Meta-analysis of five randomized clinical trials comparing sirolimus- versus paclitaxel-eluting stents in patients with diabetes mellitus

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CRD summary
This review concluded that sirolimus-eluting stents significantly reduced the incidence of target lesion revascularisation and restenosis in patients with diabetes mellitus when compared with paclitaxel-eluting stents, with no significant differences in cardiac death, myocardial infarction and stent thrombosis. The uncertain quality and small size of the included trials make the reliability of the authors' conclusions unclear.

Authors' objectives
To compare the efficacy and safety of sirolimus-eluting stents with paclitaxel-eluting stents in patients with diabetes mellitus.

Searching
PubMed, EMBASE, and Cochrane Central Register of Controlled Trials were searched from January 2001 to April 2009 for publications in any language; search terms were reported.

Study selection
Randomised controlled trials (RCTs) that were head-to-head comparisons of sirolimus-eluting stents with paclitaxel-eluting stents in patients with diabetes mellitus were eligible for inclusion.

The primary outcome was target lesion revascularisation (defined as any revascularization procedure, percutaneous or surgical, involving the target lesion). Secondary outcomes were cardiac death, myocardial infarction, stent thrombosis, and the angiographic outcome of binary restenosis (50% or more).

All the included trials were multi-centred, conducted in Europe or Korea. All the participants had diabetes and coronary artery disease. The mean age of participants ranged from 61 to 68 years (where reported), the proportion of females ranged from 16 to 45%, and the proportion with insulin-dependent diabetes ranged from 13 to 41% (where reported). The mean length of the stent segments ranged from 19 to 33mm. The mean minimal luminal diameter ranged from 0.5 to 1.1mm. The mean stenosis diameter ranged from 59 to 81%. The mean number of stents ranged from 1.1 to 1.4.

The authors did not report how many reviewers performed study selection.

Assessment of study quality
A formal validity assessment was not made, although some relevant information was reported.

Data extraction
The numbers of events for each outcome were extracted in order to calculate odds ratios (OR) and 95% confidence intervals (CI), using an intention-to-treat analysis.

Two independent reviewers performed the extraction, with disagreements resolved by consensus.

Methods of synthesis
Odds ratios were pooled using fixed-effect (Mantel-Haenszel) or random-effects (DerSimonian and Laird) models. Between trial heterogeneity was determined using the Cochrane Q and I² statistics. Sensitivity analyses were performed by removing individual trials from the analyses.

Publication bias was assessed for the primary outcome using the adjusted rank correlation test (Begg and Mazumdar) and visually using a funnel plot.
Results of the review

Five RCTs were included in the review (n=1,173 patients, range 153 to 400). All the RCTs were open-label trials, since blinding was considered to be impossible. Most trials were designed exclusively for patients with diabetes, but one represented a post hoc analysis. Angiographic follow-up ranged from six to eight months; clinical follow-up ranged from six to 24 months.

Target lesion revascularisation was needed in significantly fewer patients with sirolimus-eluting stents than those with paclitaxel-eluting stents (OR 0.41, 95% CI 0.26 to 0.64); there was no evidence of publication bias. Sensitivity analyses did not change the results. Sirolimus-eluting stents were also significantly more effective than paclitaxel-eluting stents in reducing angiographic binary restenosis (OR 0.30, 95% CI 0.19 to 0.48), which was associated with a greater reduction of late luminal loss with sirolimus-eluting stents (demonstrated using angiographic follow-up data in four RCTs). There were no significant differences between sirolimus-eluting stents and paclitaxel-eluting stents for stent thrombosis, cardiac death or myocardial infarction.

All the analyses were performed using a fixed-effect model and included data from all five RCTs; none showed significant heterogeneity ($I^2=0\%$).

Authors' conclusions

Sirolimus-eluting stents were superior to paclitaxel-eluting stents in reducing the incidence of target lesion revascularisation and restenosis in patients with diabetes, with no significant differences in cardiac death, myocardial infarction and stent thrombosis.

CRD commentary

The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched in any language. But it appeared that unpublished studies were not considered. However, a formal assessment of publication bias found no evidence of publication bias for the primary outcome. Although data extraction was carried out with efforts to reduce error and bias, it was not clear whether this process applied to other aspects of the review process.

A formal trial quality assessment was not performed and few relevant details were reported. Relevant study details were reported, particularly of the included patients. Statistical heterogeneity was assessed and there was no evidence for heterogeneity. The statistical method used for the meta-analysis of the RCTs seemed appropriate. A sensitivity analysis was only performed for the primary outcome.

In view of some potential limitations arising from the review process, uncertainties about the quality of included trials and their small size, the extent to which the authors' conclusions are reliable is unclear.

Implications of the review for practice and research

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

**Research**: The authors identified a need for studies with longer term follow-up and larger studies with more power.

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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.