Heart, Lung and Circulation (2017) xx, 1–9
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2017.08.008

REVIEW

Percutaneous Coronary Intervention Versus Surgery in Left Main Stenosis–A Meta-Analysis and Systematic Review of Randomised Controlled Trials

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Received 10 April 2017; received in revised form 18 July 2017; accepted 4 August 2017; online published-ahead-of-print xxx

Objective To investigate the safety and efficacy of percutaneous coronary interventions (PCI) versus coronary artery bypass graft (CABG) surgery for left main coronary artery (LMCA) disease.

Methods Six randomised controlled trials (RCTs) were reviewed by searching PubMed/Medline, Embase and the Cochrane Library. Estimates were pooled according to random effects model. Binary outcomes were reported as risk ratio (RR) and continuous outcomes were reported as mean difference (MD) with 95% confidence interval (CI).

Results 3794 patients were randomised into PCI and CABG arms. Mean age of the total population was 64.7 years, 74.4% were male and mean Logistic EURO score (LES) was 2.9. When compared with CABG, patients treated with PCI had reduced risk of major adverse cardiovascular events (MACE) at 30 days: (RR: 0.55; 95% CI, 0.41–0.75; $p < 0.001$; $I^2 = 0$) but similar risk at 1 year (RR: 1.15; 95% CI, 0.92–1.45; $p = 0.22$; $I^2 = 0$). Five years MACE rates favoured CABG (RR: 1.32; 95% CI, 1.13–1.53; $p < 0.001$; $I^2 = 0$) driven by a higher rate of target vessel revascularisation (TVR) (RR: 1.71; 95%CI, 1.38–2.12; $p < 0.001$; $I^2 = 0$) and myocardial infarction (MI) (RR: 1.97; 95%CI, 1.28–3.04; $p < 0.001$; $I^2 = 22$). Percutaneous coronary intervention was comparatively a safer procedure with lower rates of periprocedural adverse events including MI, stroke, bleeding events and need for blood transfusions.

Conclusion Percutaneous coronary intervention reduced MACE at 30 days with comparable MACE at 1 year. However, CABG was a more effective modality when considering mid- to long-term outcomes. Percutaneous coronary intervention is a safer procedure with regards to periprocedural adverse events.

KeyWords Left main coronary artery • Percutaneous coronary intervention • Coronary artery disease • Coronary bypass surgery • Coronary revascularisation

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Please cite this article in press as: Khan SU, et al. Percutaneous Coronary Intervention Versus Surgery in Left Main Stenosis–A Meta-Analysis and Systematic Review of Randomised Controlled Trials. Heart, Lung and Circulation (2017), http://dx.doi.org/10.1016/j.hlc.2017.08.008

Introduction

Both the American and European Cardiology Society guidelines suggest that the suitability for elective percutaneous coronary intervention (PCI) of left main coronary artery (LMCA) stenosis should be based on the SYNTAX (SS) Score. While coronary artery bypass grafting (CABG) receives a class I (LOE-B) recommendation for all SS groups, the 2011 American guidelines give class II a, II b and III evidence (LOE B) for low (SS $\leq$ 22), intermediate (SS 23–32) and high SS (SS $>$ 32), respectively [1]. The 2014 European guidelines are somewhat more lenient and give Class I, IIa and III evidence (all LOE B) indication for low, intermediate and high SS respectively [2]. In a meta-analysis of the four randomised control trials (RCTs) of LMCA revascularisation, Capodanno et al. reported that PCI was non-inferior to CABG when risk of MACE, death, and MI were compared; however repeat revascularisation was higher among PCI patients (odds ratio (OR), 2.25 95% CI 1.54–3.28) [3]. Another meta-analysis of 24 studies showed PCI was a safer alternative to CABG for LMCA stenosis [4]. A recent meta-analysis of five RCTs suggested that PCI with drug eluting stents (DES) is equally safe for revascularisation of unprotected left main coronary artery disease (ULMCA) with the caveat that most studies enrolled subjects with low surgical risk [5].

Because of the difference in the results between latest trials: Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) and NOBLE (Nordic Baltic British Left Main Revascularization), there was a need to update the evidence from all the major RCTs [6,7]. Previous meta-analyses were limited by insufficient outcomes, short follow-up durations and lack of safety profile evaluation. To overcome these limitations, we are presenting a meta-analysis incorporating the data from all RCTs comparing PCI with CABG for LMCA stenosis.

Methods

Data Sources

Two authors (SUK and HR) independently conducted the literature search. The search was done by using Pub Med/MEDLINE, Embase and Cochrane library from January 1980 to December 2016. The following search terms were used: ''left main disease'', ''left main artery'', ''stents'', ''Drug eluting stents'', ''bare-metal stents'', ''coronary artery bypass graft'', ''CABG'', ''Cardiovascular events''. The search was restricted for human, RCTs, meta-analysis and systematic reviews. The meta-analysis is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Figure 1 explains the selection process of the studies.

Selection Criteria and Quality Assessment

Eligible studies had to meet the following inclusion criteria: 1. RCTs reporting outcomes of interest (as below) in patients with LMCA stenosis undergoing PCI vs CABG; 2. Randomised participants in included trials were $\geq$18 years old; 3 Only full text articles were included.

Data extraction was done using a standardised collection form including study design, characteristics, events and sample size. Data was either directly extracted from the study or was calculated from the available variables. Risk of bias assessment was done at the study level and methodological quality assessment was done independently according to Cochrane Collaboration tool by two authors (SUK and ML) (Supplementary) [8].

Outcome Measures

Primary Efficacy Outcome

- Major adverse cardiac events (MACE): a composite of myocardial infarction (MI), stroke, all-cause mortality and target vessel revascularisation (TVR).

Secondary Efficacy Outcomes

- Myocardian infarction, stroke, all-cause mortality, cardiovascular (CV) mortality, TVR, ischaemia driven revascularisation, symptomatic graft occlusion and stent thrombosis (GOST) and length of hospital stay.

Safety Outcomes

- Periprocedural adverse events: Myocardial infarction, stroke, all-cause mortality, bleeding events, bleeding requiring transfusions, arrhythmia (supraventricular and ventricular), renal failure and other adverse events (a composite of mechanical intubation >48 hours, post pericardiotomy syndrome, infection or need for other surgical and radiological procedures).

There was considerable heterogeneity with regards to definitions of endpoints. We defined endpoints as reported in the included studies.

Statistical Analysis

Outcomes were pooled by generic invariance methods and the random effects model was used for final reporting of the estimates [9]. Binary outcomes are reported as RR and absolute risk difference (ARD), whereas, continuous outcomes are calculated as MD with 95% CI. Given the RR and ARD represent the same data, we focussed on RR estimates in the current review. However RR and ARD estimates are reported in Tables 2 and 3, respectively. A p-value of 0.05 is set as significant. Heterogeneity was assessed using Q statistics and $I^2 > 50\%$ was consistent with a high degree of heterogeneity. All the analyses were done based on the intention to treat principle.

Mixed effect regression (methods of moment) was carried out to assess the impact of mean age, female (%), diabetes mellitus (DM) (%), mean LES, mean distal left main occlusion (%) and follow-up duration (months) keeping MACE as the

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