

Optimal revascularization for left main coronary artery disease—coronary artery bypass grafting versus percutaneous coronary intervention

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Coronary artery bypass grafting (CABG) has historically been the standard of care for management of left main coronary artery disease (LMCAD). Studies have demonstrated a survival advantage when CABG has been compared to optimal medical management alone in LMCAD (1-3). With improvements in medical therapy as well as innovative stent technology there has been a growing interest in the role of percutaneous coronary intervention (PCI) in patients with LMCAD (4-7). A sub-group analysis of the Synergy between PCI with TAXus and cardiac surgery (SYNTAX) trial supported the use of CABG as the standard of care for patients with high or intermediate SYNTAX scores due to lower rates of major adverse cardiac and cerebrovascular events, myocardial infarction, and repeat revascularization when compared to PCI. In patients with mild disease or a lower SYNTAX score, however, PCI appeared to be a reasonable alternative with adequate results at 5-year follow-up (8).

Such results of sub-analyses of larger randomized trials formed the basis for two recently published trials comparing CABG *vs.* PCI in LMCAD—Nordic-Baltic-British Left Main Revascularization (NOBLE) and Evaluation of XIENCE *vs.* Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) (9,10). These trials were designed to test the hypothesis that PCI was non-inferior to CABG among LMCAD patients.

In the NOBEL trial, the authors demonstrated that major adverse cardiac events occurred with a frequency of 19% in the CABG group (81 events) in comparison to 29% in the PCI group (121 events); the hazard ratio associated with this difference was 1.48 [95% confidence interval (CI), 1.11–1.96], exceeding the limit for non-inferiority, and CABG was concluded to be superior to PCI (P=0.0066). At 5 year follow up, CABG had an all-cause mortality of 9% *vs.* 12% in the PCI group (1.07, 0.67–1.72, P=0.77), 2% *vs.* 7% (2.88, 1.40–5.90, P=0.0040) for non-procedural myocardial infarction, 10% *vs.* 16% (1.50, 1.04–2.17, P=0.032) for any revascularization, and 2% *vs.* 5% (2.25, 0.93–5.48, P=0.073) for stroke (9). Importantly, the investigators excluded periprocedural myocardial infarction as a major adverse cardiac event, which has led to significant criticism in the setting of its prognostic implications. The argument used to justify this exclusion is that prior trials had failed to identify periprocedural myocardial infarction as a significant contributor to a worse clinical outcome (11). The investigators concluded that CABG was superior to PCI for the management of LMCAD (9).

In the EXCEL trial, the composite rate of death, stroke, or myocardial infarction at 30 days occurred in 7.9% of the patients in the CABG group and in 4.9% in the PCI group (P<0.001 for non-inferiority). The composite rate of death, stroke, or myocardial infarction at 3 years occurred in

14.7% of patients in the CABG group and in 15.4% of the patients in the PCI group ($P=0.02$ for non-inferiority) (10). These findings seemed to be influenced by the lower incidence of periprocedural myocardial infarction in the CABG *vs.* PCI groups (5.9% *vs.* 3.6%, $P=0.02$). This is an important observation since the NOBLE trial did not include periprocedural myocardial infarction in their analysis. Nevertheless, the difference in the incidence of myocardial infarction could be explained by the fact that a higher enzyme level was utilized as a threshold for diagnosis in the PCI group (11).

After 3 years of follow-up, the rates of death, stroke, myocardial infarction, or ischemia-driven revascularization occurred in 19.1% of the patients in the CABG group and in 23.1% in the PCI group ($P=0.01$, non-inferiority). The authors concluded that PCI was non-inferior when compared to CABG for the management of LMCAD with low or intermediate SYNTAX scores (10).

In a recent meta-analysis by Upadhyay and colleagues which included 4,595 LMCAD patients from 5 randomized controlled trials, CABG was associated with fewer major adverse cardiac events and need for repeat revascularization compared to PCI (12). In a recent meta-analysis published by Nerlekar and colleagues comparing PCI *vs.* CABG for LMCAD there was no difference in mortality, myocardial infarction, or cerebrovascular events between groups ($P=0.73$) (13). Additionally, even though a similar definition for periprocedural myocardial infarction compared to the EXCEL trial was used, there was a higher incidence of myocardial infarction with PCI than with CABG although this difference was not statistically significant ($P=0.08$).

While the findings of the NOBLE and EXCEL trials were discordant from each other, it is central to note the differences in long-term follow-up (5 years *vs.* 3 years, respectively). Numerous studies have demonstrated that the survival advantage of CABG is realized in the long-term and this has significant implications for the design and interpretation of contemporary randomized trials that seek to compare CABG to PCI. For example, the FREEDOM trial, which compared CABG to PCI among diabetics, began to show a divergence in the primary outcome of the composite of death from any cause, nonfatal myocardial infarction, or nonfatal stroke after 2 years (14). A similar finding was observed in the ASCERT study that compared CABG to PCI by combining registries of the Society of Thoracic Surgeons and American College of Cardiology (15). Moreover, the STICH trial, which showed

no difference between optimal medical management and CABG among patients with a reduced ejection fraction at 1 year, showed a significant survival advantage for CABG at 10 years (16). The conclusion from these landmark trials is that care must be taken when examining the short-term results of randomized trials that seek to compare CABG and PCI. CABG provides a long-term survival advantage, and the long-term results of NOBLE and EXCEL are needed prior to accepting PCI as an acceptable alternative for management of LMCAD.

A second important consideration when interpreting the results of the NOBLE and EXCEL trials is the use of arterial conduits. Numerous studies have demonstrated a survival advantage with multiple arterial grafting during CABG not only when compared to single arterial grafting, but also when compared to PCI (17,18). Thus, a limitation in both the NOBLE and EXCEL trials is that the type of CABG performed may not have necessarily been the "gold standard." For example, in EXCEL, while 98.8% of patients received a single internal mammary artery, only 28.8% received bilateral internal mammary artery grafting. Thus, one could extrapolate that the long-term results comparing CABG to PCI in EXCEL would be highly in favor of CABG if a greater proportion of multiple arterial grafting was utilized.

In conclusion, the NOBLE and EXCEL trials examined the role of CABG *vs.* PCI in LMCAD and had discordant findings with the NOBLE trial demonstrating superiority with surgery and the EXCEL trial demonstrating non-inferiority of PCI. While the NOBLE trial had a longer follow-up, the overall follow-up time in both trials was relatively short. Previous studies comparing CABG to either PCI or optimal medical management have highlighted the importance of long-term follow-up and such longitudinal analyses of NOBLE and EXCEL are necessary prior to accepting PCI as an effective alternative for management of LMCAD. At best, PCI can be considered in LMCAD either in patients who are not surgical candidates or potentially in high-risk patients with low SYNTAX scores. The optimal revascularization strategy for LMCAD will continue to be an issue of investigation in the future, and the results of long-term follow-up must be sought after and carefully examined to best assess the true comparative effectiveness of CABG versus PCI in patients with LMCAD.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Lee PH, Ahn JM, Chang M, et al. Left Main Coronary Artery Disease: Secular Trends in Patient Characteristics, Treatments, and Outcomes. *J Am Coll Cardiol* 2016;68:1233-46.
2. Ragosta M. Left main coronary artery disease: importance, diagnosis, assessment, and management. *Curr Probl Cardiol* 2015;40:93-126.
3. Harskamp RE, Wang TY, Bhatt DL, et al. Hospital patterns of medical management strategy use for patients with non-ST-elevation myocardial infarction and 3-vessel or left main coronary artery disease. *Am Heart J* 2014;167:355-362.e3.
4. Cavalcante R, Sotomi Y, Zeng Y, et al. Coronary bypass surgery versus stenting in multivessel disease involving the proximal left anterior descending coronary artery. *Heart* 2017;103:428-33.
5. Ahn JM, Roh JH, Kim YH, et al. Randomized Trial of Stents Versus Bypass Surgery for Left Main Coronary Artery Disease: 5-Year Outcomes of the PRECOMBAT Study. *J Am Coll Cardiol* 2015;65:2198-206.
6. Boudriot E, Thiele H, Walther T, et al. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. *J Am Coll Cardiol* 2011;57:538-45.
7. Morice MC, Serruys PW, Kappetein AP, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. *Circulation* 2010;121:2645-53.
8. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 2013;381:629-38.
9. Mäkikallio T, Holm NR, Lindsay M, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. *Lancet* 2016;388:2743-2752.
10. Stone GW, Sabik JF, Serruys PW, et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. *N Engl J Med* 2016;375:2223-35.
11. Ruel M, Farkouh ME. Why NOBLE and EXCEL Are Consistent With Each Other and With Previous Trials. *Circulation* 2017;135:822-4.
12. Upadhaya S, Baniya R, Madala S, et al. Drug-eluting stent placement versus coronary artery bypass surgery for unprotected left main coronary artery disease: A meta-analysis of randomized controlled trials. *J Card Surg* 2017;32:70-9.
13. Nerlekar N, Ha FJ, Verma KP, et al. Percutaneous Coronary Intervention Using Drug-Eluting Stents Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Stenosis: A Meta-Analysis of Randomized Trials. *Circ Cardiovasc Interv* 2016;9.
14. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* 2012;367:2375-84.
15. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. *N Engl J Med* 2012;366:1467-76.
16. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. *N Engl J Med* 2016;374:1511-20.
17. Habib RH, Dimitrova KR, Badour SA, et al. CABG Versus PCI: Greater Benefit in Long-Term Outcomes With Multiple Arterial Bypass Grafting. *J Am Coll Cardiol* 2015;66:1417-27.
18. Weiss AJ, Zhao S, Tian DH, et al. A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting. *Ann Cardiothorac Surg* 2013;2:390-400.

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