Clinical safety and efficacy of everolimus-eluting stents compared to paclitaxel-eluting stents in patients with coronary artery disease

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CRD summary
The review concluded that everolimus-eluting stents were superior to paclitaxel-eluting stents for safety and efficacy at one year follow-up for patients with coronary artery disease. The authors' conclusions reflect the evidence presented, but lack of reporting of review methods and lack of quality assessment of the included trials mean the reliability of the conclusions is uncertain.

Authors' objectives
To evaluate the safety and efficacy of everolimus-eluting stents compared with paclitaxel-eluting stents for patients with coronary artery disease.

Searching
PubMed, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from January 2001 to August 2010 for relevant articles. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared everolimus-eluting stents with paclitaxel-eluting stents in patients with obstructive coronary artery disease and reported clinical outcomes were eligible for inclusion.

The primary outcome of interest was a composite of major adverse cardiac events (cardiac death, non-fatal myocardial infarction, and ischemia-driven target lesion revascularisation either by percutaneous or surgical intervention) occurring within one year of follow-up. Secondary endpoints included all-cause mortality, cardiac death, non-fatal myocardial infarction, ischaemia-driven target lesion revascularisation, ischaemia-driven target vessel revascularisation and stent thrombosis at one year.

In all included trials, from 300 to 600mg of clopidogrel was administered before treatment; maintenance therapy of clopidogrel for six to 12 months was provided for both intervention groups. The mean age of the included patients ranged from 62 to 63.6 years; the proportion of men ranged from 65.7 to 79%. There was baseline equivalence between treatment arms within trials for cardiac risk factors (current smoker, diabetes, hypertension, hypercholesterolemia, and prior myocardial infarction).

The authors did not state how studies were selected for inclusion.

Assessment of study quality
The authors did not state that they assessed trial quality.

Data extraction
Data for the relevant outcomes were extracted and used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Analyses were performed on an intention-to-treat basis.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
Data were pooled using either a Mantel-Haenszel fixed-effect model or a DerSimonian and Laird random-effects model according to the presence or absence of heterogeneity. Heterogeneity was assessed using Cochran's test. Sensitivity analyses were conducted removing individual trials from the main analyses.

Publication bias was assessed for the primary outcome according to methods by Begg and Mazumdar.
Results of the review
Four RCTs (n=6,788 patients) were included in the review (4,247 in the everolimus-eluting stent group and 2,541 in the paclitaxel-eluting stent group).

There were significantly fewer major adverse cardiac events (including cardiac death, myocardial infarction and ischaemia driven target revascularisation) at one year of follow-up with everolimus-eluting stents compared with paclitaxel-eluting stents for patients with coronary artery disease (OR 0.57, 95% CI 0.46 to 0.70; four RCTs). There was no evidence of publication bias for this outcome. Sensitivity analyses did not significantly alter the results (data not reported).

At one year, rates were also lower for everolimus-eluting stents compared with paclitaxel-eluting stents for ischaemia-driven target lesion revascularisation (OR 0.48, 95% CI 0.37 to 0.64), ischaemia-driven target vessel revascularisation (OR 0.60, 95% CI 0.47 to 0.75), myocardial infarction (OR 0.57, 95% CI 0.42 to 0.76) and definite or probable stent thrombosis (OR 0.34, 95% CI 0.20 to 0.59). Both early (within one month) and late (one month to one year) stent thrombosis occurred in fewer patients with everolimus-eluting stents compared with paclitaxel-eluting stents (early OR 0.25, 95% CI 0.11 to 0.58; late OR 0.37, 95% CI 0.16 to 0.89).

There were no significant differences between everolimus-eluting stents and paclitaxel-eluting stents for all-cause and cardiac mortality at one year follow-up.

There was no evidence of statistical heterogeneity for any of the analyses.

Authors’ conclusions
Everolimus-eluting stent use resulted in reduced rates of ischaemia-driven target lesion revascularisation, myocardial infarction and stent thrombosis compared with paclitaxel-eluting stents for patients with coronary artery disease, which led to a reduction in major adverse cardiac events at one year after initial procedure.

CRD commentary
The review question was clear with appropriate inclusion criteria. Several relevant sources were searched. It appeared that only published studies were eligible for inclusion, but analysis found no evidence of publication bias. Methods used to assess studies for inclusion and extract data were not described, so it was not known whether steps were taken to reduce reviewer error and bias.

The quality of the included trials was not assessed, so it was difficult to determine the reliability of the evidence presented. Combining trials in meta-analyses appeared appropriate; statistical heterogeneity was assessed. The authors noted as a limitation that three of the included trials used an older version of paclitaxel-eluting stent, while one trial used a later version of paclitaxel-eluting stent.

The authors’ conclusions reflect the evidence presented, but lack of reporting of review methods and lack of quality assessment of the included trials mean the reliability of their conclusions is uncertain.

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

Research: The authors stated that studies with longer follow-up are required to provide additional information as to the efficacy and safety of everolimus-eluting stents for patients with coronary artery disease.

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