# News and Views from the Literature

## Interventional Cardiology

### Unprotected Left Main Percutaneous Coronary Intervention

**Reviewed by Panayotis Fasseas, MD, David R. Holmes, Jr, MD**
*Division of Internal Medicine and Cardiovascular Diseases, Mayo Clinic and Mayo Foundation, Rochester, MN*
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Coronary artery bypass graft surgery (CABG) has been considered the treatment of choice for patients with unprotected left main coronary artery (ULM) disease. The superiority of surgical revascularization in these patients has been established by several trials.[1–3] Initially, percutaneous coronary intervention (PCI) for ULM disease was characterized by relatively high procedural morbidity and mortality and disappointing long-term event-free survival.[4–7] However, improvements in interventional techniques and equipment, particularly the introduction of intracoronary stents, and adjunctive pharmacotherapy have renewed interest in ULM PCI. A number of recent single-center studies have reported encouraging results. The following is a review of the Unprotected Left Main Trunk Intervention Multicenter Assessment (ULTIMA) registry, an international multicenter registry of ULM PCI.

### Long-Term Clinical Outcomes After Unprotected Left Main Trunk Percutaneous Revascularization in 279 Patients

Tan WA, Tamai H, Park SJ, et al.
*Circulation.* 2001;104:1609–1614.

#### Study Methods

The ULTIMA registry investigators have collected procedural and outcome data on consecutive ULM patients treated with PCI at 25 high-volume sites between July 1993 and July 1998. To minimize an overwhelming contribution by any single center, a maximum enrollment of 50 patients per center was allowed.[8] All data, including demographic and clinical data, in-hospital and 1-year event rates, and primary indication for PCI, were collected and analyzed by a coordinating center. Treatment data included use of adjunctive pharmacotherapy, PCI strategy (primary, bailout, etc), and use of cardiopulmonary support as an adjunct to PCI. Procedural cineangiogram analysis was performed by an angiographic core laboratory. Baseline data included left ventricular ejection fraction (LVEF), left main lesion characteristics (length, location, percent of vessel diameter stenosis pre- and posttreatment), and number of diseased vessels.

In addition, a subgroup at low risk for procedure was identified (age < 65 years, LVEF > 30%, absence of cardiogenic shock).

#### Results

Two hundred seventy-nine consecutive patients who had ULM PCI were studied. The low-risk subgroup contained 89 patients (32%). The baseline demographic and angiographic data are summarized in Tables 1 and 2. Fewer patients in the low-risk group had peripheral vascular

**Table 1**
**Baseline Demographic Characteristics**

| | All (n = 279) | Low-Risk Subset (n = 89) |
|---|---|---|
| Demographics | | |
| Age (y) (mean ± SD) | 66.1 ± 12.9 | 54.2 ± 9.2 |
| Male (%) | 65.3 | 68.5 |
| Hypertension (%) | 45.4 | 32.6 |
| Diabetes mellitus (%) | 21.2 | 20.2 |
| PVD (%) | 10.3 | 7.9 |
| Creatinine ≥2 mg/dL (%) | 5.8 | 2.2 |
| COPD (%) | 8.7 | 2.2 |
| Prior CABG (%) | 9.4 | 5.6 |
| Clinical presentation | 14.7 | 1.1 |
| Acute MI (%) | 14.7 | 1.1 |
| Cardiogenic shock (%) | 13.7 | 0 |
| CABG eligibility | | |
| Inoperable (%) | 16.6 | 4.5 |
| High risk (%) | 28.9 | 7.9 |

CABG, coronary artery bypass surgery; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease; SD, standard deviation.

disease, renal failure (serum creatinine ≥ 2.0 mg/dL), chronic obstructive pulmonary disease, or history of prior CABG or were not eligible for CABG. The aforementioned group was characterized by a higher mean LVEF, the absence of significant mitral regurgitation (MR), less distal left main coronary artery involvement, less severe lesion calcification, and lower prevalence of multivessel disease. Data regarding right coronary artery patency were unavailable for 132 patients.

More than half of the patients received a stent either as primary therapy (65.2%) or for a bailout indication (3.6%), and only 15% were treated with percutaneous transluminal coronary angioplasty alone. The use of support devices, such as intraaortic balloon counterpulsation (IABC), temporary pacing, percutaneous cardiopulmonary support (CPS), and pulmonary artery catheterization was less common in the low-risk group. Notably, only 41.7% of patients received ticlopidine and 4.3% were treated with abciximab.

There were 38 in-hospital deaths (13.7%), the majority of which occurred in patients who had presented initially with acute myocardial infarction (AMI) prior to PCI. The 1-year actuarial incidence of all-cause mortality was 24.2%. Clinical presentation with AMI and cardiogenic shock, MR grade 3 or 4, serum creatinine ≥ 2 mg/dL, LVEF ≤ 30%, and severe lesion calcification were identified as correlates of all-cause mortality by multivariate analysis. In the low-risk subgroup, the 1-year mortality was 3.4%; most important, there were no periprocedural deaths. The incidence of the combined endpoint of death, myocardial infarction (MI), and CABG was also lower in this subgroup (16.9% vs 34.6%). Among the 240 hospital survivors, the 1-year rates of death, MI, and CABG were 12.2%, 8.7%, and 8.7%, respectively. The independent correlates of post-discharge mortality were in-hospital non-ST segment elevation MI (NSTEMI), decreased LV function (LVEF ≤ 30%), and ineligibility for CABG.

## Discussion

The long-term prognosis for medically treated patients with significant left main coronary artery disease is poor. In the late 1970s, the Veterans Administration Cooperative Study and the European Coronary Surgery

**Table 2**
**Baseline Angiographic Characteristics**

| | All (n = 279) | Low-Risk Subset (n = 89) |
|---|---|---|
| LVEF (mean ± SD) | 51.3 ± 16 | 58.5 ± 10.6 |
| LVEF < 40% (%) | 28.0 | 2.9 |
| Grade 3 or 4 MR (%) | 4.1 | 0 |
| Three-vessel disease (%) | 32.5 | 22.0 |
| Lesion calcification (%) | 8.9 | 3.4 |
| Lesion length, mm (mean ± SD) | 4.64 ± 2.90 | 4.96 ± 3.00 |
| Reference diameter, mm (mean ± SD) | 3.97 ± 0.80 | 4.00 ± 0.80 |
| Lesion location | | |
| Ostial (%) | 44.0 | 55.3 |
| Midshaft (%) | 26.9 | 29.9 |
| Distal (%) | 58.3 | 49.4 |
| % Stenosis before PCI | 68.5 | 62.6 |
| % Stenosis after PCI | 12.6 | 7.2 |

LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PCI, percutaneous coronary intervention; SD, standard deviation.

Study showed a significant survival benefit for CABG compared with medical management.[1,3] The results of these trials, in combination with the unfavorable procedural and long-term outcomes documented by the early series of ULM PCI studies, established surgical revascularization as the standard of care for the management of these patients.[4,5] However, over the last decade the number of reports of ULM PCI with significantly better short- and long-term outcomes has been increasing. This change in practice was supported by progress in interventional techniques, equipment (stents, lower-profile delivery systems, etc), and improvements in adjunctive pharmacotherapy (aspirin, thienopyridines, glycoprotein IIb/IIIa inhibitors, etc). In particular, the introduction of intracoronary stents has eliminated the problem of elastic recoil and dramatically reduced the incidence of acute closure, two potentially serious complications associated with ULM PCI.

*Independent predictors of in-hospital and long-term mortality were identified and may be useful for prospective risk stratification.*

The earliest reports of ULM stenting were based either on compassionate use in high-surgical-risk patients or on its use as a bailout for procedure-related acute left main coronary artery dissection.[9,10] However, more recent reports have included lower-risk patients who were offered ULM PCI as an alternative to CABG. Wong and colleagues reported a series of 55 patients, of whom eight were considered to be at high surgical risk (previous stroke, renal failure, depressed LV function).[11] Thirty patients (55%) had distal left main disease with significant involvement of the bifurcation. All patients were premedicated with aspirin and ticlopidine, and each received a stent. The procedural success rate was 100%, and none of the patients required hemodynamic support (IABC or percutaneous CPS). There were no in-hospital complications (MI, CABG, death, or stent thrombosis). The 2-year survival rate was 98%, and the event-free survival rate was 81%. The primary limitation of this study was the lack of angiographic follow-up.

Park and colleagues have published a series that included 127 consecutive patients with normal LV function who underwent ULM stenting and 6-month angiographic follow-up.[12] Aspirin and ticlopidine were administered to all patients prior to the procedure. The restenosis rate (≥50% diameter stenosis by quantitative coronary angiography) was 19%. There were no procedure-related deaths, and the 2-year survival and event-free rates were 97% and 87%, respectively.

Silvestri and coworkers performed a similar study involving 140 patients, 47 of whom were high-risk CABG candidates.[13] All patients received antiplatelet treatment. The reported procedural success rate was 100%. Angiographic follow-up was obtained at 6 months. One-month mortality was 0% in the low-risk group and 9% in the high-risk group. The overall repeat revascularization rate was 17.4% at 6 months. One year actuarial survival rates were 89% and 97.5% in the high- and low-risk groups, respectively. Glycoprotein IIb/IIIa inhibitors were not utilized in this cohort.

These studies have established several important facts:

1. ULM stenting can be safely performed in low-risk patients with minimal periprocedural complications.
2. It is associated with low long-term morbidity and mortality rates.
3. This procedure can be performed without the need for invasive hemodynamic support (IABC or CPS).

The results of the ULTIMA registry investigations support the aforementioned findings. In addition, they provide valuable data on high-risk patients undergoing ULM PCI. This group of patients is characterized by a higher rate of procedural complications and a higher incidence of major adverse clinical events. Independent predictors of in-hospital and long-term mortality were identified and may be useful for prospective risk stratification. This may be particularly useful information for clinicians when discussing the relative merits of ULM PCI versus CABG.

Despite the recent advances in the percutaneous treatment of ULM disease, there are several issues that need to be addressed. The most important is the problem of restenosis. In their series, Wong and Silvestri reported a 6-month angiographic restenosis rate of 17%–19%.[12,13] Although these rates are similar to those seen in other coronary segments, given the anatomic location, the consequences of restenosis can be severe. The ULTIMA investigators recommend routine angiographic surveillance within the first 6 months following ULM PCI. However, there are no uniform recommendations as to how often and for how long these patients should undergo screening coronary angiography. This issue may become less important with the advent of drug-eluting stents if their impact on restenosis is confirmed. The roles of

*Controlled randomized clinical trials are unlikely, given the prohibitive sample size and cost limitations.*

lesion debulking and intravascular ultrasound need to be further defined in randomized trials. Although there are some reports favoring their use in ULM PCI, they are based on small, nonrandomized, single-center trials.[12,14]

*Study Limitations*

The ULTIMA investigators acknowledge a number of important limitations to this study. The registry's design and the absence of a surgical control group limit the outcome analysis to comparisons with historical controls. However, such controlled randomized clinical trials are unlikely, given the prohibitive sample size and cost limitations. The use of platelet glycoprotein IIb/IIIa inhibitors was limited in this study (4.3%); additional benefit in periprocedural outcomes might be expected with more liberal use of these agents.[15,16] ■

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# Atherosclerosis

## Exploring the Relationship Between Hyperlipidemia and Aortic Stenosis

**Reviewed by Arthur E. Weyman, MD**
*Cardiac Unit, Massachusetts General Hospital, Boston, MA*
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Valvular aortic stenosis is a relatively common disorder, occurring in between 2% and 7% of the population older than 65 years. Aortic stenosis is most frequently caused by progressive calcification and degeneration of the aortic cusp. The disease typically shows a progressive course, which accelerates after the threshold to mild stenosis has been crossed. Similar pathologic mechanisms of aortic valve stenosis and atherosclerosis have been reported, but the relationship of cardiovascular risk factors to progression of aortic stenosis has been inconsistent.

### Progression of Aortic Valve Calcification: Association with Coronary Atherosclerosis and Cardiovascular Risk Factors

Pohle K, Mäffert R, Ropers B, et al.
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In this study the investigators used electron beam tomography (EBT) to quantitate the degree of aortic valve calcification in a group of 104 patients (age 64.7 ± 8 years, 89 male) to determine the rate of progression and the influence of cardiovascular risk factors on the course of calcium accumulation. They also investigated the influence of the low-density lipoprotein cholesterol (LDL) level, other standard cardiovascular risk factors, and the extent of coronary calcification on the progression of aortic valve calcification, as quantified by EBT. Patients were selected because of a positive EBT scan for aortic valve calcium and coronary calcium. Aortic valve calcium was quantified using a volumetric score. EBT was repeated at a