Role of Percutaneous Coronary Intervention in the Treatment of Left Main Coronary Artery Disease

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Revascularization with coronary artery bypass graft surgery is the choice of therapy in patients with left main (LM) coronary artery stenosis. During the last decade, the introduction of drug-eluting stents, together with antiplatelet and antithrombotic treatments, has improved the outcome of percutaneous coronary interventions (PCIs) by reducing the number of repeat revascularizations and the risk of stent thrombosis. Many institutions inside and outside the United States have adopted stent treatment of unprotected LM coronary artery disease as a more routine strategy. However, coronary bypass surgery has improved as well by using more arterial grafts, better perioperative care, and optimizing medical treatment postoperatively. The advances in stent technique may reduce the gap between coronary surgery and PCIs further, but the results of the Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization study, randomizing patients with LM coronary artery disease between coronary bypass grafting and PCIs, will be needed to test whether PCIs is noninferior to coronary bypass surgery.

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INTRODUCTION

The selective injection of contrast media into the right coronary artery by Mason Sones in 1958, and the resulting ability to evaluate the coronary anatomy, introduced a new era in cardiovascular medicine. It created diagnostic and therapeutic possibilities that ultimately shaped much of cardiovascular medicine practiced today.

Coronary bypass surgery (CABG) was introduced only a few years after the availability of coronary angiography[1] and provided an opportunity to revascularize patients with coronary obstructions. Several trials compared CABG with medical therapy and a meta-analysis with individual patient data showed that patients undergoing CABG had a significantly lower mortality rate after 10 years (risk reduction = 17%).[2] Only 6% had left main (LM) disease, but the reduction in mortality in this group was 33% and the absolute survival benefit was 19.3 months. The Coronary Artery Surgery Study trial also demonstrated improvements at 15 years in both overall survival and median survival with CABG compared with medical therapy (37% vs 27% and 13.3 vs 6.6 years, respectively).[3]

Mortality was reduced by CABG and thus became the standard of care for more than 30 years. The treatment guidelines recommend CABG as the most appropriate revascularization strategy for patients[4] with unprotected LM disease. A recent network meta-analysis also confirmed that among patients with stable coronary artery disease, CABG reduces the risk of death, myocardial infarction, and subsequent revascularization compared with medical treatment.[5]

Percutaneous coronary intervention (PCI) was introduced by Gruntzig in 1977 but PCI was initially considered only for patients with single-vessel disease and not for patients with LM coronary artery

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disease. The main stem of the coronary tree is of vital importance to provide blood to the myocardium, as it supplies at least 70% of the blood to the left ventricle.[6] The most common site of LM stenosis is the midportion or distally at the bifurcation. A complication of PCI would lead to a major myocardial infarction and high mortality rate. Late restenosis could also influence the late results of the intervention for LM stenosis to a higher extent than it would do for other anatomical situations. The "Appropriateness Criteria for Coronary Revascularization" indicate that PCI is inappropriate for patients with LM coronary artery disease. PCI should only be considered for patients who are not eligible for CABG (Patel et al, 2012).[7]

However, major advancements have been made in the clinical practice of PCI, and the application of PCI has been expanded to include patients with LM disease. The introduction of bare-metal stents lowered the incidence of abrupt vessel closure and restenosis but mortality at 1-2-year follow-up was still high and ranged from 3%-31%.[8]

The introduction of drug-eluting stents (DES) lowered the risk of restenosis further, and there are indications that PCI with new-generation DES may improve survival compared with medical treatment.[5] Owing to the development and refinement of techniques, PCI for unprotected LM coronary artery stenosis became a safe procedure at least for selected patients and in experienced hands. The introduction of intravascular ultrasound enables the evaluation of angiographically indeterminate lesions with criteria now set forward as to what constitutes an indication for revascularization. Other studies have demonstrated a low risk of sudden death or stent thrombosis after LM stenting with DES.[9] Single-center registries, propensity-matched cohorts and meta-analyses of registries have been published showing improved outcomes.[10,11]It is clear from these studies and the run-in phase of the SYNTAX trial that many institutions inside and outside the United States have adopted stent treatment of unprotected LM disease as a more routine strategy.[12] The rates of major adverse cardiac and cerebrovascular events at 1 year of studies that randomized patients between PCI and CABG are listed in the Table. None of these studies showed a significant difference between CABG and PCI.

The 5-year results of the "all-comers" SYNTAX trial showed that PCI with paclitaxel-eluting stents in a cohort of 1800 patients with 3-vessel disease and LM coronary artery disease was inferior to CABG for the end point major adverse cardiac and cerebrovascular events (MACCE).[13] The trial had a randomized cohort of 705 patients with LM coronary artery disease and is thereby currently the largest randomized, controlled trial comparing PCI with CABG. Most patients with significant LM stenosis had, in addition, significant narrowing of at least one of the other major coronary vessels. Isolated LM disease is an unusual clinical entity, in the SYNTAX study only 91 (13%) patients had isolated LM coronary artery disease. The other patients had associated 1- (n = 138, 20%), 2- (n = 218, 31%), or 3-vessel disease (n = 258, 37%). This heterogeneity is the reason that, although overall MACCEs in the LM subgroups were pre-specified and powered, the SYNTAX trial used a hierarchical statistical testing plan, whereby testing of the LM subgroup would occur only if the primary end point was met. Further analysis beyond the primary end point are rendered observational and hypothesis-generating only.

In the SYNTAX trial, patients with LM coronary artery disease could be subdivided into even smaller groups according to the SYNTAX score. The SYNTAX score allows quantification of the complexity (eg, number of lesions, total occlusion, bifurcations or trifurcations, aorto-ostial stenosis, tortuosity, lesion length, calcification, thrombus, and small vessels or diffuse disease) of the LM coronary artery disease[6] using a downloadable calculator or the SYNTAX score website www.syntaxscore.com.

At 5-year follow-up, the MACCE rate in patients with PCI LM with low or moderate disease complexity (low and intermediate SYNTAX scores) was similar to patients randomly assigned to CABG. However, in patients with high SYNTAX scores ($\geq$33), the MACCE rate was significantly increased in the PCI arm. In the group of patients with high SYNTAX scores, MACCE, cardiac death, and revascularization were all significantly increased in patients receiving PCI.[14] Procedure-related stroke is

Table. Major Adverse Cardiac and Cerebrovascular Events of PCI and CABG at 1 Year in Randomized Trials

Trial	First Author	*n*	MACCE CABG (%)	MACCE PCI (%)	*P*
Le Mans	Buszman (2008)[24]	105	25	31	0.47
SYNTAX	Morice et al[25]	705	14	16	0.44
Boudriot et al	Boudriot et al[26]	201	14	19	0.33
PRECOMBAT	Park et al[27]	600	6	9	0.36

PRECOMBAT, Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease.