Drug-eluting balloon angioplasty for in-stent restenosis: a systematic review and meta-analysis of randomised controlled trials


CRD summary
The authors concluded that drug-eluting balloons were useful to treat in-stent restenosis in previously implanted bare-metal and drug-eluting stents and resulted in reduced risk of major adverse cardiac events and target lesion revascularisation. The conclusions should be considered as reliable but the evidence base comprised just five trials and the authors identified several ongoing relevant studies.

Authors' objectives
To review the effectiveness of drug-eluting balloons to treat in-stent restenosis.

Searching
EMBASE, PubMed, BIOS and Web of Science were searched from 2005 to November 2012. Abstracts and conference proceedings from five relevant scientific meetings were searched from 2006 to 2011. Review articles and reference lists were checked for eligible studies. Five key websites were handsearched. No language restrictions were applied. Search strategies were reported in an appendix.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared drug-eluting balloon with any comparator treatment (plain balloon angioplasty or drug-eluting stents). Outcomes of interest were a composite of major adverse cardiac events, target lesion revascularisation, all cause mortality, myocardial infarction, late lumen loss and in-stent restenosis. Studies that used drug-eluting balloons for de novo stenoses were not included.

All included trials used paclitaxel-eluting balloons compared with uncoated balloons or TAXUS Liberte stent. Stent types included drug-eluting stents and bare-metal stents. All trials focused on patients with stable coronary artery disease or acute coronary syndrome and follow-up ranged from six to 60 months. Elements included in the composite outcome major adverse cardiac events and definitions of target lesion revascularisation varied between trials.

Two researchers independently evaluated studies for inclusion.

Assessment of study quality
Study quality was assessed based on evaluating randomisation, allocation concealment, intention-to-treat analysis, blinded outcome assessment, premature stopping of enrolment and reporting about dropout numbers. An overall quality score was not used but studies were graded as insufficient, sufficient or good quality on each item (no further details on the criteria for these decisions were provided).

It was not clear how many researchers assessed study quality.

Data extraction
Relative risks and associated 95% confidence Intervals were extracted or calculated for each outcome. Where shorter and longer term outcomes were reported, longer term (five year) data were used for analyses.

It was not clear how many researchers extracted data.

Methods of synthesis
A DerSimonian and Laird random-effects model was used to estimate the pooled impact as a risk ratio of drug-eluting balloons versus comparator treatments. Continuity corrections were used where no event occurred in one group. Heterogeneity was assessed using I² and a value of more than 50% was considered to represent moderate heterogeneity. Subgroup analyses were used for the different comparators and for bare metal stent versus drug-eluting stent. Publication bias and small study effects were not assessed due to the small number of included studies.
**Results of the review**

Five RCTs (801 participants) were included in this review. Three studies compared drug-eluting balloons with conventional balloon angioplasty and two studies compared drug-eluting balloons with first-generation drug-eluting stents. The included trials were rated as sufficient or good quality on all of the quality criteria.

Most of the reported endpoints were significantly reduced for drug-eluting balloons compared with the control groups. For the composite outcome of major adverse cardiac events, the relative risk was 0.46 (95% CI 0.31 to 0.70; $I^2=53\%$). For target lesion revascularisation the relative risk was 0.34 (95% CI 0.16 to 0.73; $I^2=74\%$). The relative risk for angiographic in-segment restenosis was 0.28 (95% CI 0.14 to 0.58; $I^2=78\%$). There was a statistically significant lower mortality risk for drug-eluting balloons compared with controls (RR 0.48, 95% CI 0.24 to 0.95; $I^2=0\%$).

There was no statistically significant difference in myocardial infarction or late stent thrombosis.

Subgroup analyses results were reported in the full paper. Influence analyses indicated no single trial was unduly responsible for influencing the results.

The authors reported that formal tests of heterogeneity did not detect major variations but commented on the considerable clinical heterogeneity present (comparator, setting, follow-up duration).

**Authors' conclusions**

Drug-eluting balloons are useful to treat in-stent restenosis in previously implanted bare-metal stents and drug-eluting stents, resulting in reduced risk of major adverse cardiac events and target lesion revascularisation.

**CRD commentary**

The review addressed a clear clinical question. Searches and inclusion criteria were appropriate and covered the major databases and grey literature without language restrictions. Review processes were partly described and this made it difficult to rule out reviewer error or bias. The included trials were assessed for quality and appeared to be generally reliable. However, criteria used were not described fully and it was unclear how the gradings were applied.

The analyses appeared broadly appropriate and the authors' conclusions followed from the data presented. The conclusions should be considered as reliable but the evidence base consisted of just five trials and the authors identified several ongoing relevant studies.

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

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

**Research:** The authors drew attention to ongoing and prospective trials which should be considered in any further review of the area.

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