Meta-analysis comparison (nine trials) of outcomes with drug-eluting stents versus bare metal stents in patients with diabetes mellitus

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CRD summary
This review compared outcomes of drug-eluting stent and bare-metal stent implantation in diabetic patients. The authors concluded that drug-eluting stents resulted in lower risk of in-stent restenosis and target lesion revascularisation and decreased incidence of myocardial infection during follow up with no impact on mortality or stent thrombosis. In general, the conclusions are likely to be reliable.

Authors' objectives
To assess the effects of drug-eluting stents on follow-up events in diabetic patients (insulin treated and non insulin treated) compared with bare metal stents.

Searching
MEDLINE via PubMed and Cochrane Central Register of Controlled Trials were searched from 2002 to May 2008; search terms were reported. Bibliographies, abstracts from relevant meetings and recent (within two years) editorials and reviews were examined for additional studies.

Study selection
Randomised studies that reported outcomes of drug-eluting stent (all types) implantation compared to bare metal stents in diabetic patients (or subgroups of diabetic patients) during follow up of at least six-months post procedure were eligible for inclusion. To be eligible, reported study outcomes needed to include results of angiographic follow up for all patients or ischemia-driven angiography. Studies were excluded if raw data were not available or where duplicate publication occurred.

Published double-blind randomised studies were included. Most included studies reported on sub-populations of diabetic patients using Sirolimus (six studies) or Paclitaxel (three studies) drug-eluting stents. Mean age ranged from 62 to 67 years. Most participants were male. Reported outcomes included death from any cause, myocardial infarction, in-stent restenosis, target lesion revascularisation and stent thrombosis. Median duration of clinical follow up was 12 months (mean 16 months and range eight to 24 months). Co-therapies included aspirin and clopidogrel or antiplatelet therapy with ticlopidine. Main clinical, angiographic and procedural characteristics were comparable for drug-eluting stent and bare metal stent patients.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed in terms of adequacy of allocation concealment, whether intention to treat analysis was performed and whether there was blind assessment of outcome measures.

The authors did not state how the validity assessment was performed.

Data extraction
Data were extracted by two independent reviewers; disagreements were resolved through discussion with a third. Where necessary, absolute numbers were re-calculated from percentages.

Methods of synthesis
The pooled odds ratio (OR) and corresponding 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel method for fixed-effect and the DerSimonian-Laird method for random-effects meta-analysis. Statistical
heterogeneity was assessed using the Q test and I² test. Only fixed-effect estimates were reported. All analyses were based on intention to treat. Publication bias was investigated using funnel plot analyses. Subgroup analyses were carried out for insulin and non-insulin treated patients.

**Results of the review**

Nine double blind RCTs (n=1,141) were included in the review.

There was no statistically significant heterogeneity between studies for any of the reported outcome measures. Funnel plot analyses showed no evidence of publication bias. Results for quality assessment were not reported.

Drug-eluting stents were associated with statistically significant decreases in the occurrence of target lesion revascularisation (OR 0.23, 95% CI: 0.16 to 0.33, p<0.00001) and in the occurrence of angiographic in-stent restenosis (OR 0.13, 95% CI: 0.09 to 0.20, p<0.00001), compared with bare metal stents. The effects were similar for sirolimus-eluting and paclitaxel-eluting stents. Statistically significant decreases in occurrence of in-stent restenosis were also shown in both non insulin treated and insulin treated subgroups. There was no difference in the occurrence of stent thrombosis or death.

Drug-eluting stents were associated with statistically significant decrease in incidence of myocardial infarction during follow up compared to bare metal stents (OR 0.48, 95% CI: 0.26 to 0.87, p=0.02). Results showed that 25 diabetic patients needed to be treated with drug-eluting stents to prevent one myocardial infarction and five patients needed to be prevent one target lesion revascularisation.

**Authors’ conclusions**

Diabetic patients treated with drug-eluting stents had lower risk of in-stent restenosis and target lesion revascularisation, and lower incidence of myocardial infarction during follow-up than those who received bare metal stents. No differences were shown for occurrence of death or stent thrombosis.

**CRD commentary**

This review had clearly stated inclusion and exclusion criteria in terms of participants, study design, interventions and outcomes. The authors searched relevant databases and efforts were made to identify additional studies by reviewing reference lists of relevant literature and abstracts from relevant meetings. Funnel plots showed no evidence of publication bias despite the exclusion of unpublished studies. It was unclear whether there were any language restrictions, so language bias could not be ruled out. Appropriate efforts were made to minimise reviewer bias and error during data extraction, but it was unclear whether these were adhered to during study selection and assessment. Appropriate methods were used to pool the results and to investigate statistical heterogeneity. Appropriate subgroup analyses were carried out. However, the results of the validity assessment were neither reported nor used in the synthesis of data. It was unclear whether outcomes were pooled at similar follow-up times, which may be an issue if (as the authors suggested) risk changes over time. Given the level of evidence presented the authors’ conclusions are likely to be reliable.

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

**Practice:** For diabetic patients the clinical benefits associated with implantation of drug-eluting stents may outweigh the small but significant risk of late stent thrombosis shown in observational studies.

**Research:** The authors did not state any implications for further research.

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Not stated.

**Bibliographic details**

Record Status
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.