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Left Main Artery Revascularisation: PCI As A Viable Alternative To CABG

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Abstract

The controversial choice in revascularisation modality, Coronary Artery Bypass Graft Surgery (CABG) or Percutaneous Coronary Intervention (PCI), in Left Main Coronary Artery (LMCA) disease has recently been highlighted with the publication of 10-year follow-up data in two randomised control trials (RCTs) and a large observational study (OS), as well as the ESC/EACTS taskforce new recommendations on the topic. In this review, all-cause mortality is similar across patients managed with either modality, though with increased rates of repeat revascularisation following PCI. The complexity of the lesion, by location or SYNTAX score, was frequently shown to affect outcomes. With modern ongoing advancements, PCI may be more strongly considered in certain patient cohorts requiring future LMCA revascularisation.

Keywords: Revascularisation, Left Main Coronary Artery Disease

Short Communication

The choice of Coronary Artery Bypass Graft Surgery (CABG) compared to Percutaneous Coronary Intervention (PCI) in revascularisation of Left Main Coronary Artery (LMCA) disease has been recently highlighted following the publication of long-term outcome data of two seminal Randomised Control Trials (RCTs) and a number of recent meta-analyses. We present a brief overview of the key literature on this topic, with a comparison of RCT findings, observational cohort studies, and meta-analyses.

Two key RCTs, the PRECOMBAT and SYNTAX trials, have both recently published the findings of their 10-year follow-up comparing CABG with PCI for management of LMCA disease. Both interestingly demonstrated similar results, finding no difference in all-cause mortality between the two groups, though with higher rates of repeat revascularisation in the PCI group [1,2].

The PRECOMBAT trial of 600 patients in Korea compared PCI with DES (sirolimus-eluting) and CABG, with a significant proportion having complex disease; 22.3% had high SYNTAX scores, and 64.6% had distal LMCA disease. It showed no significant difference in all-cause mortality rates (14.5% and 13.8% for the PCI group and CABG group respectively), or in the primary outcome of MACCE of 29.8% *vs*. 24.7%. Revascularisation rates, both overall and those rates driven by ischaemia, were higher in the PCI group (21.3% overall and 16.1% ischaemia-driven) compared to the CABG group (10.6% overall and 8% ischaemia-driven). In subgroup analysis, patients with concomitant triple-vessel and LMCA disease showed higher MACCE rates at 10 years post-PCI compared to post-CABG, however SYNTAX score was not shown to be associated with a significant difference in MACCE or all-cause mortality, with only increased rates of ischaemia-driven revascularisation being observed in patients with higher SYNTAX score lesions managed with PCI [2].

The SYNTAX trial, a randomised control trial with 10-year follow-up, compared 1800 patients with LMCA or triple-vessel disease managed with paclitaxel-eluting stents (n=903) versus CABG (n=897). 10-year follow-up data was available for 93% of the PCI group and 95% of the CABG group. Among patients with LMCA disease, all-cause mortality, the primary outcome, was not significantly different between both PCI (27%) and CABG (28%) groups. On subgroup analysis, there was no association found between SYNTAX score and all-cause mortality, though patients with triple-vessel disease and a high SYNTAX score had a higher rate of all-cause mortality when managed with PCI. Specific causes of mortality, rates of MI, and MACCE were not assessed in the 10-year SYNTAX follow-up [1].

Another RCT with similar results is the NOBLE trial, which had a 5-year follow-up of a Northern European cohort of 1184 patient divided equally between PCI and CABG interventions. This study again demonstrated similar all-cause mortality between the two study groups (9% in both groups), despite the PCI group again demonstrating higher rates of non-procedural MI (8% in PCI group vs. 3% in CABG group, $p<0.01$), and need for revascularisation (17% in the PCI group *vs.* 10% in the CABG group, $p<0.01$). The primary endpoint measured was MACCE, finding that CABG was superior to PCI ($p<0.01$), with 28% in the PCI group and 10% in the CABG group in subgroup analysis by SYNTAX score, scores

over 33 (representing 9% of the study population) showed no statistically significant difference in MACCE in the PCI group (33%) compared to the CABG group (25%) ((p=NS) but a statistically significant difference favouring CABG for lower SYNTAX scores over PCI, with MACCE rates of 27% in the PCI group and 14% in the CABG group (p<0.01).

A further key RCT is the EXCEL trial, with a cohort of 1905 patients with low to intermediate lesion complexity. While at three-year follow-up, no difference in all-cause mortality was observed (HR 1.34, p=NS), at five-year follow-up, there was a higher incidence of mortality in the PCI group (13%) compared to the CABG group (9.9%) (OR 1.38, CI 1.03-1.85). Rates of ischaemia-driven revascularisation were also significantly higher in the PCI group compared to the CABG group (16.9 *vs.* 10%, p<0.01). The primary endpoint of the EXCEL trial was a composite of death, stroke, or MI, and was not significantly different between the two groups at 5 years (22.0% in the PCI group *vs.* 19.2% in the CABG group, p=NS) [3].

These RCTs are supported by observational data collected in the 10-year follow-up of the MAINCOMPARE study of 2,240 patients in Korea. The propensity-matched analysis similarly showed no difference in all-cause mortality (HR 1.09, CI 0.87-1.36) but significantly increased risk of target-vessel revascularisation following PCI for LMCA disease (HR 4.07, CI 3.43-6.44, p<0.01). These observations were maintained during subgroup analysis comparing CABG with PCI with BMS (mortality, p=NS; revascularisation HR 10.70, CI 3.80-29.90, p<0.01) or PCI with DES (mortality, p=NS; revascularisation HR 5.96, CI 2.51-14.10, p<0.01). This cohort again highlighted the importance of lesion location, with a significant reduction in mortality risk in the CABG cohort compared to the PCI cohort when lesions were located distally (HR 1.44, CI 1.06-1.96), while no difference was seen in those with shaft or ostial lesions (HR 0.71, CI 0.47-1.07) [4,5].

Another large observational study, the SWEDEHEART study, followed a cohort of 11,137 Swedish patients with LMCA disease for a median of 4.7 years (IQR 2.1-7.6), 9,364 of whom were managed with CABG and 1,773 of whom were managed with PCI. After adjustment for known and unknown confounders using inverse probability weighting and instrumental variable analyses, MACCE was found to be higher in the PCI group compared to the CABG group (HR 2.8, CI 1.8-4.5), including mortality (HR 1.5, CI 1.1-2.0), MI (HR 6.1, CI 1.4-26.3), and new revascularisation (HE 14.0, CI 5.8-33.6). In analysis of subgroups, a statistically significant difference was seen in mortality and MACCE with more complex disease, with increased rates of mortality and MACCE seen in patients with concomitant two or three vessel disease, when compared to LMCA disease only or one vessel concomitant disease (p<0.001) [6].

There are a number of insightful meta-analyses. Key recent publications again support the contention that both PCI and CABG should be considered as possible modalities for LMCA disease. All-cause mortality was shown to be similar across both modalities in long-term follow-up of 5-10 years [7–11], though with increased rates of repeat revascularisation in those who underwent PCI [7–11], particularly for distal disease [12].

Last year, the ESC/EACTS taskforce published their recommendations following a review of updated data for revascularisation strategy in LMCA disease with SYNTAX score <33; as the EACTS had previously withdrawn their support for the 2018 guideline when new data emerged. The new guidelines give a class I recommendation for CABG and class IIa recommendation for PCI for this patient cohort, with a Level A of evidence for both recommendations [13].

Overall, this literature (Table 1) demonstrates that PCI is a viable alternative to the historical use of CABG for LMCA disease. While the vast majority of RCTs, OSs, and meta-analyses demonstrate no significant difference in mortality at 5-10 years of follow-up, with the notable exception of the EXCEL RCT, many do demonstrate increased rates of MACCE and unplanned revascularisation. Importantly, the lesion location and complexity were frequently found to influence outcomes, which is reflected in the current ESC/EACTS guidelines which give a level of Class III recommendation for the use of PCI to high SYNTAX score LMCA lesions, though a Class IIa for PCI to low to moderate SYNTAX score lesions. Thus, there is clearly data which suggest that the use of PCI for LMCA disease may be considered more strongly, particularly with longer-term follow-up data of up to 10-years now available across RCTS, OSs, and meta-analyses to inform clinician decisions.

In consideration of this data, there are some limitations of which to be aware. There are a number of sources of heterogeneity between studies, including the patient cohorts, the inclusion and exclusion criteria, local guidelines and practices, and the technological and medical advancements available at the time of each study. Particularly trials conducted earlier and with longer-term follow-up data did not have the benefit of many advances which are commonplace today and which have improved patient outcomes, including newer generation drug-eluting stents, the use of fractional-flow reserve measurements, and intravascular ultrasound. The rigorousness of RCTs presents useful comparisons, as all patients included had to be candidates for either procedure; cohort studies, in contrast, may be skewed by inclusion of patients who were only suited to one revascularisation technique (eg., as poor surgical candidates or with higher comorbidities), despite authors using statistical analysis tools such as propensity-matching to account for this to some degree.

Overall, mortality appears similar in both groups across the majority of studies, while MACCE, particularly driven by need for revascularisation, tends to be higher in the PCI group, likely driven by lesion complexity and location. In light of emerging evidence and ongoing advancements, the answer regarding the revascularisation technique of choice for LMCA disease remains a dynamic one.

			Differences in risk for key outcomes				
Literature		**Follow-up** (years)	**Mortality**	**MACCE**	**Revascularisation**	**MI**	**Findings according to lesion location or complexity, PCI vs CABG**
PRECOMBAT ***(HR [95%CI])***	RCT	10	NS	NS	**↑ PCI group** *Ischaemia driven: 1.98 [1.21-3.21] Any: 2.04 [1.33-3.11]*	NS	High SYNTAX score: Ischaemia-driven revascularisation increased (p<0.01)
SYNTAX	RCT	10	NS	NA	NA	NA	NS
NOBLE ***(p-value)***	RCT	5	NS	**↑ PCI group** *p<0.01*	**↑ PCI group** *Target lesion: p=0.04*	**↑ PCI group** *p<0.01*	Low SYNTAX score: MACCE increased (p<0.01). High SYNTAX scores: p=NS.
EXCEL ***(OR [95%CI])***	RCT	5	**↑ PCI group** *(1.38 [1.03-1.85]*	NS	**↑ PCI group** *Ischaemia-driven: p<0.01*	NS	Excluded patients with SYNTAX >32
MAINCOMPARE ***(p-value)***	OS	10	NS	NS	**↑ PCI group** *P<0.01*	NA	Distal lesions: Mortality and MACCE increased. Ostial/shaft lesions: NS
SWEDEHEART ***(HR [95%CI])***	OS	5	**↑ PCI group** *(1.5 [1.1-2.0])*	**↑ PCI group** *(2.8 [1.8-4.5])*	**↑ PCI group** *(14.0 [5.8-33.6])*	**↑ PCI group** *(6.1 [1.4-26.3])*	NA

Legend: MACCE (Major Adverse Cardiac and Cerebrovascular Events), MI (Myocardial Infarction), NA (not applicable/analysed), NS (not significant), OS (Observational Study), PCI (Percutaneous Coronary Intervention), RCT (Randomised Control Trial)

Table 1: Comparison of key literature in this review.

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