Efficacy and safety of drug-eluting stents: current best available evidence

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CRD summary
This review concluded that drug eluting stents compared to bare metal stents substantially reduce in-stent restenosis and repeat revascularization for patients at low risk of subsequent restenosis, with no effect on medium-term mortality or myocardial infarction rates. Lack of reporting of review methods and limited synthesis of data make the reliability of the authors' conclusion difficult to determine.

Authors' objectives
To evaluate the effectiveness and safety of drug-eluting stents (DES) in the management of symptomatic obstructive coronary artery disease.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Current Contents, DARE, NHS EED, Science Citation Index and International Network of Agencies for Health Technology Assessment databases were searched from January 1986 to June 2005. Search terms were reported. No language restrictions were applied. Hand searching of bibliographies, scientific meeting abstracts and related journals were also conducted.

Study selection
Randomised controlled trials (RCTs) comparing sirolimus or paclitaxel eluting stents with bare metal stents (BMS) in adult patients undergoing single or multiple vessel stenting and reporting at least one outcome, with at least six months follow-up, were eligible for inclusion. Clinical outcomes of interest were: event rate or event-free survival; major adverse cardiac events (MACE); major adverse cardiac and cerebrovascular events (MACCE); target vessel failure or other composites of events. These other composite outcomes included death, acute myocardial infarction (AMI), target vessel revascularization (TVR), target lesion revascularization (TLR) and repeat treatment (percutaneous transluminal coronary angioplasty (PCTA), stent or coronary artery bypass graft (CABG)). Radiological outcomes of interest were binary restenosis and/or late loss/late loss index (measuring minimal lumen diameter differences immediately post-procedure and at follow-up). Patients with a recent history of myocardial infarction or a low ejection fraction were excluded.

Interventions in the included studies were various types of sirolimus-eluting balloon expandable stents and paclitaxel eluting stents. The proportion of male participants in the included studies ranged from 69% to 88%. Risk of restenosis ranged from low to intermediate. Prevalence of diabetes ranged from 15% to 29%. Quantitative coronary angiography follow up was undertaken in 43% to 97% of participants. Length of follow-up ranged from six months to 12 months. Most studies enrolled patients with de novo lesions in a native coronary artery. All patients were additionally given aspirin indefinitely and antiplatelet drugs for at least two to six months.

The authors did not state how papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using published critical appraisal checklists. In addition studies were graded A (high) to D (low), based on the level of evidence. The authors did not state how the validity assessment was performed.

Data extraction
Data on the number of patients treated with each type of stent and key outcomes were extracted. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative synthesis, taking into account the source and strength of evidence. Each study...
was described in the text and additional descriptive information was presented in tables.

**Results of the review**

Eleven RCTs (n=5,287) were included in the review (n=2,731 for DES; n=2,556 for BMS). The authors reported that the trials were well conducted, with random treatment allocation, blinding of allocation for most trials and clinical follow-up rates of more than 90%.

The authors reported that “evidence suggests the restenosis rate on routine follow-up angiography was substantially lower with DES than with BMS with consequent reductions in rates of target-lesion revascularization and major adverse cardiac events”.

There were no statistically significant differences between DES and BMS groups for death rates (11 RCTs).

Late loss (measured in mm) was statistically significantly lower for DES groups than BMS groups (10 RCTs, p=<0.001 to 0.0001; one RCT, p=<0.001).

DES groups reported statistically significantly lower rates of restenosis (eight RCTs, p=<0.001 to 0.0001; one RCT, p=<0.001) and MACE (two RCTs, p=<0.001 to 0.0001; four RCTs, p=0.006 to 0.0002; one RCT, p=<0.001) than BMS groups.

**Cost information**

Estimated additional costs for using DES as opposed to BMS range from a cost saving to $2,800 per person.

**Authors’ conclusions**

The current best available evidence from RCTs suggests that DES in comparison to BMS substantially reduces the incidence of in-stent restenosis and for the need for repeat revascularization procedures when used in patients who are at low risk of subsequent restenosis, without any effect on medium-term mortality or rates of myocardial infarction. DES appears to be safe over the short and medium term but there is a paucity of data to enable firm conclusions to be drawn.

**CRD commentary**

Inclusion criteria were clearly defined in terms of interventions, participants, outcomes and study design. Several relevant sources were searched and search terms reported. Efforts were made to reduce language bias but no efforts were made to reduce publication bias. Methods used to select studies, assess validity and extract data were not described, so it is not known whether efforts were made to reduce reviewer errors and bias. Validity was assessed using specified established criteria but results of the validity assessment were poorly reported and limited to the adequacy of randomisation. Characteristics of the included studies were presented in tables. The authors did not report why they undertook a narrative analysis rather than a meta-analysis. The results of each study were reported in a table with some data also reported in the text, although the authors only conducted a minimal synthesis of the data. The lack of reporting of review methods, lack of details of validity assessment and limited synthesis of data make the reliability of the authors’ conclusion difficult to determine.

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

Practice: The authors stated that although there is a significant impact of DES on coronary artery surgery volume compared to BMS, the two techniques should be regarded as complementary and not as competitive strategies for myocardial revascularization.

Research: The authors stated that future research should focus on regularly updating existing meta-analyses, as well as performing cumulative meta-analysis, to evaluate the long-term safety and efficacy of drug-eluting stents. The research should incorporate the outcomes of recently published trials and longer-term outcomes of existing trials.

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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.