Drug-eluting versus bare-metal stent for treatment of saphenous vein grafts: a meta-analysis

CRD summary
This generally well-conducted review found observational studies showed lower risk of target vessel revascularisation, myocardial infarction, stent thrombosis and mortality in patients with saphenous vein graft lesion using drug-eluting versus bare-metal stents. The authors acknowledged observational studies were prone to selection bias and the findings were not supported by underpowered controlled trials. These conclusions reflect the uncertainties surrounding the evidence.

Authors' objectives
To compare the efficacy of drug-eluting stents versus bare-metal stents for the treatment of saphenous vein graft lesions.

Searching
EMBASE, MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), International Pharmaceutical Abstracts, and Web of Science were searched from 2002 up to March 2010. Search terms were reported. Abstracts and conference proceedings from meetings of the American College of Cardiology (2006 to 2010), European Society of Cardiology (2006 to 2009), Transcatheter Cardiovascular Therapeutics, and the American Heart Association were scanned. Reference lists of selected articles were manually searched. Primary authors were contacted for further information. Other internet based sources were assessed (Google Scholar, www.tctmd.com, www.theheart.org).

Study selection
Randomised controlled trials (RCTs) and non-RCTs that directly compared drug-eluting stents versus bare-metal stents (with and without the use of protection devices) in patients with saphenous vein graft stenosis were eligible for inclusion. The primary outcome of interest was target vessel revascularisation (or target lesion revascularisation). Secondary outcomes were myocardial infarction, stent thrombosis, or mortality.

Included studies were of patients aged from 65 to 75 years. Graft age ranged from 11 to 12.6 years in the RCTs and from 7.5 to 12.9 years in the observational studies (where reported). Drug-eluting stents used paclitaxel and/or sirolimus. Where reported, 0 to 100% of procedures used protection devices.

Two reviewers independently screened studies for inclusion, with final inclusion of studies based on agreement of both reviewers.

Assessment of study quality
Two reviewers assessed the quality of RCTs according to the Jadad scale, but the results were not reported in the review.

Data extraction
Two reviewers extracted data on the number of outcome events to calculate odds ratios (ORs) and their 95% confidence intervals (CIs). Primary authors were contacted for further information where necessary. Disagreements were resolved by re-checking the data.

Methods of synthesis
A random-effects model was used to pool odds ratios and their 95% confidence intervals. Separate analyses were undertaken for RCTs and observational studies. Where no events occurred in one treatment arm, continuity correction was used. Analyses were based on an intention-to-treat basis.

Statistical heterogeneity was assessed using $I^2$; where this was evident, stratified analyses were undertaken by type of drug-eluting stents used in the drug-eluting stent treatment arms, publication date, study size, and duration of follow-up. Sensitivity analyses were undertaken to include only updated unpublished data from the RCTs.
Publication bias was assessed in the RCTs using the Egger's test and funnel plots.

**Results of the review**

Three RCTs (n=202 patients) and 26 observational registries (n=7,347 patients) were included in the review. The authors reported that all included trials had sufficient quality. The median follow-up in the RCTs ranged from 18 to 32 months (where reported). Follow-up in the observational studies ranged from six to 48 months (where reported).

**Target vessel revascularisation (or target lesion revascularisation):** There were fewer occurrences of target vessel revascularisation in patients who received drug-eluting compared with bare-metal stents; the difference was not significant for the three RCTs (OR 0.50, 95% CI 0.24 to 1.00; $I^2=16.2\%$), but was statistically significant for the observational studies (OR 0.62, 95% CI 0.49 to 0.79; 26 studies). There was evidence of heterogeneity among the observational studies ($I^2=56.3\%$).

**Myocardial infarction:** Three RCTs showed no statistically significant differences in the occurrence of myocardial infarction between patients who received drug-eluting stents and those who received bare-metal stents, but there was evidence of heterogeneity ($I^2=64.8\%$). The observational studies showed fewer incidences of myocardial infarction in the drug-eluting compared with the bare-metal stent group (OR 0.68, 95% CI 0.49 to 0.95; $I^2=23\%$; 19 studies).

**Stent thrombosis:** Two RCTs showed no statistically significant difference between drug-eluting and bare-metal stents in the occurrence of stent thrombosis, but there was evidence of heterogeneity ($I^2=68.2\%$). The observational studies showed significantly fewer incidences of stent thrombosis in the drug-eluting stent than the bare-metal stent group (OR 0.58, 95% CI 0.38 to 0.84; $I^2=0\%$; 12 studies).

**Mortality:** Three RCTs showed no statistically significant difference in mortality rates between drug-eluting and bare-metal stents, but there was evidence of substantial heterogeneity ($I^2=75.8\%$). The observational studies showed statistically significantly fewer deaths in patients who received drug-eluting stents compared with those who received bare-metal stents (OR 0.69, 95% CI 0.55 to 0.85; $I^2=19\%$; 23 studies).

Sensitivity analyses showed statistically significantly fewer incidences of target vessel revascularisation in the drug-eluting stent compared with the bare-metal stent group (OR 0.40, 95% CI 0.16 to 0.96; $I^2=48\%$; three RCTs), but results for other outcomes were not significantly altered. Stratified analyses showed that publication date and study size influenced effect size.

There was no evidence of publication bias for RCTs reporting target vessel revascularisation.

**Authors' conclusions**

Observational studies showed that drug-eluting stents may decrease the rate of target vessel revascularisation, rate of myocardial infarction, stent thrombosis and death in patients with saphenous vein graft lesions, but this was not supported by data from three small RCTs. These findings could reflect patient selection bias in the observational studies or represent a true finding that was not detected by the underpowered RCTs.

**CRD commentary**

A substantial search of the literature was undertaken and included a search for published and unpublished data, which reduced the potential for missed data. It was unclear whether any language restrictions were introduced. Publication bias was assessed; the authors acknowledged the limitations of the results due to the small sample bias. Each stage of the review process was undertaken in duplicate, thereby reducing the potential for reviewer error and bias.

The quality of the RCTs was not reported, so it was unclear how robust the findings were. The authors acknowledged that only a small number of underpowered RCTs were included in the analyses. Separate pooling of the RCTs and observational studies was appropriate, but the findings from the separate analyses were conflicting, and confidence intervals were wide for some outcomes using RCT data only. There was some evidence of heterogeneity, which was investigated appropriately. The authors also acknowledged that observational data were prone to bias, and that most studies had short follow-up durations.
This was a generally well-conducted review. The authors’ conclusions reflect the uncertainties surrounding the available evidence and highlight the need for caution when interpreting the findings.

Two authors disclosed financial links with Abbott Vascular (manufacturers of coronary stents).

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

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