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EDITORIAL COMMENT

Myocardial Revascularization for Left Main Coronary Artery Disease

A Step Toward Individualized Treatment Selection*

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Significant left main disease (LMD) is observed in 4% to 7% of patients undergoing diagnostic coronary angiography (1). The extent of myocardium subtended to the left main coronary artery amounts to ~80% of the left ventricle in a right-dominant coronary system (~100% in case of left-coronary dominance), and as a result, significant LMD is associated with poor prognosis if left untreated (2). LMD has conventionally represented an indication for coronary artery bypass grafting (CABG). At the time of the first description of percutaneous dilation of a stenosis in the left main stem by Grüntzig in 1979 (3), CABG had already been shown to be effective in improving survival compared with medical treatment alone among patients with LMD, resulting in a Class I indication for surgical revascularization. Even 1 decade ago, percutaneous coronary intervention (PCI) in patients with LMD was not recommended by guidelines on both sides of the Atlantic (4,5), whereas more recently, PCI has emerged as a valid alternative to CABG among patients with low and intermediate anatomic complexity (SYNTAX [Synergy Between PCI With TAXUS and Cardiac Surgery] score ≤32) (6,7).

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In this issue of the *Journal*, Cavalcante et al. (8) provide new evidence for the treatment of LMD by pooling individual patient-level data from 2 randomized clinical trials: PRECOMBAT (Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease trial) and SYNTAX. A total of 1,305 patients with LMD, randomized to either PCI or CABG, were followed prospectively for 5 years. Major adverse cardiovascular and cerebrovascular events (MACCE), a composite of all-cause death, myocardial infarction, stroke, and any revascularization, were increased through 5 years among patients assigned to PCI compared those who underwent CABG (28.3% vs. 23.0%, respectively; $p = 0.045$). The difference was largely related to a higher risk of repeat revascularization with PCI (19.5% vs. 10.8%, respectively; $p < 0.001$), whereas the composite safety endpoint including all-cause death, myocardial infarction, and stroke occurred at a comparable frequency (14% vs. 15.1%, respectively; $p = 0.45$). Similarly, there were no significant differences between PCI and CABG for the individual components of all-cause mortality and myocardial infarction.

Although the overall outcomes are consistent with those of previous reports and meta-analyses (9,10), the present study adds several important aspects. First, of 4 randomized trials comparing PCI with drug-eluting stents (DES) versus CABG for LMD published to date, this pooled analysis entails approximately 80% of the entire patient population ($n = 1,305$ of 1,611). Therefore, the 5-year follow-up is of importance as it informs the long-term safety, efficacy, and durability of the 2 procedures. In this regard, the equipoise between PCI and CABG for the safety composite endpoint is clinically meaningful and reassuring as both myocardial infarction and stroke are associated with impaired prognosis, whereas repeat revascularization procedures mainly affect

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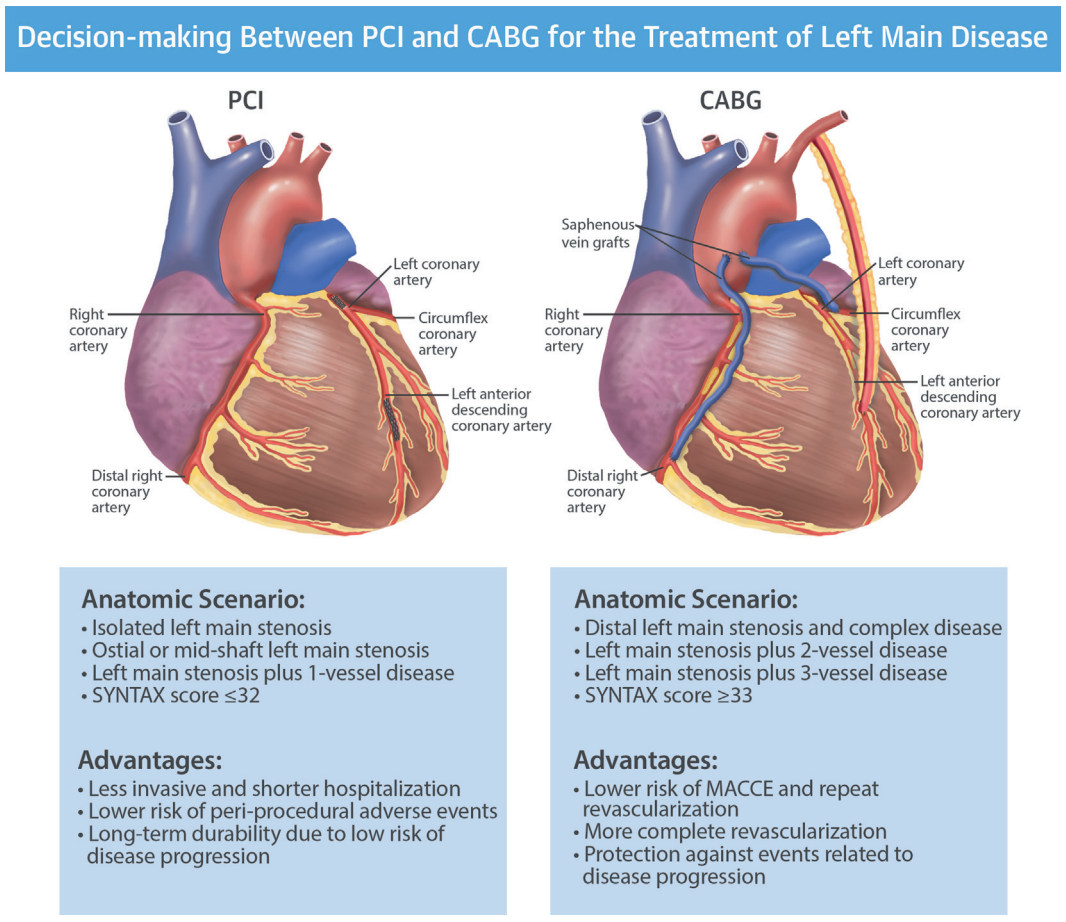
FIGURE 1 **Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting in Patients With Left Main Disease**



CABG = coronary artery bypass grafting; MACCE = major adverse cardiovascular and cerebrovascular events; PCI = percutaneous coronary intervention; SYNTAX = Synergy Between PCI With TAXUS and Cardiac Surgery trial.

quality of life. Second, the availability of patient-level data enabled the exploration of relevant subgroups and risk score assessment. Among patients with low-to-intermediate SYNTAX scores (≤32), representing nearly 70% of the overall population, PCI was found to be as safe and effective as CABG, with comparable rates of MACCE. Notably, there were fewer cardiac deaths among patients undergoing PCI, yielding a significant interaction between the 2 revascularization techniques and SYNTAX score terciles (p interaction = 0.016). Similarly, in the subgroup of patients with isolated LMD or LMD and involvement of a single vessel, PCI resulted in a lower risk of death (hazard ratio [HR]: 0.40; 95% confidence interval [CI]: 0.20 to 0.80; p = 0.029) and cardiac death (HR: 0.33; 95% CI: 0.12 to 0.88; p = 0.025) than CABG. Although the benefit of decreased mortality of PCI relative to CABG in lower-risk subsets is intriguing, the play of chance cannot be excluded, and a prudent interpretation asks for mechanistic reasons. Of note, there was no specific subgroup in which CABG outperformed PCI with respect to long-term mortality.

Another main finding of the study was that the SYNTAX II score provided a better discrimination for 5-year mortality than the original SYNTAX score, suggesting that the combination of clinical and anatomic patient characteristics allows for a more nuanced and individualized approach in treatment selection. When the outcomes were analyzed according to the SYNTAX II score, PCI and CABG yielded similar rates of mortality in patients in whom the score recommended both techniques or CABG, whereas mortality rates were higher with CABG when PCI was recommended (5.8% for PCI vs. 19.1% for CABG; p = 0.018).