Off-label use of drug-eluting versus bare metal stents: a lesion-specific systematic review of long-term outcomes

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CRD summary
This review concluded that rates of mortality, myocardial infarction and stent thrombosis were similar in patients with bare metal stents and those with drug-eluting stents. Rates of target lesion revascularisation were lower in patients with drug-eluting stents. These conclusions should be interpreted with caution given the low methodological rigour of most of the included studies and concerns about review methods.

Authors' objectives
To compare the efficacy and safety with the off-label use of drug-eluting stents versus bare metal stents.

Searching
PubMed and The Cochrane Library were searched from May 2000 to April 2008. Search terms were reported. Four relevant web sites (www.acc.org, www.theheart.org, www.tctmd.com, www.clinicaltrialresults.org) were searched for studies. Only published studies in English were considered.

Study selection
Studies that evaluated off-label use of drug-eluting stents and bare metal stents and reported at least one lesion-specific outcome were eligible for inclusion. Eligible studies needed to have at least six-month follow-up. Only studies with at least 25 patients were eligible. The efficacy outcome was target lesion revascularisation. Target vessel revascularisation was used as a surrogate measure when target lesion revascularisation was not reported. Safety outcomes included overall mortality, myocardial infarction and stent thrombosis.

Of included studies, indications with off-label use included left main lesions, saphenous vein grafts, in-stent restenosis, ostial lesions, bifurcation lesions, chronic total occlusions, small vessels, long lesions and calcified lesions. Most studies were from registry databases. Some randomised controlled trials (RCTs) were included. The mean age of included patients was 63 years. Most patients were male. Compared to patients with bare metal stents, patients with drug-eluting stents were more likely to have diabetes mellitus, hypertension and renal insufficiency. Eight per cent of patients with bare metal stents had a prior coronary artery bypass grafting (CABG) and 4.9% of patients with drug-eluting stents had a prior CABG. Fifty-two per cent of patients with bare metal stents had multivessel disease and 64% of patients with drug-eluting stents had this condition. Use of heparin, beta blockers and angiotensin converting enzyme inhibitors was similar between patients who received drug-eluting stents and those who received drug-eluting stents.

Two reviewers independently assessed studies for inclusion.

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

Data extraction
Data were extracted on the number of patients in each group who experienced an event. It appeared that one reviewer performed data extraction.

Methods of synthesis
Weighted event rates, with 95% confidence intervals (CIs), were calculated separately for groups with bare metal stents and drug-eluting stents using a fixed-effect model. The inverse variance weighting method was employed. Subgroup analyses were conducted by lesion types, as well as registry studies only.

Results of the review
One hundred and twelve studies were included (13,699 patients with drug-eluting stents and 8,739 patients with bare
metal stents). Most studies were registry studies. The number of included RCTs was not reported. Sample size ranged from 25 to 2,484. Most outcomes were reported at six to 12 month and three-year follow-ups.

**Efficacy:** The rate of target lesion revascularisation was 19.6% (95% CI 17.8% to 21.6%) in patients who received bare metal stents and 7.5% (95% CI 6.5% to 8.7%) in patients who received drug-eluting stents at six to 12 month follow-up. At two-year follow-up, the rate of target lesion revascularisation was 16.9% (95% CI 10.3% to 26.6%) in patients who received bare metal stents and 6.6% (95% CI 4.5% to 9.5%) in patients who received drug-eluting stents. At two-year follow-up, the rate of myocardial infarction was 5.0% (95% CI 1.9% to 13.0%) in patients who received bare metal stents and 3.7% (95% CI 2.7% to 5.1%) in patients who received drug-eluting stents.

**Safety:** Overall mortality at six to 12 month follow-up was 3.3% (95% CI 2.6% to 4.3%) for patients who received bare metal stents and 2.8% (95% CI 2.2% to 3.6%) for those who received drug-eluting stents. Overall mortality rates were similar at three-year follow-up between patients who received bare metal stents and those who received drug-eluting stents: 18.8% (95% CI 13.5% to 24.1%) versus 15.3% (95% CI 8.5% to 26.0%). Rates of myocardial infarction were 6.5% (95% CI 5.2% to 8.0%) in patients who received bare metal stents and 6.0% (95% CI 5.0% to 7.1%) in patients who received drug-eluting stents at six to 12 month follow-up. Overall stent thrombosis rates were 1.8% (95% CI 0.8% to 3.8%) in patient who received bare metal stent and 1.7% (95% CI 1.2% to 2.4%) in those who received drug-eluting stents at six to 12 month follow-up.

Results of subgroup analyses were reported.

**Authors' conclusions**
Rates of mortality, myocardial infarction and stent thrombosis were similar between patients who received bare metal stents and those who received drug-eluting stents. Rates of target lesion revascularisation were lower in patients who received drug-eluting stents.

**CRD commentary**
The review's inclusion criteria were clear. Relevant databases were searched. The decision to restrict the review to published studies in English may have increased the possibility of language and publication biases. It appeared that only one reviewer performed data extraction, so biases and errors in this review process could not be ruled out. No formal validity assessment was performed. Most of the included studies were observational studies (studies with this type of design are of low methodological rigour). The authors stated that some RCTs were included in the review, but it was unclear how many. All RCTs were treated as observational cohorts in the analyses. Given the diversity of included studies, deriving a single pooled event rate from these studies may be not have been appropriate. It was unclear whether statistical heterogeneity between included studies was assessed in the pooled analyses.

The authors' conclusions should be interpreted with caution given the low methodological rigour of most of the included studies and concerns in the review methods.

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

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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.