Drug-eluting vs bare-metal stents in primary angioplasty: a pooled patient-level meta-analysis of randomized trials

CRD summary
This review concluded that drug-eluting stents were associated with reductions in target vessel and lesion revascularisation, but not mortality, compared with bare-metal stents. Limited generalisability, lack of statistical power in some outcomes and the omission of data from two trials must be acknowledged when considering the results of the review.

Authors' objectives
To evaluate the long-term safety and effectiveness of drug-eluting stents compared with bare-metal stents in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction (STEMI).

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 2000 to June 2011; search terms were reported. Conference abstracts published in four relevant journals and presentations at conferences of five societies were also searched for additional studies.

Study selection
Completed randomised controlled trials (RCTs) that compared drug-eluting stents and bare-metal stents in primary percutaneous coronary intervention for STEMI were eligible for inclusion. Eligible studies had at least 50 participants and over one year follow-up in at least 90% of participants.

The mean age of participants was approximately 61 years. Across the studies, approximately 77% were male, 43% were hypertensive, 15% were diabetic and 37% had hypercholesterolaemia. Three types of stent were used: Cypher, Taxus and Endeavor. Where specified, the drug-eluting stents most commonly used Sirolimus or Paclitaxel. Between 52% and 100% of patients were receiving glycoprotein IIb/IIIa inhibitors. The use of routine angiographic follow-up was highly variable. All studies used concomitant aspirin indefinitely and clopidogrel for at least six months.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
The data obtained from trialists were checked for completeness and consistency and compared with results from publications. Any queries were resolved by contact with trialists.

Data extraction
Individual patient data was sought from trial investigators for the primary end point of mortality, and secondary end points of reinfarction, target-vessel revascularisation and definite or probable stent thrombosis at long-term follow-up. Hazard ratios (HR) or mean differences and 95% confidence intervals (CI) were calculated depending on outcome.

Methods of synthesis
Pooled hazard ratios or weighted mean differences (WMD) and 95% CI were calculated using a fixed-effect Mantel-Haenszel model. Heterogeneity was assessed using \( I^2 \); Survival analyses were conducted using the Cox regression analysis stratified according to trial; the method used resulted in the study period being split into a specified number of time intervals, and the effect of drug-eluting stents estimated within each of the intervals. Choice of time intervals was based on estimates of fully time-dependent regression. Kaplan-Meier survival curves were presented with event rates reported as estimated probabilities.

Results of the review
Individual patient data was available for 11 of the 13 included RCTs (6,298 patients; 3,980 drug-eluting stents and 2,318 bare-metal stents). Duration of follow-up ranged from three to six years.
There was no significant difference between drug-eluting stents and bare-metal stents in terms of mortality at a mean of 1,201 days follow-up (HR 0.85, 95% CI 0.70 to 1.04) or cardiac mortality (HR 0.84, 95% CI 0.65 to 1.09; nine trials). There was also no significant difference in rates of reinfarction (HR 1.12, 95% CI 0.88 to 1.41) or stent thrombosis (HR 1.13, 95% CI 0.86 to 1.47). The hazard ratios for these outcomes changed over time and in the longer-term, drug-eluting stents was associated with a significant increase in reinfarction rate (HR 2.06, 95% CI 1.22 to 3.49) and stent thrombosis (HR 2.81, 95% CI 1.28 to 6.19). Drug-eluting stents significantly reduced the need for target-vessel revascularisation (HR 0.57, 95% CI 0.50 to 0.66) and target lesion revascularisation (HR 0.54, 95% CI 0.45 to 0.64; seven trials).

**Authors’ conclusions**

Compared with bare-metal stents, drug-eluting stents were associated with a significant reduction in target-vessel revascularisation and target-lesion revascularization at long-term follow-up. No significant differences in overall or late mortality were observed, but the point estimate favoured drug-eluting stents at all time periods.

**CRD commentary**

The review addressed a clear question supported by appropriate inclusion criteria. Relevant sources were searched with an attempt to identify unpublished data, but a major database (EMBASE) was not searched. It was not clear whether study selection was conducted in duplicate, so there was potential for selection bias and missed studies. Consistency and completeness of individual patient data was assessed appropriately.

Appropriate methods of synthesis were used, but there were no sensitivity analyses where summary data from the trials (where individual patient data was not available) were included, so the impact of these studies was unknown. The authors acknowledged that the included trials had selected populations and the results of the review could not be generalised to all patients undergoing primary percutaneous coronary intervention for STEMI. They also acknowledge that the analyses were underpowered to show a statistically significant difference in mortality between the groups. Therefore, there were some limitations that must be kept in mind when considering the results of the review.

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

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

**Research**: The authors stated that randomised trials were needed to evaluate newer-generation drug-eluting stents for patients undergoing primary percutaneous coronary intervention for STEMI, especially when combined with more potent and/or prolonged dual antiplatelet therapy.

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