Impact of the everolimus-eluting stent on stent thrombosis: a meta-analysis of 13 randomized trials


CRD summary
The authors concluded that everolimus-eluting stents were associated with a large and significant reduction in stent thrombosis compared with non-everolimus-eluting stents. Similar effects of less magnitude were found with target vessel revascularisation and myocardial infarction. The authors’ conclusions should be interpreted cautiously as they over-simplify the review results (given variation in comparator subgroup results).

Authors’ objectives
To evaluate whether everolimus-eluting stents reduce stent thrombosis and other cardiac outcomes compared to other drug-eluting stents.

Searching
MEDLINE, Scopus and The Cochrane Library databases and internet sources were searched without language or date restrictions. Additional searches of conference proceedings were performed. References of relevant reviews were checked for additional studies. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared everolimus-eluting stents with non-everolimus-eluting stents and reported frequency of stent thrombosis were eligible for inclusion. Comparisons that included nonpermanent polymer drug-eluting stents were excluded.

Most patients were male. Mean ages ranged from 62 to 67 years. Where reported, rates of patients with diabetes mellitus ranged from 14% to 100%, complex lesion from 11% to 100% and acute presentation from 21% to 65%. Most common comparators were sirolimus-eluting stents followed by paclitaxel-eluting stents and zotarolimus-eluting stents. Nearly all studies reported using clopidogrel for between six and 12 months. Definitions of outcomes were reported. Studies were published between 2007 and 2011.

Two reviewers selected studies for inclusion.

Assessment of study quality
Risk of bias assessment covered selective reporting, incomplete outcome data, outcome blinding, allocation concealment, sequence generation and other bias.

The authors did not report how many reviewers assessed study quality.

Data extraction
Data on outcomes of interest (stent thrombosis, target vessel revascularisation, myocardial infarction and cardiac death) were extracted to calculate risk ratios (RR) and risk differences (RD) on an intention-to-treat basis. Study authors were contacted in case of missing data.

The authors did not report how many reviewers extracted data.

Methods of synthesis
Pooled risk ratios and absolute risk differences were calculated using a random-effects meta-analysis. Heterogeneity was assessed using $I^2$ and Cochran’s Q. Publication bias was assessed using Egger’s and Begg’s tests. Sensitivity analyses were conducted to assess the robustness of the findings. The association between baseline risk and outcomes of interest were explored using a meta-regression.

Results of the review
Thirteen RCTs (17,101 patients) were included. Follow-up ranged from nine to 48 months (mean 21.7 months). Risk of bias was generally low. Sequence generation was deemed adequate in all trials. Risk of bias associated with allocation concealment, outcome blinding and incomplete outcome data was low in more than 80% of trials.

Risk of stent thrombosis was significantly lower for patients who received everolimus-eluting stents compared to non everolimus-eluting stents (RR 0.55, 95% CI 0.38 to 0.78; 11 RCTs). There was no evidence of significant heterogeneity ($I^2=19.4\%$)

Risks of myocardial infarction (RR 0.78, 95% CI 0.64 to 0.96; $I^2=25.8\%$) and target vessel revascularisation (RR 0.77, 95% CI 0.64 to 0.92; $I^2=43\%$) were significantly lower in patients who received everolimus-eluting stents compared to non everolimus-eluting stents (13 RCTs). There was no statistically significant difference between the groups in cardiac death.

Results of sensitivity analyses and meta-regression were reported. Treatment effect varied by comparator. Significant differences were seen favouring everolimus-eluting stent versus paclitaxel-eluting stents (four RCTs) but not when compared with sirolimus-eluting stents (eight RCTs) or zotarolimus-eluting stents (one RCT).

**Authors’ conclusions**
The authors concluded that everolimus-eluting stents were associated with a large and significant reduction in stent thrombosis compared with non-everolimus-eluting stents. Similar effects of less magnitude were found with target vessel revascularisation and myocardial infarction.

**CRD commentary**
The review question and selection criteria were clear. Several bibliographic sources were consulted. Published and unpublished data were sought. Two reviewers selected the studies. It was unclear whether study selection was done in duplicate and what steps were taken to minimise error and bias during data extraction and quality assessment.

Results of the quality assessment were reported. All studies were RCTs and risk of bias was generally low. The number of included patients was large. Methods of synthesis appeared appropriate. Sources of heterogeneity and the robustness of the findings were explored using a range of methods.

The overall conclusions appeared to over-simplify the review results, given variation in comparator subgroup results; these indicated that significant effects were found only when everolimus-eluting stents were compared with paclitaxel-eluting stents. For this reason the authors' conclusions should be interpreted cautiously.

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

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

**Research**: The authors stated that analyses using individual patient data would allow a better evaluation of differences in the composite endpoint of cardiac death or myocardial infarction and the timing of stent thrombosis with respect to dual-antiplatelet therapy duration and/or cessation. They stated that further research was needed to explore the extent of the review findings to other second-generation drug-eluting stents. Longer term data would also provide further understanding on the durability of the review results and their extension to other patient populations.

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**Bibliographic details**

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.