Efficacy and safety of drug-eluting stents in patients with acute ST-segment-elevation myocardial infarction: a meta-analysis of randomized controlled trials

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CRD summary
The review found that drug-eluting stents used with percutaneous coronary intervention for acute ST-segment elevation myocardial infarction did not increase stent thrombosis (at least in the first 48 months) and reduced rates of other cardiac adverse events compared with bare metal stents. These conclusions require some caution in interpretation due to limitations in the review including a suboptimal literature search.

Authors' objectives
To compare the efficacy and safety of drug-eluting versus bare metal stents in patients having primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction.

Searching
PubMed was searched to May 2010. Search terms were reported. The websites of the American College of Cardiology, the American Heart Association, the European Society of Cardiology, Transcatheter Cardiovascular Therapeutics and EuroPCR were searched for abstracts and expert presentations. Reference lists of retrieved studies and relevant reviews were checked. Authors were contacted, along with other specialists, for additional studies. There were no language restrictions.

Study selection
Randomised controlled trials (RCTs) that compared drug-eluting versus bare metal stents in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction were eligible for inclusion. Eligible trials were required to report at least six months follow-up.

The age of participants in the included trials ranged from 59 to 65 years. Drug-eluting stents contained paclitaxel and/or sirolimus (where reported). Participants also received thienopyridine therapy for three to 12 months.

Outcomes reported in the review were death, recurrent myocardial infarction, target-vessel revascularisation, in-stent restenosis, stent thrombosis and major adverse cardiac events (a composite outcome that varied across trials). There were few data on rates of stent thrombosis occurring later than two years after percutaneous coronary intervention.

Two reviewers independently selected the studies.

Assessment of study quality
Trial quality was evaluated using the Jadad scale, assessing the adequacy of reported randomisation, double blinding, and withdrawals or drop-outs. Each trial was awarded a score out of a maximum of 5 points. Trials that scored fewer than 3 points were excluded.

Two reviewers independently assessed study quality, with disagreements resolved by discussion.

Data extraction
Risk ratios (RRs) and 95% confidence intervals (CIs) were extracted or calculated.

Two reviewers independently extracted the data, with disagreements resolved by discussion.

Methods of synthesis
Trials were combined to calculate pooled risk ratios and 95% confidence intervals. Heterogeneity was assessed using $\chi^2$, $T^2$, and $I^2$. Fixed-effect models were used unless there was significant heterogeneity ($\chi^2<0.05$), in which case random-
effects models were used.

Subgroup analyses were conducted to investigate the effect of type of drug eluting stent, duration of thienopyridine therapy, and duration of follow-up on major adverse cardiac events.

Publication bias was assessed for major adverse cardiac events and stent thrombosis, using a funnel plot and/or the fail-safe number.

**Results of the review**

Thirteen RCTs were included in the review (4,246 patients received drug-eluting stents and 2,523 received bare stents); trial size ranged 80 from 3,008 patients. All trials were of acceptable quality (Jadad score at least 3). Mean duration of follow-up ranged from six to 48 months.

Drug-eluting stents significantly reduced major adverse cardiac events (RR 0.59, 95% CI 0.47 to 0.73, 13 RCTs), recurrent myocardial infarction (RR 0.76, 95% CI 0.58 to 0.98; 12 RCTs), target vessel revascularisation (RR 0.47, 95% CI 0.39 to 0.56; 11 RCTs) and in-stent restenosis (RR 0.32, 95% CI 0.25 to 0.39; seven RCTs) compared with bare metal stents. There was no significant difference between the stent groups for overall deaths (13 RCTs) or stent thrombosis (13 RCTs).

There was significant statistical heterogeneity (p=0.01) for the analysis of major adverse cardiac events, so a random-effects model was used. There was no significant statistical heterogeneity for other outcomes.

The funnel plot for major adverse cardiac events suggested publication bias, although when trials were subgrouped by type of drug-eluting stent or by duration of thienopyridine therapy, the asymmetry decreased.

The results of subgroup analyses were also reported in the review.

**Authors’ conclusions**

Drug-eluting stents used with percutaneous coronary intervention for acute ST-segment elevation myocardial infarction did not increase stent thrombosis (at least in the first 48 months) and reduced rates of other cardiac adverse events compared with bare metal stents.

**CRD commentary**

The objectives and inclusion criteria of the review were clear in most respects, although the review outcomes were not clearly pre-specified. Relevant sources were searched for studies without restriction by language or publication status. However, only one database was searched, which meant that some studies may have been missed. Steps were taken to minimise the risk of reviewer bias and error (independent duplicate methodology) at all stages of the review.

Few details were provided about the characteristics and quality of individual trials (such as participant gender, drop-out rates, individual quality scores, methods of allocation concealment). Over 60% of participants received drug-eluting stents and most participants (n=3,006) were derived from a single trial. Only one trial had follow-up for longer than 24 months. Appropriate statistical techniques were used to combine the trials and assess statistical heterogeneity and publication bias. Subgroup analyses were used to explore differences between the trials. The authors’ interpretation of subgroup analyses (as if they were head-to-head comparisons) did not appear reliable; statistical heterogeneity was higher in some of the subgroups than in the main analyses. However, findings in the main analyses were consistent and heterogeneity was low in most cases.

The authors’ conclusions require some caution in interpretation due to limitations in the review, including a suboptimal search, lack of detail about trial quality and possible publication bias.

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

**Practice:** The authors stated that use of drug-eluting stents in ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention is safe with respect to stent thrombosis in the first 48 months.
Research: The authors stated that trials are needed of drug-eluting stents in ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with follow-up longer than 48 months, to investigate the possibility of very late stent thrombosis.

Funding
The Major State Basic Research Development Program of China, grant number 2010CB732605.

Bibliographic details

PubMedID
20978561

Original Paper URL
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2953216/?report=abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Angioplasty, Balloon, Coronary /adverse effects /instrumentation /mortality; Chi-Square Distribution; Coronary Restenosis /etiology /prevention & control; Drug-Eluting Stents; Evidence-Based Medicine; Humans; Metals; Middle Aged; Myocardial Infarction /mortality /therapy; Odds Ratio; Prosthesis Design; Randomized Controlled Trials as Topic; Recurrence; Risk Assessment; Risk Factors; Stents; Thrombosis /etiology /prevention & control; Time Factors; Treatment Outcome

AccessionNumber
12010008094

Date bibliographic record published
13/04/2011

Date abstract record published
12/10/2011

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.