

## Recent Advances in the Management of Left Main Coronary Artery Disease

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### Clinical Problem

The left main coronary artery refers to the proximal segment of the left coronary artery that arises from the left aortic sinus and bifurcates into the left anterior descending artery and left circumflex artery. It supplies at least 75% of the left ventricle and as a result, occlusion of this vessel puts a patient at high risk for cardiovascular and cerebrovascular events [1]. Without revascularization, 3 year survival can reach as low as 37 percent [2].

### Treatment Strategies

Early clinical trials for treatment of left main disease demonstrated that Coronary Artery Bypass Grafting (CABG) is superior to medical therapy [3]. Since then, CABG remained the gold standard treatment for left main disease. Percutaneous Coronary Intervention (PCI) was reserved for patients that were not surgical candidates. As PCI evolved from bare metal stents to drug-eluting stents, traditional treatment strategies of left main disease were challenged.

Advanced approaches now offer high-risk patients with left main disease, who were poor candidates for either intervention, PCI treatment with hemodynamic support. This includes patients with depressed left ventricular function and severe comorbidities [4]. An intra-aortic balloon pump or more recently, Impella, a percutaneous left ventricular assisted device, increases cardiac output during the procedure and reduces complications and mortality [5].

### Evidence from Previous Trials

The PRECOMBAT, NOBLE, SYNTAX trials directly compared PCI versus CABG in the treatment of left main disease [6].

The PRECOMBAT trial [7] enrolled 600 patients with left main disease who underwent either PCI with sirolimus-eluting stents or CABG. The primary endpoint was a major cardiac or cerebrovascular events after 1 year. The study found PCI to be noninferior to CABG. The difference was attributable to high rate of ischemia driven revascularization in the PCI group. This study had a follow up after 5 years and found PCI to be noninferior to CABG. This study however, had a limited power and results must be interpreted with caution.

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The NOBLE trial [8] enrolled 1201 patients with left main disease who underwent either PCI with biolimus-eluting stents or CABG. The primary endpoint was major cardiac or cerebrovascular event after 5 years. The study found CABG to be superior to PCI, the difference being attributable to frequent revascularization in the PCI group. This study, however, excluded peri-procedural myocardial infarctions occurring within 30 days from their trial design [9].

The SYNTAX trial [10] enrolled 1800 patients with left main and three vessel disease. 705 with left main disease underwent PCI with paclitaxel-eluting stent or CABG with a primary endpoint of major cardiovascular and cerebrovascular events in 1 year. The study found CABG to be superior to PCI after 1 year. The SYNTAX trial was followed up after 5 years [11] and PCI was found to be noninferior to CABG in a subset of left main disease patients with a SYNTAX score < 33. SYNTAX scores are numerical grades corresponding to the complexity of coronary artery disease. Also at the 5 year follow up, patients in the PCI group had a lower stroke but higher revascularization rate than the patients who underwent CABG. However, since the primary endpoint was met, the findings were from a subgroup of a subgroup, they were considered hypothesis generating.

### Current Guidelines

In 2014, two groups published their recommended guidelines for revascularizations. The first group included European Society of Cardiology/European Association for Cardio-Thoracic Surgery [12], and the second group included the American College of Cardiology Foundation/American Heart Association/ American College of Physicians/American Association for Thoracic Surgery/Preventive Cardiovascular.

Nurses Association/Society for Cardiovascular Angiography and Interventions/Society of Thoracic Surgeons [13]. Both groups had very similar recommendations. They believed PCI was a reasonable strategy in patients with a SYNTAX score  $\leq 22$ , patients with low anatomical complexity. However, they preferred CABG over PCI in all other patient populations.

### EXCEL Trial

The EXCEL trial [14] is the latest study in left main disease that utilizes the low SYNTAX score subgroup identified in the SYNTAX trial. This study randomly assigned 1905 patients with left main coronary artery disease as well as a low to intermediate anatomical complexity, a SYNTAX score < 32, to undergo either PCI with fluoropolymer based cobalt chromium everolimus-eluting stents or CABG. The primary endpoint of the study was death from any cause, stroke or MI at 3 years. There was a secondary endpoint of death, stroke, MI or ischemia driven revascularization at 3 years, and an additional secondary endpoint of death, stroke, or MI at 30 days. The study found that after 3 years, PCI was noninferior to CABG. The secondary endpoint of death, stroke, MI or ischemia driven revascularization after 3 years occurred more often in the PCI group. At 30 days, the end point occurred less often in the PCI group due to the lower rate of MI. This study is a hallmark in establishing that PCI is a safe alternative to CABG.

The EXCEL trial most significantly differed from previous trials because it used the newest procedural techniques. The trial used newer stents with a lower rate of thrombosis and utilized intravascular ultrasonography guided imaging in PCI group. It also used newer surgical techniques in the patients undergoing CABG, including off pump surgery, arterial revascularization, transesophageal ultrasonography, all associated with lower rates of surgery related deaths. This trial also used the largest sample size to date.

### Areas of Uncertainty

The EXCEL trial needs longer follow up to assess the long term events after revascularization, at 5 and 10 years. To complete the scope of left main disease treatment, future studies must investigate patients with higher anatomical complexity or a higher SYNTAX score. Also, future trials should explore effect of post-procedure medications on study outcomes.

## Conclusions

Multiple trials have not only shown evidence that PCI is a safe alternative treatment for left main coronary artery disease in select patients, but has also become an optimal treatment. The gold standard of treatment of left main coronary artery disease has begun shifting away from CABG towards PCI with second generation drug-eluting stents.

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