Efficacy and safety of drug-eluting stents in chronic total coronary occlusion recanalization: a systematic review and meta-analysis

CRD summary
The authors concluded that drug-eluting stents used in chronic total occlusion were associated with significantly fewer major adverse cardiac events and fewer occurrences of target vessel revascularisation, restenosis and stent occlusion compared with bare metal stents. The review was generally well conducted and the authors’ conclusions appear appropriate.

Authors' objectives
To compare the efficacy and safety of drug-eluting stents with bare-metal stents used in chronic total occlusion recanalisation.

Searching
MEDLINE and the Cochrane Library databases were searched between January 2002 and May 2009 for articles in any language. Search terms were reported. The conference proceedings and websites of the American College of Cardiology, the American Heart Association, the European Society of Cardiology, Transcatheter Cardiovascular Therapeutics and EuroPCR were also searched.

Study selection
Studies of drug-eluting stents (sirolimus or paclitaxel) compared with bare-metal stents for chronic total occlusion recanalisation were eligible for inclusion. Studies had to provide clinical or angiographic outcome data over at least six months follow-up after stent implantation.

The relevant outcomes included major adverse cardiac events, target vessel revascularisation, death, myocardial infarction, and stent thrombosis.

The included studies compared paclitaxel, sirolimus or a mixture of paclitaxel and sirolimus drug-eluting stents with bare-metal stents. The mean reference vessel diameter was 2.60mm to 3.61mm, and the occlusion length was 16mm to 32.5mm (where reported). The majority of included patients had an average duration of occlusion of at least 12 weeks. The prevalence of diabetes ranged from 14 to 33% and the proportion of previous myocardial infarction varied from 35 to 73% (where reported). The mean age of patients ranged from 58 to 70 years and the proportions of male patients varied from 63 to 89% (where reported).

Two authors independently undertook the selection process; disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
Quality assessment was undertaken by two reviewers using the Cochrane Collaboration tool for RCTs and the Newcastle-Ottawa scale for non-randomised controlled studies. Disagreements were resolved by discussion with a third reviewer.

Data extraction
Two authors independently extracted data on major adverse cardiac events, target vessel revascularisation, death, myocardial infarction and stent thrombosis. These were used to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

Methods of synthesis
The pooled risk ratios, together with 95% confidence intervals, were calculated using a random-effects meta-analysis. Statistical heterogeneity was assessed using the Cochran Q and I$^2$ statistic. Publication bias was assessed using funnel
plots, Begg’s correlation and Egger’s regression.

Sensitivity analysis was undertaken to assess the importance of individual studies on the results.

The number-needed to treat (NNT) was also estimated.

**Results of the review**

Fourteen comparative studies were included in the review (n=4,394 patients): two RCTs, one non-randomised controlled study, three retrospective cohorts, and eight historically controlled studies. The quality of the RCTs was deemed moderate, and the quality of the non-randomised studies ranged from 4 to 7 out of 8. There was no evidence of publication bias for major adverse cardiac events, restenosis or stent reocclusion, although there was some evidence of publication bias with target vessel revascularisation (in terms of funnel plot assessment, although Begg’s test and Egger’s test did not show statistical significance).

**Cardiac outcomes and death:** Compared with bare-metal stents, drug-eluting stents had significantly less major adverse cardiac events (RR 0.41, 95% CI 0.29 to 0.58; $I^2=73%$; NNT=9; 13 studies; figures taken from the forest plot not the text). There was no difference between bare-metal and drug-eluting stents in terms of myocardial infarction or death. The benefit in terms of major adverse cardiac event risk reduction was sustained with drug-eluting stents up to three years.

**Vessel outcomes:** Compared with bare-metal stents, drug-eluting stents had significantly less target vessel revascularisation (RR 0.45, 95% CI 0.34 to 0.60; $I^2=62%$; NNT=10; 13 studies; figures taken from the forest plot not the text), restenosis (RR 0.25, 95% CI 0.16 to 0.41; $I^2=72%$; NNT=5; 10 studies), and stent re-occlusion (RR 0.30, 95% CI 0.18 to 0.49; $I^2=0%$; NNT=14; seven studies). Compared with bare-metal stents, drug-eluting stents had a higher rate of stent thrombosis (RR 2.79), but the results were not statistically significant. The benefit in terms of target vessel revascularisation reduction was sustained with drug-eluting stents up to three years. Follow-up angiography was undertaken in 75% of patients, with a higher number of restenosis in the bare-metal stent group (358 patients) compared with the drug-eluting stent group (106 patients).

**Sensitivity analysis:** Exclusion of individual studies had no significant effect on overall results.

**Authors’ conclusions**

Drug-eluting stents used in chronic total occlusion were associated with significantly fewer major adverse cardiac events and fewer occurrences of target vessel revascularisation, restenosis and stent occlusion compared with bare-metal stents. Although there was a statistical trend toward a higher risk of stent thrombosis with drug-eluting stents, further evidence is needed to confirm this.

**CRD commentary**

Inclusion criteria for the review were clearly defined and several relevant databases were searched without language restrictions. Publication bias was assessed, and there was little evidence to indicate its presence in any of the analyses. Two authors performed study selection, data extraction and quality assessment, which should have minimised the possibility of error and bias in the analysis.

Quality assessment indicated the moderate quality of most of the included studies, which the authors acknowledged. Studies were combined using random-effects meta-analysis; sources of heterogeneity were explored, which was appropriate.

The review was generally well conducted and the authors’ conclusions appear appropriate.

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

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

**Research:** The authors stated that further research is needed to assess the rate of stent thrombosis with drug-eluting
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