propose a “thought experiment.” In this exercise, we will evaluate 2 potential outcomes from the 705-patient UPLM subset of the SYNTAX trial. Each hypothetical outcome assumes an expected benchmark 5-year survival in the CABG arm of 83% based on historical studies of CABG for UPLM revascularization.1,93

In scenario 1, at 5 years, mortality in the CABG arm is 17% (the benchmark), and mortality in DES patients is 35% higher, or 23% (P=0.039). With this outcome, the probability value is “significant,” but the number needed to treat to save 1 life is rather high, at 16.6. Now imagine that you are in a conference room with 16 of your colleagues. You each have important UPLM disease. Are all 16 of you willing to undergo bypass surgery, with all of its pain and morbidity, to save 1 life? I find I get a mixed reaction when I pose this question to patients and physicians. An analogy might be a 16-soldier squad at the start of a 5-year war. All 16 soldiers are each given a choice. At the end of the war, either 15 will be unharmed but 1 dead or, on day 1 of the war, all 16 are wounded, but all will survive for 5 years. Would all 16 soldiers agree to accept significant injuries for the 1 survivor? Clearly, their sergeant would not endorse this choice! Whatever your opinion, the answer is not black and white.

In scenario 2, the 5-year mortality in the CABG group remains at our benchmark of 17%, but DES mortality is now a whopping 50% higher, at 25.3% (P=0.0058). Now, the number needed to treat is a bit more palatable at 12. Would all 12 patients accept the wounds of surgery to save 1 life? Perhaps many would, but even with a 50% reduction in mortality, many would still have second thoughts.

From this exercise, we see that it would take a very unlikely ≥50% increase in mortality in the stent arm of the upcoming randomized trials before CABG becomes close to an unequivocal treatment choice. My point is that probability values are helpful, but a significant probability value does not always determine clinical significance, particularly when such radically different strategies as CABG and PCI are compared.

This point can be further illustrated by the recent “public” reaction to the New York State Registry comparing DES with CABG that received significant attention in the lay press.94 In this nonrandomized registry, after adjustment, PCI patients were reported to have a 20% higher mortality compared with the CABG group. However the mortality differences were 7.3% versus 6% (P=0.03), a 1.3% absolute difference. This 1.3% absolute mortality difference yields a number needed to treat of 77. If we need to do 77 bypasses to save 1 life, I believe that the mortality benefit is clinically meaningless,

Another perspective on SYNTAX is to question the clinical significance of repeat revascularization rate differences in the UPLM subgroup. Although these differences were statistically worse at 1 year in the stent group (12% versus 6.7%; P=0.02), the absolute difference of 5.3% is extremely small. This means that the number of CABGs needed to prevent 1 repeat revascularization is 19. Most of my patients would rather have 2, 3, or even 5 stent procedures to avoid 1 bypass surgery. Yet in SYNTAX, one had to perform 19 CABGs to prevent 1 PCI. Viewed another way, 18 of the 19 CABGs were unnecessary. The small benefit with respect to revascularization came at the cost of a 9-fold increase in stroke (0.3% versus 2.7%; P=0.009). When one adds the increased morbidity of CABG to the equation, the argument for stenting UPLM disease becomes quite convincing.

Choosing PCI or CABG for the Patient With UPLM

Despite our intense effort to bring evidence-based medicine to decisions on revascularization strategies, I believe that we must still bring a great deal of healing arts to this science. For the majority of my patients, the major driving force behind the revascularization strategy I recommend is the anatomy as documented in the catheterization laboratory.

I have a strong disposition toward CABG if (1) 1 or more total occlusions of the left coronary artery are present in addition to the UPLM; (2) severe multivessel disease is present in small, tortuous vessels in addition to the UPLM, especially if these vessels are heavily calcified; (3) the UPLM lesion involves both limbs of the distal bifurcation; (4) the left main coronary artery is small (ie, <3 mm in diameter) and both the proximal LAD and circumflex arteries are ≥2.5 mm; and (5) the patient is intolerant of prolonged antplatelet therapy.

I have a strong preference for PCI with DES if (1) the UPLM lesion is located at the left main ostium or mid-shaft; and (2) the UPLM lesion is located at the distal bifurcation, but 1 limb is relatively disease free, allowing use of the crossover technique; (3) the UPLM lesion involves both limbs of the distal bifurcation, but the left main is large (≥3 mm) and not heavily calcified; and (4) the patient has significant comorbid conditions putting him or her at increased risk for CABG.

These predominantly anatomic considerations form the basis of my treatment recommendations. Other risk factors such as the presence of diabetes mellitus or poor left ventricular function are included in my decision making but carry considerably less weight. I must emphasize, however, that the strategies outlined above are my opinion based largely on experience. Current American College of Cardiology/American Heart Association/Society for Cardiac Angiography and Interventions Practice Guidelines consider UPLM stenting a class III indication (meaning it should not be undertaken) in patients eligible for CABG and a class IIa indication (meaning the weight of evidence/opinion is in favor) in patients not eligible for CABG.

Conclusions

The diseased UPLM lies at the crossroads of new technology development. The impact of DES in reducing restenosis has made UPLM a ripe target for PCI. When performed by experienced interventionalists in high-volume centers, procedural risks are very low. Early (1-year) mortality in multiple registries, 1 small randomized trial, and a large subgroup of the SYNTAX trial is promising and, in appropriately selected patients, appears similar to CABG but with less procedural morbidity. There remains much room for technological improvement, including improved stent platforms, stent coatings, antiproliferative drugs, and antithrombotic strategies. Continued late follow-up of large multicenter trials will be required before UPLM stenting is accepted as a standard of care. However, provided that the patient understands the risks and long-term data deficiencies, I believe that the current available data support continued use and study of DES in UPLM patients with suitable anatomy who are either at high risk for CABG or are strongly adverse to surgery.

Disclosures

Dr Teirstein is a consultant for and has research grants from Cordis, Boston Scientific, and Medtronic and has received honoraria payment for speaking from Medtronic and Cordis.

References

8. Park SJ, Hong MK, Lee CW, Kim JJ, Song JK, Kang DH, Park SW, Mintz GS. Elective stenting of unprotected left main coronary artery


Response to Teirstein

Craig R. Smith, MD

Dr Teirstein’s excellent review, far more comprehensive than mine, contributes a number of noteworthy references. Editorial differences in emphasis aside, however, I see little fundamental disagreement on the existing body of knowledge, and I will generously agree that the results are “encouraging” for left main coronary artery percutaneous coronary intervention (PCI). Dr Teirstein provides technical details supporting my assertion that left main coronary artery anatomy is challenging for PCI outside the ostium and shaft (the majority of patients). Dr Teirstein concludes his discussion of PCI with an outstanding section on informed consent, including the important observation that “it is extremely challenging to obtain consent from patients who are acceptable candidates for CABG,” and mentions that the process can be helped by independent consultation with a surgeon. Alas, I must encourage readers to stop there. Dr Teirstein’s section on the argument against bypass surgery is based on obvious and unarguable differences in morbidity between PCI and surgery, combined with a worst-case exegesis on the liabilities of the saphenous vein graft. I have shown that PREVENT IV is an outlier. I have stated that left main coronary artery stenosis should be bypassable with the use of bilateral internal mammary arteries in most cases. I share Dr Teirstein’s regret that this is not more widely practiced. I bypass the left side of the coronary circulation with the internal mammary arteries >80% of the time, which does not make me uniquely gifted; I have cited references illustrating even higher usage. Readers should conclude that a role exists for both PCI and for surgery. The options must be weighed thoroughly and thoughtfully and discussed with patients.
Percutaneous Revascularization Is the Preferred Strategy for Patients With Significant Left Main Coronary Stenosis
Paul S. Teirstein

Circulation. 2009;119:1021-1033
doi: 10.1161/CIRCULATIONAHA.107.759712
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/119/7/1021

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/