A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents

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CRD summary
This review compared bare metal stents (BMS) with anti-mitotic drug-eluting stents. The authors concluded that sirolimus and polymeric paclitaxol-eluting stents decreased angiographic restenosis and major adverse cardiac events compared with BMS, but there was no difference in mortality or myocardial infarction. Larger studies with longer-term follow-up are required. These conclusions are likely to be reliable.

Authors' objectives
To compare the benefits and safety of bare metal stents (BMS) to antimitotic drug-eluting stents (DES).

Searching
PubMed was searched from December 1998 to April 2004 for studies published in English; the search terms were reported. Internet searches were also conducted and the reference lists of identified studies and recent reviews were checked. Trials published as abstracts were included.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. The studies had to report medium-term follow-up results (6 to 12 months after the index percutaneous coronary intervention). Data on long-term (greater than 12 months) follow-up were excluded. Follow-up coronary angiography was performed on 43 to 97% of enrolled patients 6 to 9 months after the index surgery.

Specific interventions included in the review
Studies that compared antimitotic DES with BMS were eligible for inclusion. Only studies of stents eluting sirolimus or paclitaxol were included in the main analysis. DES studies were classified by the antimitotic drug used and polymer coating (sirolimus, polymeric paclitaxol, non-polymeric paclitaxol and others).

Participants included in the review
Studies of adults undergoing percutaneous coronary interventions were eligible for inclusion. The mean age, where reported, ranged from 56 to 66 years, and 67 to 94% of the participants were male. In all of the included studies the patients had de-novo lesions in a native coronary artery. Multilesion percutaneous interventions were excluded from all included studies, as were patients with a recent myocardial infarction or low ejection fraction. The majority of the participants had a low risk of angiographic restenosis.

Outcomes assessed in the review
The primary outcomes assessed in the review were all-cause mortality, myocardial infarction, target-lesion revascularisation, major adverse cardiac events, in-lesion restenosis or in-stent restenosis, edge restenosis and safety (acute, subacute and late thrombotic complications, and late incomplete stent apposition). The definitions used for the outcomes were given in the paper.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The studies were assessed for randomisation, concealment of treatment allocation, blinding and the proportion of patients followed up. The authors did not state who performed the validity assessment.
Data extraction
One reviewer extracted the data and two reviewers independently verified the data extracted. Any disagreements were resolved by consensus. Odds ratios (ORs) and 95% credibility intervals (CrIs) were extracted for each study. Where the number of patients undergoing repeat angiography was not stated, the reviewers assumed all enrolled patients had undergone angiography.

Methods of synthesis
How were the studies combined?
The studies were grouped by eluted drug and carrier polymer. Pooled ORs and 95% CrIs were calculated using a hierarchical Bayesian random-effects model. Low-information prior distributions were used, increasing the weight of data from the RCTs in the final distribution.

How were differences between studies investigated?
Forest plots of the OR and 95% CrI for each study included in the main meta-analyses were presented. A sensitivity analysis was performed using different low-information prior distributions. Differences among the studies were discussed in the paper. Primary analyses were repeated after including two RCTs of stents eluting QP2 (7-hexanoyltaxol) and dactinomycin.

Results of the review
Eleven RCTs (n=5,103) were included.

The studies were randomised, with adequate concealment of treatment allocation and clinical follow-up rates of more than 90%. Eight RCTs were double-blinded, two single-blinded and one unblinded.

All DES.
There was no statistically significant difference between DES and BMS in mortality (OR 1.11, 95% CrI: 0.61, 2.06) or myocardial infarction (OR 0.92; 95% CrI: 0.65, 1.25). DES was associated with statistically significantly lower rates of major adverse cardiac events (7.8% with DES versus 16.4% with BMS; OR 0.42, 95% CrI: 0.32, 0.53) and angiographic restenosis rates (8.9% with DES versus 29.3% with BMS; OR 0.18, 95% CrI: 0.06, 0.40).

Sirolimus DES.
There was no statistically significant difference between DES and BMS in mortality or myocardial infarction. Sirolimus DES was associated with statistically significant reductions in major adverse cardiac events (6.8% with DES versus 21.0% with BMS; OR 0.28, 95% CrI: 0.17, 0.41), target lesion revascularisation (3.5% with DES versus 18.5% with BMS; OR 0.15, 95% CrI: 0.02, 0.46) and rate of angiographic restenosis (6.2% with DES versus 36.9% with BMS; OR 0.06, 95% CrI: 0.0, 0.34).

Polymeric paclitaxel DES.
There was no statistically significant difference between DES and BMS in mortality or myocardial infarction. Polymeric paclitaxel DES was associated with statistically significant reductions in major adverse cardiac events (8.7% with DES versus 6.7% with BMS; OR 0.47, 95% CrI: 0.25, 0.71), target lesion revascularisation (3.3% with DES versus 12.2% with BMS; OR 0.23, 95% CrI: 0.10, 0.42) and rate of angiographic restenosis (7.1% with DES versus 23.5% with BMS; OR 0.23, 95% CrI: 0.07, 0.40).

Non-polymeric paclitaxel DES.
There was no statistically significant difference between DES and BMS in mortality, myocardial infarction, target lesion revascularisation or angiographic restenosis. Non-polymeric paclitaxel DES reduced major adverse cardiac events in comparison with BMS (7.7% with DES versus 9.5% with BMS; OR 0.64, 95% CrI: 0.42, 1.00).

The results were similar after using a range of low-information prior distributions.
Authors' conclusions
Sirolimus and polymeric paclitaxol-eluting stents decreased angiographic restenosis and major adverse cardiac events in comparison with BMS, but there was no difference in mortality or myocardial infarction rates.

CRD commentary
The review question was clear in terms of the study design, intervention and outcomes. By restricting the search to English language studies identified through a limited search, relevant studies might have been missed. The methods used to select studies and assess validity were not described, so it is not known whether any efforts were made to reduce errors and bias. Methods were used to minimise bias in the data extraction process. Validity was assessed using established criteria.

The nature of the data used to produce the prior distribution was unclear. It appeared that this distribution was discarded in favour of a low-information distribution, thus reducing the influence of what was presumably data from lower quality studies. If this was the case, it might have been more informative to have undertaken a sensitivity analysis to demonstrate the influence of the initial prior distribution. By using a low-information distribution and removing the influence of other data, the results were in essence a standard meta-analysis of the 11 RCTs. Although statistical heterogeneity was not formally assessed, consistency in the direction of treatment effect was illustrated using forest plots. The authors' conclusions appear to be supported by the evidence presented and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that larger studies with longer-term follow-up are needed and that further research is required to assess restenosis (including edge restenosis) and repeat revasularisation. They also suggested that the principal investigators of the major DES trials should collaborate on an analysis of individual patient data to quantify treatments effects in specific subgroups.

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