What is the risk of stent thrombosis associated with the use of paclitaxel-eluting stents for percutaneous coronary intervention: a meta-analysis

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CRD summary
This review investigated the differences in risk for stent thrombosis from the use of paclitaxel-eluting stents versus bare metal stents in people with coronary artery disease. The authors concluded that the evidence suggests no difference between the two types of stents. Limitations in some aspects of the review methodology mean that this conclusion should be treated with caution.

Authors' objectives
To investigate the risk of stent thrombosis associated with the use of paclitaxel-eluting stents (PES), compared with bare metal stents (BMS).

Searching
MEDLINE, EMBASE, CRISP, the meta Register of Controlled Trials and The Cochrane Library were searched from 2001 to 2004; the search terms were given. Relevant journals and abstracts from international cardiology meetings and conferences were handsearched. The Science Citation Index was used to check references within identified articles. Authors of identified studies and experts were also contacted.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared the use of PES with BMS were eligible for inclusion. Studies were excluded if both treatment groups received PES, if sirolimus was used, where paclitaxel was given orally, or where other analogues of paclitaxel were used. Both polymer and non-polymer stents were used in the included studies. In some studies, aspirin, clopidogrel, cilostazol, ticlopidine or glycoprotein IIb/IIIa inhibitors were also administered.

Participants included in the review
Studies on people with coronary artery disease, undergoing stent implantation, were eligible for inclusion. In the included studies, the median age of the participants ranged from 58 to 66 years and between 62% and 94% were men. Where given, between 23% and 54% were current smokers, 10% to 31% were diabetic, and 26% to 43% had had a previous myocardial infarction. Details of the coronary lesions were given in the paper.

Outcomes assessed in the review
To be included, the studies had to assess thrombosis using angiographic data for at least 30 days' follow-up. The primary outcome of interest was stent thrombosis. This was defined as either angiographically documented thrombosis or, where angiographic data were unavailable, an event in which the study investigators clinically presumed that thrombosis had occurred. Any identified stent-associated thrombosis, occurring up to one year of follow-up, was included in the outcome data. The duration of follow-up ranged from 6 to 12 months in the included studies.

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 authors stated that as all the included studies were double-blind RCTs, formal quality assessments were not
conducted.

**Data extraction**

Two reviewers independently abstracted the data. Any discrepancies were resolved with a third reviewer. Data were extracted from the individual studies and used to calculate risk ratios (RRs) with 95% confidence intervals (CIs). Where studies evaluated more than one treatment, it appeared that each was considered separately in the analysis using the same control group for each comparison. The data were extracted on an intention-to-treat basis.

**Methods of synthesis**

How were the studies combined?

A summary RR with 95% CIs was calculated using a fixed-effect model. Where there were no events in a single arm, the automatic ‘zero cell’ correction method was used. Publication bias was investigated using Eggar's funnel plot.

How were differences between studies investigated?

Cochran’s Q statistic was used to investigate heterogeneity. Subgroup analyses were performed based on differences between duration of concomitant antiplatelet treatment, longer (mean length >12 mm) and shorter coronary lesions, or higher and lower doses of paclitaxel.

**Results of the review**

Eight double-blind RCTs (3,817 participants) reporting 13 treatment comparisons were included.

There was no evidence of statistically significant heterogeneity among the studies (P=0.82) and no evidence of publication bias (P=0.86).

There was no statistically significant difference in the risk of thrombosis between the PES and BMS (RR 1.06, 95% CI: 0.55, 2.04, P=0.86).

Similarly, in the subgroup analyses, there was no increased risk of thrombosis in the four studies that used aspirin and clopidogrel together for 6 months, in the three studies that used a higher dose of paclitaxel, or in the two studies that enrolled people with longer coronary lesions.

**Authors' conclusions**

Evidence suggests that a standard dose PES do not increase the risk of stent thrombosis in comparison with BMS.

**CRD commentary**

The inclusion criteria for this review were clear. The sources searched for studies appeared comprehensive and unpublished studies were included in the review, although the authors made no mention of any language restrictions. However, tests for publication bias were negative. The method of selecting studies for the review was not described, thus it is possible that decisions made at this stage could introduce reviewer error and bias into the review. The authors chose not to assess the quality of the included studies although this might have been useful, particularly as some of the included studies had not undergone peer review. The decision to statistically pool the data seems appropriate, and the apparent differences between the studies were considered in subgroup analyses. However, when pooling the studies, it appears that the authors have used data from the same control groups in more than one comparison; it is possible that this could distort the results of the analysis. In view of these comments, the authors’ conclusions should be interpreted with some degree of caution.

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

The authors did not state any implications for practice or further research.
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