Effect of drug-eluting stents in patients with acute ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: a meta-analysis of randomised trials and an adjusted indirect comparison


CRD summary
This review concluded that patients undergoing percutaneous coronary intervention for ST-segment elevation myocardial infarction had reduced incidence of target vessel revascularisation and recurrent myocardial infarction when treated with drug-eluting compared with bare-metal stents; there was no increase in cardiac death or stent thrombosis. These conclusions are likely to be reliable.

Authors' objectives
To evaluate the use of drug-eluting stents compared with bare-metal stents after percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction.

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to July 2009. Search terms were reported. Scientific abstracts in four cardiology journals and seven relevant websites were also searched. There were no language restrictions.

Study selection
Randomised controlled trials (RCTs) that compared drug-eluting stents with bare-metal stents and reported clinical outcomes were eligible for inclusion. Trials were required to have a minimum follow-up of three months.

The primary efficacy outcome was target vessel revascularisation and the primary safety outcome was stent thrombosis. Secondary outcomes were cardiac death and recurrent myocardial infarction. Per-protocol definitions were used for all outcomes.

Included trials assessed paclitaxel-eluting or sirolimus-eluting stents; a few patients in one trial received zotarolimus-eluting stents. All trials used a clopidogrel dose of 300 to 600mg. Included patients had mean ages ranging from 59 to 64 years. Most RCTs were single-centre. Approximately half the trials included routine angiographic follow-up. All trials used aspirin therapy (given for one to twelve months); all trials used glycoprotein IIb/IIIa inhibitors in 50 to 100% of patients.

Two reviewers independently selected the studies at the abstract screening stage, with differences resolved by a third reviewer. Methods for final inclusion decisions were not reported, but it appeared that two independent reviewers were involved.

Assessment of study quality
Trials were evaluated using the following criteria: randomisation, allocation concealment, use of intention-to-treat analysis, sample-size calculation and description of losses to follow-up.

The authors did not state how many reviewers performed the assessment.

Data extraction
Data were extracted to permit the calculation of odds ratios (OR) with 95% confidence intervals (CI).

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
Pooled odds ratios with 95% confidence intervals were calculated using a Mantel-Haenszel fixed-effect model except where statistically significant heterogeneity was present. Statistical heterogeneity was assessed using $\chi^2$ and $I^2$; where it was present, a DerSimonian and Laird random-effects model was employed. This was also used as a sensitivity analysis in the case of analyses with statistically significant results.

The impact on outcomes of dual antiplatelet therapy discontinuation, publication status, sample size, multiple enrolling centres and length of follow-up were assessed using tests for interaction. For target vessel revascularisation, interaction with routine angiographic follow-up was also assessed. The association between baseline risk of target vessel revascularisation (incidence in control groups) and number needed to treat (NNT) to prevent one target vessel revascularisation was assessed using a weighted least-squares regression. An adjusted indirect comparison was used to investigate differences between sirolimus-eluting and paclitaxel-eluting stents using bare-metal stents as a common comparator. Sensitivity analyses were used to explore the impact of removing each trial from the analyses.

Publication bias was assessed using funnel plot analyses and rank correlation tests.

Results of the review
Thirteen RCTs (n=7,244 patients) were included in the review. Nine trials reported appropriate randomisation methods and seven described allocation concealment. All trials reported losses to follow-up. One trial used of intention-to-treat analyses; these were modified analyses in two instances. Mean follow-up ranged from six to 12 months.

Target vessel revascularisation occurred in 7.48% of patients (542 patients). Treatment with drug-eluting stents was associated with a statistically significantly reduced incidence of target vessel revascularisation (OR 0.43, 95% CI 0.35 to 0.51; NNT17, 95% CI 15 to 20; $I^2 =33\%$) compared with bare-metal stents (5.11% versus 11.27%).

There was also a statistically significant benefit of drug-eluting stents in recurrent myocardial infarction (OR 0.73, 95% CI 0.56 to 0.96; $I^2=0\%$) compared with bare-metal stents (3.03% versus 3.70%). Similar results were obtained using random-effects analyses.

There were no statistically significant differences in the incidence of stent thrombosis or cardiac mortality between the groups.

Subgroup analyses revealed a larger reduction in target vessel revascularisation in trials with fewer than 300 patients (p=0.03) and in trials using routine angiographic follow-up (p=0.01).

The adjusted indirect comparison found a benefit of sirolimus-eluting compared with paclitaxel-eluting stents for target vessel revascularisation (OR 0.59, 95% CI 0.40 to 0.89), but no statistically significant differences for other outcomes.

There was no evidence of publication bias in any of the analyses.

Authors’ conclusions
In patients undergoing percutaneous coronary intervention for ST-segment elevation myocardial infarction, treatment with drug-eluting stents was associated with a reduced incidence of target vessel revascularisation and recurrent myocardial infarction. There was no increase in cardiac death or stent thrombosis at one-year follow-up. Sirolimus-eluting stents were associated with greater reductions in target vessel revascularisation than paclitaxel-eluting stents.

CRD commentary
The review question and the inclusion criteria were clear. Several relevant databases and other sources were searched without restrictions, reducing the chances of selection biases or omission of relevant studies. The authors reported using methods designed to reduce reviewer bias and error in the selection of studies, but it was not clear if such methods were also employed for the assessment of validity and the extraction of data. The quality assessment used appropriate criteria. The synthesis used appropriate methods, including assessment and exploration of heterogeneity.

Despite some shortcomings in the reporting of review methodology, the authors’ conclusions reflect the results of the
Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that results at longer follow-up are required for the included trials. An appropriately powered direct comparison of sirolimus-eluting and paclitaxel-eluting stents in patients undergoing percutaneous coronary interventions for ST-segment elevation myocardial infarction is also needed.

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