

Aminian

Which Intervention for Patients with Left-Main Coronary Artery Disease?

- Until now, data have been limited regarding the very long term (beyond 5 years) outcomes of PCI versus CABG in patients with left main coronary artery disease. Moreover, two long-

term studies (NOBLE and EXCEL) showed conflicting results at 3 years and even more discordant results at 5 years, including all-cause mortality, which was higher with PCI in EXCEL but similar in NOBLE.

- Just the fact that the debate remains a hot topic represents a major paradigm shift, given that only a decade ago guidelines on both sides of the

Atlantic held that elective PCI was contraindicated (Class III) for any patient with LMCAD who was otherwise eligible for surgery. For them, the 2009 appropriate use criteria deemed PCI “not a reasonable approach and unlikely to improve the patients’ health outcomes or survival.”

Still Equipoise between percutaneous intervention and surgery ?

- Now there is 10-year follow-up from the PRECOMBAT trial. This study by Park et al. represents the longest follow-up ever reported in a large randomized, controlled trial

specifically designed to compare revascularization modalities in patients with LMCAD (Reference 1).

- The results: there was no significant difference between PCI and CABG surgery based on the incidence of major adverse cardiac or cerebrovascular events – specifically the primary endpoint composite of death from any cause, myocardial

infarction, stroke, or ischemia-driven TVR.

- The same lack of significance was true for the major secondary endpoint, a composite of death, MI, or stroke. Importantly, data were consistent at 2, 5, and 10 years (**Table**), which is reassuring, given other extended follow-up studies reporting a trend of late catch-up or

even crossover in the incidence of the primary composite outcome or all-cause mortality favoring CABG over PCI.

**PRECOMBAT: Cumulative Incidence of the
Primary Endpoint* at Published
Timepoints**

	PCI	CABG	HR (95% CI)
2-year report	12.2%	8.1%	1.50 (0.90- 2.52)
5-year report	17.5%	14.3%	1.27 (0.84- 1.90)
10-year report	29.8%	24.7%	1.25 (0.93- 1.69)

***Death from any cause, myocardial infarction, stroke, or ischemia-driven target-vessel revascularization.**

- With a median follow-up of 11.3 years, the biggest difference between the two approaches was seen for ischemia-driven TVR, which was 2-fold higher after PCI (16.1% vs. 8.0%).**

Not the Final Word

- The authors acknowledged that the study remains largely underpowered for its primary endpoint. Therefore, rather than a firm conclusion, the PRECOMBAT results should be considered hypothesis-generating.

Nevertheless, as Fernando Alfonso, MD, PhD, and Adnan Kastrati, MD, PhD, wrote in an accompanying commentary

to the 10-year results, (**Reference 2**)“The lack of differences in the primary outcome (that included TVR) in the intention-to-treat analysis is highly reassuring.”

Where does that leave the debate over treatment of LMCAD?

- First, it is important to note that PRECOMBAT PCI patients received first-generation sirolimus-eluting stents.

Since NOBLE and EXCEL both used new-generation DES, their long-term follow-up data are eagerly awaited. In the meantime, a new Bayesian analysis of the 5-year data from EXCEL was published online on June 1, 2020. **(Reference3)**, The study's author, James Brophy, MD, PhD (McGill University Health Center, Montreal), concluded that whether based on EXCEL results

alone or on the totality of available evidence, PCI is associated with inferior long-term results for all events, including mortality, compared with CABG for patients with LMCAD.

- Compare that to Dr. Alfonso and Dr. Kastrati, who wrote that the 10-year PRECOMBAT results provide “compelling evidence” that clinical equipoise persists for PCI and bypass

for patients with LMCAD and low-to-intermediate anatomic complexity. However, they added, "The occurrence of revascularization failure at this critical site remains of concern, considering its prognostic implications. The higher need for TVR in the PCI arm, consistently seen in all LMCAD studies, overshadows the long-term results of this strategy."

They concluded that this issue underscores the continued importance of the heart team when considering the best approach for an individual patient and suggest the following algorithm.

A CLINICAL CHARACTERISTICS:

- Age
- Diabetes
- Left ventricular function
- STS score (better than EuroSCORE II)

ANATOMIC FEATURES:

- Completeness of revascularization
- Distal bifurcation involvement:
 - LAD and LCX ostial disease
 - LCX size. Dominance (RCA vs. LCX)
- Number of concomitant diseased vessels (1,2,3)
- SYNTAX Score and SYNTAX-2
- Specific adverse features of lesions in major vessels: (*)
 - Number of lesions
 - Lesion length
 - Chronic total occlusion
 - Major bifurcation
 - Severe calcification

B

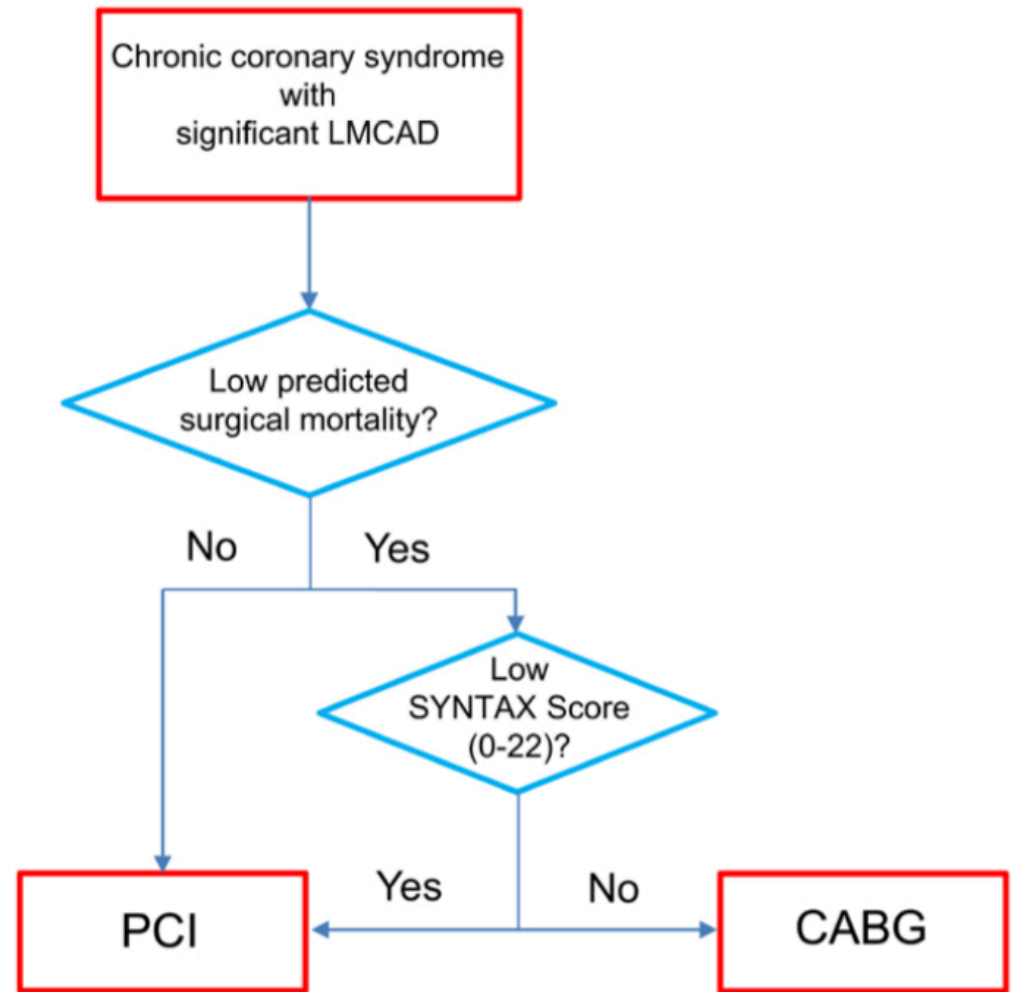


Figure. Left main coronary artery disease (LMCAD) revascularization.

Relevant variables to be considered in the clinical decision making process of elective treatment of patients with unprotected LMCAD eligible for revascularization

In summary

At 10-year follow-up, PCI and CABG had no significant differences on the primary composite endpoint (all-cause death, myocardial infarction, stroke, or target-vessel revascularization). Except for target-vessel revascularization (which was twice as common after PCI), no individual endpoint component,

including all-cause mortality (about 14% in each group), differed between study arms. Findings were consistent across most subgroups, including patients with involvement of the distal left-main bifurcation, diabetes mellitus, or greater angiographic complexity. However, patients with left-main plus 3-vessel CAD appeared to derive greater benefit from CABG.

COMMENT

These long-term data add to the growing evidence that the most severe irreversible long-term outcomes (death, stroke) are relatively similar after PCI or CABG for patients with significant left-main CAD – at least for those without concomitant 3-vessel disease. As the authors note, the

study has important limitations, including low statistical power, use of older-generation DES, and perhaps, limited generalizability as PCIs were performed in expert centers by highly experienced operators. Given the continued uncertainty, CABG is likely to remain the dominant form of revascularization for left-main disease in our practice; however, for patients

with less complex anatomy, we would consider PCI with contemporary DES when supported by shared decision making.

References:

- 1. Park DW, Ahn JM, Park H, et al. for PRECOMBAT Investigators.**

Ten Year Outcomes After Drug-eluting Stents Versus Coronary Artery Bypass Grafting for Left Main Coronary Disease: Extended Follow-Up of the PRECOMBAT Trial. *Circulation* 2020;141:1437-46.

2. Alfonso F, Kastrati A. Ten-Year Follow-Up of Left Main Coronary Artery Revascularization: Still Equipoise Between Percutaneous

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- 3. Brophy JM.** Bayesian Interpretation of the EXCEL Trial and Other Randomized Clinical Trials of Left Main Coronary Artery Revascularization. *JAMA Intern Med* 2020 June 1 [published online ahead of print]. doi:10.1001/jamainternmed.2020.1647.

