Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis


CRD summary
This review evaluated the efficacy and safety of sirolimus-eluting, paclitaxel-eluting and bare metal stents. The authors found that overall and cardiac mortality were comparable between the stents, while sirolimus-eluting stents carried lower rates of target lesion revascularisation and myocardial infarction. This review was well conducted and the conclusions are likely to be reliable.

Authors’ objectives
To compare the efficacy and safety of sirolimus- versus paclitaxel-eluting stents.

Searching
MEDLINE, EMBASE, the Cochrane CENTRAL Register were searched from inception to March 2007, as well as websites of cardiology societies and clinical trials registers. No language restrictions were applied. Reference lists, conference abstracts, book chapters and the proceedings of the Food and Drug Administration advisory panels were checked, and manufacturers and trialists were contacted for additional studies.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with at least 6 months’ follow-up were eligible for inclusion.

Specific interventions included in the review
Studies comparing the paclitaxel-eluting Taxus stent and the sirolimus-eluting Cypher stent with each other or bare metal stents, were eligible for inclusion.

Participants included in the review
Studies of patients with silent or provoked stable angina pectoris, unstable angina pectoris or acute myocardial infarction (MI) were eligible for inclusion. Where reported, the mean age ranged from 56 to 73 years, the proportion of patients with diabetes varied from 0 to 100% (majority less than 35%), and the proportion of males ranged from 34 to 90%.

Outcomes assessed in the review
The primary outcomes were mortality (overall, cardiac, procedure-related, concomitant treatment-related, and unknown cause), fatal and nonfatal MI, death or MI, and stent thrombosis within the stented segment. The secondary efficacy outcome was the rate of target lesion revascularisation.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies; the method for resolving disagreements was not reported.

Assessment of study quality
Study validity was assessed on the basis of concealment of allocation, blinding of assessors of clinical outcomes, and intention-to-treat analysis. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two reviewers independently extracted the data, with any disagreements resolved through discussion with a third reviewer. Trialists and manufacturers of drug-eluting stents were asked to check the data extracted and provide, when needed, information on outcome data according to standardised definitions. The incidence of stent thrombosis, MI, deaths and revascularisation were extracted from each study.

Methods of synthesis
How were the studies combined?
A multivariable Bayesian hierarchical random-effects model was used to calculate pooled hazard ratio (HR) and 95% credibility intervals (Cis). A random-walk model based on piece-wise constant hazards was used to account for varying follow-up times. Studies with zero events in either arm were excluded. The numbers-needed-to-treat (NNT) and numbers needed-to-harm were calculated.

How were differences between studies investigated?
Sensitivity analyses was performed for high-quality trials, strut thickness and type of stent platform. Statistical heterogeneity was estimated from the median between-trial variance. Stratified analyses were conducted for mortality and the composite of death or MI according to the presence or absence of diabetes. A post-hoc analysis was conducted for stent thrombosis occurring before and after 30 days from stent implantation.

Results of the review
Thirty-eight RCTs (18,023 patients) were included in the review. Follow-up ranged from 1 to 4 years.

Quality: adequate methods of allocation concealment were described in 29 trials, 28 trials reported a blind adjudication of clinical outcomes, and 31 studies performed an intention-to-treat analysis.

Mortality: comparable overall mortality (38 studies; n=18,023) and cardiac mortality (36 trials, n=17 705) were observed for the three types of stent.

MI (37 trials, n=17,962): sirolimus-eluting stents were associated with a lower risk of MI than bare metal stents (HR 0.81, 95% CI: 0.66, 0.97, p=0.030; NNT 99) and paclitaxel-eluting stents (HR 0.83, 95% CI: 0.71, 1.00, p=0.045; NNT 106). The incidence of MI was similar between paclitaxel-eluting stents and bare metal stents.

Death or MI (38 trials, n=18,023): there was no significant difference between the different types of stent.

Stent thrombosis (24 trials, n=16,963): the risk of overall or early stent thrombosis was similar for the different types of stent. Stent thrombosis after 30 days of implantation occurred more often with paclitaxel-eluting stents than with bare metal stents (HR 2.11, 95% CI: 1.19, 4.23, p=0.017; NNT 100), and less often with sirolimus-eluting stents than with paclitaxel-eluting stents (HR 0.54, 95% CI: 0.26, 0.98, p=0.041; NNT 113). Rates were similar for bare metal stents and sirolimus-eluting stents.

Target lesion revascularisation (37 trials, n=17,712): compared with bare metal stents, both sirolimus- and paclitaxel-eluting stents reduced the risk of target lesion revascularisation (respectively: HR 0.30, 95% CI: 0.24, 0.37, p<0.0001, NNT 7; HR 0.42, 95% CI: 0.33, 0.53, p<0.0001, NNT 8). Sirolimus-eluting stents reduced the incidence of target lesion revascularisation by 30% compared with paclitaxel-eluting stents (HR 0.70, 95% CI: 0.56, 0.84, p=0.0021; NNT 35).

Sensitivity analyses: none of the sensitivity analyses changed the results of the main analyses.

Authors' conclusions
Sirolimus-eluting stents seem to be clinically better than bare metal stents and paclitaxel-eluting stents.

CRD commentary
This review addressed a well-defined question in terms of the study design, participants, intervention and outcomes. The authors searched several relevant database and efforts were made to identify unpublished studies, thereby limiting
the risk of publication bias, although this was not evaluated in the review. No language restrictions were applied, thus reducing the potential for language bias. The authors attempted to minimise bias and errors during the review process by carrying out the study selection and data extraction in duplicate. It was not stated clearly whether the study quality assessment was also performed in duplicate, although it seems that at least two reviewers were involved in this phase. Statistical heterogeneity was assessed and the authors stated that there was low statistical heterogeneity for the main outcomes; this supports the authors' decision to pool the studies in a meta-analysis. The authors' cautious conclusions appear appropriate and are likely to be reliable.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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