Meta-analysis of three randomized trials and nine observational studies comparing drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery disease


CRD summary
Percutaneous coronary interventions using drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery disease produced favourable outcomes for composite mortality, mortality, myocardial infarction and stroke and significantly higher risk of target vessel revascularisation. The reliability of the conclusions was unclear due to limited evidence from randomised studies and a lack of significance for several outcomes.

Authors' objectives
To evaluate the efficacy and safety of percutaneous coronary interventions using drug-eluting stents versus coronary artery bypass grafting for unprotected left main coronary artery disease.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 2001 to 2011; search terms were reported.

Study selection
Randomised controlled trials (RCT) and observational studies that comparing the efficacy and safety of percutaneous coronary interventions (PCI) using drug-eluting stents versus coronary artery bypass grafting (CABG) in patients with unprotected left main coronary artery disease were eligible for inclusion. Follow-up needed to be 12 months or more. Studies that used only bare-metal stents or combined bare-metal and drug-eluting stents were excluded. The primary outcomes were mortality, composite mortality (composite of death, myocardial infarction or stroke) and target vessel revascularisation at one year of follow-up. Secondary outcomes included myocardial infarction and stroke.

Most studies used sirolimus-eluting or sirolimus-eluting/paclitaxel-eluting stents; two trials also used zotarolimus-eluting stents. The studies had a global spread. Participant characteristics included average age of 62 to 72 years, 50% to 87% were men, 44% to 88% had hypertension, 17% to 51% had diabetes and 12% to 59% were smokers. There were some significant differences between patient groups for these and other risk factors.

The authors did not report how many reviewers performed the study selection.

Assessment of study quality
Study quality was assessed using seven criteria (prospective design, multicentre enrolment, selection bias, performance bias, attrition bias, detection bias and multivariate adjustment for potential confounders). Risk of bias was assessed as low, moderate, high or with incomplete reporting.

The authors did not report how many reviewers performed the quality assessment.

Data extraction
Numbers of events were used to calculate odds ratios (OR) with 95% confidence intervals (CI). For four studies where actual numbers of events were not reported, probabilities of end points were estimated from Kaplan-Meier curves.

Two independent reviewers performed the data extraction.

Methods of synthesis
Odds ratios were pooled using a fixed-effect model (no significant heterogeneity) and a random-effects model (significant heterogeneity) to give odds ratios with 95% confidence intervals. Statistical heterogeneity was assessed using Cochran's Q and I² statistics (I²<25% indicated no heterogeneity, I²>25% low, I²=50% moderate and I²=75% high). Numbers needed to treat (NNT) were calculated. Sensitivity analyses were performed by serially excluding
studies and to assess the effects of ethnicity, study design (RCTs versus observational studies) and the burden of coronary diseases. Publication bias was assessed using Egger’s test, with the trim-and-fill method (Duval and Tweedie) and visual inspection of funnel plots.

**Results of the review**

Twelve studies were identified (5,079 participants, range 173 to 792): three RCTs (1,506 participants, range 201 to 705) and nine observational cohort studies (3,573 participants). All 12 studies had moderate performance and detection bias and 11 studies had adequate adjustment for confounders. RCTs had a low risk of selection and attrition bias. For cohort studies attrition bias was low (four studies) or not reported (five studies) and selection bias varied (low for two studies, moderate for five and high for two).

There was a marginally significant lower risk of composite mortality for drug-eluting stents versus CABG (OR 0.70, 95% CI 0.49 to 1.00; I²=54%; 12 studies; NNT=33). The effect was not significant for the three RCTs alone.

Publication bias was found to be in favour of CABG for this outcome. There was no significant difference in risk of death for drug-eluting stents versus CABG (I²=46%; NNT=50; 12 studies). There was no significant difference in risk of myocardial infarction (seven studies) and a significantly lower risk of stroke for drug-eluting stents versus CABG (OR 0.23, 95% CI 0.09 to 0.58; six studies).

Risk of target vessel revascularisation was significantly higher for drug-eluting stents versus CABG (OR 3.52, 95% CI 2.72 to 4.56; I²=35%; 12 studies; NNT=14). The effect was significant but lower for the RCTs alone (OR 2.01, 95% CI 1.34 to 3.00) than for the non-randomised studies.

A propensity matched analysis for five studies found significant effects for death and target vessel revascularisation but not for composite mortality. Results were reported stratified by burden of coronary artery disease.

**Authors’ conclusions**

PCI with drug-eluting stents is associated with favourable outcomes for mortality, composite end point for death, myocardial infarction and stroke and a higher risk of target vessel revascularisation compared to CABG in patients with unprotected left main coronary artery disease.

**CRD commentary**

The review addressed a well-defined question in terms of study design, participants, interventions and relevant outcomes. The search was adequate but the authors did not report on any language restriction so relevant studies may have been missed. The studies were well spread globally. There was evidence for publication bias. Study quality was assessed using suitable criteria and was adequate. Efforts to reduce error and bias were reported for data extraction but not for study selection or quality assessment. Relevant data were provided.

The synthesis method was appropriate. The level of heterogeneity was not reported for two outcomes. The sensitivity analyses were appropriate and attempts were made to account for possible confounders. Relatively few RCTs were identified and subgroup analyses were appropriate for this. There was moderate heterogeneity for some meta-analyses, particularly for composite mortality.

The reliability of the conclusions was unclear due to the limited evidence from randomised studies and a lack of significance for several outcomes.

**Implications of the review for practice and research**

**Practice:** The authors noted that revised practice guidelines (2011) concluded that PCI using drug-eluting stents for unprotected left main coronary artery disease may be considered in patients with anatomical conditions associated with a low risk of PCI procedural complications, a high likelihood of good long-term outcomes and clinical characteristics that indicated an increased risk of adverse clinical outcomes. Previous guidelines recommended CABG as the standard treatment for unprotected left main coronary artery disease. They also noted that their results may not apply to the new generation drug-eluting stents.

**Research:** The authors did not specifically report any implications for research but suggested that longer follow-up was required.
Bibliographic details

PubMedID
22877423

DOI
10.1016/j.amjcard.2012.06.051

Original Paper URL
http://www.ajconline.org/article/S0002-9149(12)01706-7/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Coronary Artery Bypass /methods; Coronary Artery Disease /surgery; Drug-Eluting Stents; Humans; Randomized Controlled Trials as Topic

AccessionNumber
12012054766

Date bibliographic record published
21/12/2012

Date abstract record published
10/04/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.