Meta-analysis of long-term outcomes of drug-eluting stent implantations for chronic total coronary occlusions
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CRD summary
Compared to bare metal stents, drug-eluting stents for chronic total coronary occlusions reduced rates of stent restenosis, reocclusion, major adverse cardiovascular events and the need for repeated angiography. No difference was found for death and myocardial infarctions. Concerns about the uncertain quality of much of the evidence mean that the reliability of the conclusions is unclear.

Authors' objectives
To evaluate the balance of risk and benefit of drug-eluting stent implantation compared to bare metal stents implantation in the treatment of chronic total coronary artery occlusion.

Searching
MEDLINE, EMBASE, the Chinese Biomedical Database (to April 2009) and The Cochrane Library (to Issue three, 2009) were searched. Reference lists of retrieved papers and reviews were checked. No language restriction was applied. Main search terms were reported.

Study selection
Studies that compared drug-eluting stents implantation with bare metal stents implantation to treat patients with chronic total coronary artery occlusion diseases were included. Minimum follow-up period was six months. Studies with incomplete data, lack of baseline or follow-up data, duplicate publications and ongoing studies were excluded.

Major adverse cardiovascular events (MACEs) were the primary outcome of interest and were a composite of all-cause death, myocardial infarctions and target vessel revascularisation. Secondary outcomes were all-cause death, myocardial infarction, target vessel revascularisation, target lesion revascularisation, target vessel failure and angiographic outcomes that involved minimal lumen diameter, late lumen loss, restenosis and reocclusion. Definitions for secondary outcomes were reported.

Studies were published between 2004 and 2008 inclusive. Six studies used sirolimus-eluting stents, two used paclitaxel-eluting stents and two studies used both. Patients had a mean age of 63 years. About three-quarters were male. The proportion of patients with diabetes ranged from 10% to 33% across studies. About half had experienced a previous myocardial infarction (range from 36% to 67% across studies), a history of hypertension (39% to 79%) and nearly two-thirds had a history of hyperlipidaemia (34% to 90%). Six studies reported a mean left-ventricular ejection fraction of 57% at baseline.

Two reviewers independently selected studies for inclusion. Disagreements were resolved by discussion or with a third reviewer when necessary.

Assessment of study quality
Study quality was assessed following The Cochrane Handbook, covering randomisation, allocation concealment, blinding, reported loss to follow-up, or withdrawal and comparability at baseline.

Two reviewers independently assessed study quality. Disagreements were resolved by discussion or with a third reviewer when necessary.

Data extraction
Data on the specified outcomes were extracted to permit the calculation of odds ratios (ORs) and mean differences.

Two reviewers independently extracted data. Disagreements were resolved by discussion or with a third reviewer when necessary.
Methods of synthesis
Studies were pooled using Mantel-Hetzel fixed-effect and random-effects models. Statistical heterogeneity was assessed using $\chi^2$ and $\hat{I}^2$. A fixed-effect model was used in case of no observed heterogeneity ($\hat{I}^2=0\%$). If statistical heterogeneity was evident, a sensitivity analysis, subgroup analysis or random-effects model were applied. Publication bias was assessed with a funnel plot.

Results of the review
Ten studies (1,678 patients) were included in the review: two RCTs (327 patients) and eight non-randomised controlled studies (1,351 patients). The median follow-up period was 13 months (range six to 36 months) for clinical endpoints, and six months (six to 36 months) for angiographic endpoints.

Major adverse cardiovascular events
No significant difference was found for in-hospital major adverse cardiovascular events between drug-eluting stents and bare metal stents implantation (OR 1.07; 95\% CI 0.53 to 2.13; 1,002 patients; five studies; $\hat{I}^2=0\%$). There was a significant difference between the groups for long-term major adverse cardiovascular events (OR 0.22; 95\% CI 0.13 to 0.38; 1,678 patients; 10 studies; $\hat{I}^2=65\%$). Subgroup and sensitivity analyses yielded similar results.

Myocardial infarction and all-cause death: None of the analyses showed a significant difference in effect or any evidence of heterogeneity.

Target lesion revascularisation and target vessel revascularisation: Patients who received drug-eluting stents implantation had significantly lower long-term rates of target lesion revascularisation, target vessel revascularisation rate and target vessel failure compared with patients who received bare metal stents.

Angiographic outcomes: The following angiographic outcomes also showed statistically significant benefits of drug-eluting stents: minimal lumen diameter; late lumen loss; rates of stent restenosis; and reocclusion.

No evidence of publication bias was found.

Authors’ conclusions
Drug-eluting stents implantation improved long-term angiographic and clinical outcomes compared with bare metal stents in the treatment of chronic total coronary artery occlusion.

CRD commentary
The review question and inclusion criteria were clear. Literature searches were reasonably thorough. Studies with missing data were excluded and there was no indication that unpublished papers were sought. Therefore, studies may have been missed and there was a risk of publication bias. While a subsequent evaluation did not find evidence of it, the tests used to assess publication bias may have been unreliable as only a small number of studies were included. Study selection, data extraction and quality assessment were carried out with sufficient attempts to minimise error and bias.

Study population details were adequately provided. The limited reporting on the results of the quality assessment may have limited the reliability of the findings. Most studies were not randomised, which suggested a risk of selection bias. Studies included in the analysis were of different designs, so it was unclear whether pooling was appropriate. Heterogeneity was assessed appropriately. Only two studies reported outcomes beyond 12 months. Follow-up may have been too short and studies may have been too small to identify significant differences in clinical outcomes such as death and myocardial infarction.

Due to the non-randomised nature and uncertain quality of much of the evidence, the reliability of the conclusions is unclear.

Implications of the review for practice and research
Practice: No implications for practice were reported.

Research: More high-quality randomised controlled trials with larger samples were needed to evaluate the effect of drug-eluting stents on clinical and angiographic outcomes.
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