Twelve-month clinical outcomes of everolimus-eluting stent as compared to paclitaxel- and sirolimus-eluting stent in patients undergoing percutaneous coronary interventions, A meta-analysis of randomized clinical trials
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CRD summary
This well-conducted review found that treatment with everolimus-eluting stents was associated with decreased target-lesion revascularisation and myocardial infarction rates after 12 months compared with paclitaxel-eluting and sirolimus-eluting stents, with similar mortality. The authors' conclusions are likely to be reliable.

Authors' objectives
To assess the efficacy and safety of everolimus-eluting stents compared with paclitaxel-eluting stents or sirolimus-eluting stents in patients undergoing percutaneous coronary interventions.

Searching
MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE databases were searched up to August 2010; search terms were reported. Scientific session abstracts in the Journal of the American College of Cardiology, Circulation, the European Heart Journal and the American Journal of Cardiology were handsearched. The web sites of five cardiology organisations and http://www.clinicaltrialresults.org were also searched. Reference lists of the retrieved studies were checked for additional trials. There were no language or publication status restrictions.

Study selection
Randomised controlled trials (RCTs) that compared everolimus-eluting stents with paclitaxel-eluting or sirolimus-eluting stents in patients undergoing percutaneous coronary interventions were eligible for inclusion. Ongoing trials and trials with irretrievable data or the use of bare-metal stents in the control arm were excluded from the review. The primary outcome of the review was ischaemia-driven target-lesion revascularisation at 12-month follow-up. Secondary outcomes were death, myocardial infarction and stent thrombosis.

The included trials were conducted from 2005 to 2008. Most were multi-centre trials. The proportion of men included in the trials ranged from 67 to 77%. Included patients presenting with acute coronary syndromes ranged from 0 to 60%. Most trials compared everolimus-eluting stents with paclitaxel-eluting stents; one trial compared everolimus-eluting stents with biodegradable-polymer sirolimus-eluting stents or durable-polymer paclitaxel-eluting stents. A loading dose of 300mg to 600mg clopidogrel was given before or after percutaneous coronary interventions in all except one trial. Aspirin was prescribed indefinitely in all the trials. Antiplatelet therapy of clopidogrel was given for at least six months in most trials.

Two reviewers independently performed the study selection; any disagreements were resolved with a third reviewer.

Assessment of study quality
Two reviewers evaluated the methodological quality of the trials for adequacy of sequence generation, allocation concealment, blinding, completeness of data outcomes, presence of selective outcome reporting, other potential sources of bias and sample size calculation.

Data extraction
Data were extracted to calculate odds ratios (OR) and 95% confidence intervals (CI) for the outcomes.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated using a Mantel-Haenszel fixed-effect model. Heterogeneity was assessed using the Breslow-Day test and I². Where significant statistical heterogeneity was present, pooled summary statistics were calculated using a DerSimonian and Laird random-effects model. The numbers-needed-
to-treat (NNT) for benefit were calculated with 95% confidence intervals.

Sensitivity analyses were conducted by omitting one trial at a time.

Publication bias was evaluated using funnel plots and the Harbord and Peters tests.

**Results of the review**

Five RCTs (8,058 patients) were included in the review. Sample size calculations, allocation concealment, and incomplete data outcomes were addressed in all the trials. Adequate sequence generation was performed in four trials. All the trials were free of selective reporting and other sources of bias. The outcome assessors were blinded in four trials.

Treatment with everolimus-eluting stents was associated with statistically significant benefits compared with paclitaxel-eluting or sirolimus-eluting stents. There were reductions in target-lesion revascularisation (OR 0.56, 95% CI 0.45 to 0.70; I²=25%; NNT=40 patients, 95% CI 32 to 58) and myocardial infarction (OR 0.57, 95% CI 0.43 to 0.77; I²=0%; NNT=61 patients, 95% CI 46 to 114). There was a reduced incidence of stent thrombosis with everolimus-eluting stents with paclitaxel-eluting stents or sirolimus-eluting stents, but this change was not statistically significant (OR 0.45, 95% CI 0.20 to 1.01; I²=57%). There were no significant differences in mortality between everolimus-eluting stents and paclitaxel-eluting stents or sirolimus-eluting stents.

When the trial of sirolimus-eluting stents versus everolimus-eluting stents was omitted in the sensitivity analysis, there was a significantly reduced rate of stent thrombosis (OR 0.30, 95% CI 0.16 to 0.55; I²=0%; NNT=42 patients, 95% CI 34 to 59). No small-study effects were observed for the primary outcome of target-lesion revascularisation.

There was no evidence of publication bias observed in the Harbord or Peters tests.

**Authors’ conclusions**

At one year follow-up, treatment with everolimus-eluting stents was associated with decreased target-lesion revascularization and myocardial infarction rates compared with paclitaxel-eluting and sirolimus-eluting stents, with similar mortality.

**CRD commentary**

The review addressed a defined question. Clear criteria for the inclusion of studies were defined. Appropriate sources were searched to identify trials. There were no language restrictions. Steps were taken to minimise errors and biases for study selection and quality assessment, but were not reported for data extraction.

The authors’ decision to pool the results in a meta-analysis appeared to be justified. Potential sources of heterogeneity were explored in sensitivity analyses.

The review was generally well conducted and the authors’ conclusions are likely to be reliable.

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

**Practice:** The authors stated that the findings from the review supported the safety and efficacy of everolimus-eluting stents implantation in routine clinical practice.

**Research:** The authors stated that larger studies with longer follow-up were necessary to assess the different effects that treatment with everolimus-eluting stents had on the occurrence of stent thrombosis compared with sirolimus-eluting stents treatment.

**Funding**

None.

**Bibliographic details**

PubMedID
21315461

DOI
10.1016/j.ijcard.2011.01.015

Original Paper URL
http://www.internationaljournalofcardiology.com/article/S0167-5273(11)00345-3/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Angioplasty, Balloon, Coronary /trends; Drug-Eluting Stents /trends; Everolimus; Humans; Paclitaxel /administration & dosage; Randomized Controlled Trials as Topic /trends; Sirolimus /administration & dosage /analogs & derivatives; Treatment Outcome

AccessionNumber
12011004530

Date bibliographic record published
07/12/2011

Date abstract record published
21/05/2012

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.