Comparison of drug-eluting stents with bare metal stents in patients with ST-segment elevation myocardial infarction


CRD summary
This review concluded that early generation drug-eluting stents for ST-segment elevation myocardial infarction reduced target-vessel revascularisation, with a trend towards fewer definite stent thromboses, during the first year, but they increased stent thromboses in later years. The review was well conducted, and the conclusions seem to be reliable.

Authors' objectives
To assess the long-term effects of early generation drug-eluting stents, compared with bare-metal stents, in people with ST-segment elevation myocardial infarction, who were undergoing primary percutaneous coronary intervention, and to determine whether the benefits and risks vary over time.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to April 2011. The search terms were reported in an online appendix. Five relevant websites or trials registers, conference proceedings and reference lists of relevant papers were checked. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) or quasi-RCTs that compared sirolimus- or paclitaxel-eluting stents with bare-metal stents, in adults with ST-segment elevation myocardial infarction, were eligible for inclusion. The primary outcomes were definite stent thrombosis (confirmed by angiography or pathology) and target-vessel revascularisation. Secondary outcomes were cardiac death, procedure-related death, deaths related to other treatment, deaths from unknown causes, fatal and non-fatal myocardial infarction, a composite of myocardial infarction or death, and a composite of definite or probable stent thrombosis.

In the included trials, where given, participants' mean age ranged from 59 to 65 years; 70% to 83% were men; 10% to 28% had diabetes; 26% to 58% had hypertension; 25% to 68% were smokers; 34% to 53% had multivessel disease; mean reference-vessel diameter was 2.3mm to 3.2mm; mean number of stents was one to 1.5; mean stent diameter was 3.1mm to 3.5mm; and mean stent length was 18mm to 30mm. Most trials assessed sirolimus- or paclitaxel-eluting stents, one assessed zotarolimus for some participants. Some trials used loading doses of clopidogrel. The planned duration of dual antiplatelet therapy ranged from three to 12 months. Glycoprotein IIb or IIIa inhibitors were used for all participants in eight trials, and for 71% to 99% of participants in five other trials.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
Quality was assessed by one reviewer and checked by a second, for adequacy of concealment of allocation, blinding of outcome assessors, and intention-to-treat analysis.

Data extraction
Data were extracted to calculate risk ratios and 95% confidence intervals for outcomes at the longest follow-up, at one year and after one year. Where data on target-vessel revascularisation were missing, target-lesion revascularisation was used (one trial). Where the composite of death and myocardial infarction was not reported, cardiac death and myocardial infarction was used (two trials).

Data were extracted by one reviewer and checked by a second. Authors were contacted for additional information.

Methods of synthesis
The pooled risk ratios and 95% confidence intervals were calculated using a random-effects model. Random-effects meta-regression was used to investigate the follow-up period (one year or less versus over one year). Statistical
heterogeneity was assessed using $I^2$.

Sensitivity analyses investigated the possible effects of bias in allocation concealment, blind assessment of outcomes, intention-to-treat analysis, trial size (under 300 versus over 300 patients) and industry sponsorship; the length of treatment with dual antiplatelet therapy; and the type of drug-eluting stent. Post-hoc analysis investigated the effect of removing the largest study. The numbers needed to treat and to harm were calculated. Funnel plots and regression tests were used to assess publication bias.

**Results of the review**

Fifteen RCTs, with 7,867 participants, were included. One trial had 3,006 participants, others ranged from 65 to 745 participants. Follow-up was seven months in one trial, and one to six years in the others. Allocation concealment was adequate in four trials; nine described blinding of outcome assessors; and seven used intention-to-treat analysis. Three trials reported that they did not receive industry funding.

**Definite stent thrombosis:** There was no statistically significant difference in definite stent thrombosis between bare-metal stents and drug-eluting stents (15 trials; $I^2=0$). Analyses by study quality and characteristics showed only minor variations in effect. At one year, the difference in risk of definite stent thrombosis was not statistically significant (14 trials; $I^2=0$). After one year, the risk was greater in the drug-eluting stent group (RR 2.10, 95% CI 1.20 to 3.69; nine trials; $I^2=0$). There was a positive interaction for the difference over time ($p=0.009$).

**Target-vessel revascularisation:** Drug-eluting stents reduced the risk of target-vessel revascularisation (RR 0.51, 95% CI 0.43 to 0.61; 14 trials; $I^2=24\%$). Subgroup analyses indicated a greater effect in small than in large trials, and during the first year (RR 0.46, 95% CI 0.38 to 0.55; 14 trials; $I^2=6.4\%$) than after one year (RR 0.75, 95% CI 0.59 to 0.94; 11 trials; $I^2=0$), with a positive test for interaction over time ($p=0.007$).

Sensitivity analyses, of higher quality trials, had similar results to the main analyses for both primary outcomes, for time dependent effects, as did post-hoc analyses that excluded the largest trial. Other sensitivity analysis results were reported. Funnel plots showed no evidence of publication bias for stent thrombosis, but suggested missing trials for target-vessel revascularisation.

**Secondary outcomes:** There was no statistically significant effect on myocardial infarction overall, but there was a positive interaction over time ($p=0.010$), with a reduced risk of myocardial infarction at one year or less with drug eluting stents (RR 0.73, 95% CI 0.57 to 0.94), but no statistically significant difference beyond one year. Definite or probable stent thrombosis had similar results as for definite thrombosis, with a positive test for interaction over time ($p=0.015$). There was no evidence of time dependent effects for other outcomes.

**Authors' conclusions**

Early generation drug-eluting stents in primary percutaneous intervention for ST-segment elevation myocardial infarction reduced target-vessel revascularisation, with a trend towards fewer definite stent thromboses, in the first year, but these benefits were offset by an increase in stent thromboses in later years.

**CRD commentary**

The aims of this review were clearly stated with the inclusion criteria. The search covered a number of relevant sources including published and unpublished studies, in any language. This is likely to have reduced any language or publication bias, but the tests suggested that trials may have been missing for one of the primary outcomes. The methods included efforts to prevent reviewer error or bias. Quality was assessed and the methods of synthesis were appropriate. Heterogeneity was investigated. The authors suggested that methodological problems within trials and possible selective reporting of outcomes could have overestimated the effects of drug-eluting stents on target-vessel revascularisation.

The review appears to have been well conducted and the conclusions seem to be reliable.

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

**Practice:** The authors stated that the long-term safety of drug-eluting stents should be improved.

**Research:** They did not state any implications for research.
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