

## Stenting or bypass grafting for left main coronary artery disease: considering short- and long-term trade-offs of each procedure for individualised patient care



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It is universally accepted that patients with significant left main coronary artery (LMCA) disease should receive coronary revascularisation regardless of the spectrum of clinical presentation. However, the optimal revascularisation strategy for such patients has been the subject of intense investigation for decades. Although coronary artery bypass graft (CABG) surgery has been the standard of care for the treatment of LMCA disease for nearly 40 years, percutaneous coronary intervention (PCI) treatment has undergone considerable therapeutic evolution over time and has changed the therapeutic paradigm in the field. Particularly since the widespread use of drug-eluting stents (DES), PCI for LMCA disease has become much more technically feasible and has shown favourable short- and long-term clinical outcomes. Several randomised clinical trials (RCT) have compared PCI with DES and CABG for the treatment of LMCA disease and have generally shown comparable rates of mortality and composite safety outcomes between the two strategies, though more frequent repeat revascularisations with PCI and more frequent stroke with CABG<sup>1</sup>. However, until recently, none of these has been adequately powered or has included contemporary

PCI devices. In recent years, lesion assessment and procedural optimisation have become more accurate using invasive imaging or functional tools. In addition, the concomitant development of adjunctive pharmacotherapies, involving periprocedural antithrombotic agents, antiplatelet therapy, statins, or other secondary preventive drugs, has substantially contributed to enhancing PCI outcomes for LMCA disease. In this context, the results of the EXCEL (Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) and the NOBLE (Nordic-Baltic-British Left Main Revascularization Study) RCT, which represent the largest and most contemporary data, have been long awaited<sup>2,3</sup>. Unexpectedly, the two trials apparently showed disparate findings: EXCEL found PCI to be non-inferior to CABG, while NOBLE noted CABG to be superior to PCI, adding some uncertainty regarding clinical decision making between PCI and CABG for patients with LMCA disease. Overall, the available studies were of variable size and were powered for varying composite endpoints at different time periods. All were underpowered for low-frequency events, such as mortality. Against

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this background, a meta-analysis to determine whether there are significant differences in the risk of mortality and other individual or composite endpoints between PCI and CABG in patients with LMCA would be informative.

In this issue of AsiaIntervention, Iqbal and colleagues report a pairwise meta-analysis of six updated RCT comparing PCI and CABG for unprotected LMCA disease<sup>4</sup>.

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In addition to the EXCEL and NOBLE trials, the final 10-year results of the LE MANS trial were also included. Estimation of relative treatment effect was stratified into short-term (one-year) and long-term follow-up among a total of 4,717 patients treated with either PCI or CABG. Sensitivity analyses were performed for different endpoint definitions (e.g., myocardial infarction) and the type of stent used. Major findings were as follows: no difference in mortality regardless of follow-up period, higher rates of non-procedural myocardial infarction with PCI at long-term follow-up (risk ratio [RR]: 1.73, 95% confidence interval [CI]: 1.27-2.35) but not at one year (RR: 1.17, 95% CI: 0.77-1.76), higher rate of stroke with CABG at one year (RR: 0.39, 95% CI: 0.21-0.70) but not at long-term follow-up (RR: 0.86, 95% CI: 0.44-1.69), and higher rate of repeat revascularisation with PCI regardless of follow-up period. Finally, the long-term follow-up rate for the composite of these four endpoints was higher in PCI-treated patients (RR: 1.25, 95% CI: 1.12-1.39) and was attributable to the results of those who had a SYNTAX score of 33 or more. The authors should be congratulated for their sophisticated efforts on analyses, as they contributed to the robustness of the study. The findings provide further solid evidence of the relative strengths and limitations of each revascularisation strategy for patients with LMCA disease: PCI offers an early safety advantage and acceptable long-term survival, while CABG offers longer-term durability as well as greater protection from future myocardial infarction. In the same context, a substantial interaction between treatment effect and time for the risk of major adverse events in the recent EXCEL and NOBLE trials deserves attention, i.e., late catch-up in EXCEL or late divergence in NOBLE on the treatment effect of CABG over PCI during follow-up<sup>5</sup>. Limited follow-up could have penalised the CABG group in all of the available trials because the long-term benefits of CABG over PCI may not be fully evident until five to 10 years after the procedure. Whether treatment differences between PCI and CABG will continue to accrue or will be attenuated with longer-term follow-up should be the subject of further investigation.

PCI practices have changed significantly since the landmark SYNTAX trial. Small vessels, generally those with a diameter  $\leq 2.0$  mm, are currently not considered large enough for revascularisation. In addition, revascularisation in lesions with diameter stenosis of 50-70% has become less frequent, as these lesions are now commonly known to have functional insignificance. Together with the fact that >60% of patients were eligible for PCI in the EXCEL screening registry, the practical threshold in choosing PCI for LMCA disease is likely to be less stringent in contemporary

real-world practice. However, the optimal choice of revascularisation modality for LMCA disease should be made after discussion among Heart Team members, taking into account eligibility for PCI or CABG, the specific circumstances of each patient, and individual preferences. CABG practices have also changed significantly towards considerable reduction in operative mortality and perioperative complications<sup>6</sup>. Patients who would benefit from durable grafts (e.g., those with a complex anatomy, severe left ventricular dysfunction, or diabetes) should be seriously considered as recipients. Because current guidelines on revascularisation for LMCA disease largely rely on the SYNTAX score<sup>7,8</sup>, and do not clearly address a considerable group of patients who may experience positive outcomes with either CABG or PCI, the selection of the optimal treatment strategy should be more patient-centred, based on the short- and long-term trade-offs of each procedure as shown in the results of the current meta-analysis.

### Conflict of interest statement

The authors have no conflicts of interest to declare.

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