Meta-analysis of stent thrombosis after drug-eluting stent implantation: 4-year follow-up

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CRD summary
The authors concluded that the safety profile of drug-eluting stents was similar to bare metal stents in terms of stent thrombosis. There was no evidence of increased risk of late and very late thrombosis for drug-eluting stents. The conclusions appear reliable but should be viewed with caution given possible language bias.

Authors' objectives
To compare the effect of drug-eluting stents with classic bare metal stents on the occurrence of early, late and very late stent thrombosis during an extended follow-up for up to four years.

Searching
PubMed, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for publications in English. Reference lists of identified articles and cardiology conference proceedings were hand searched. Relevant internet resources were reviewed (www.tctmd.com, www.theheart.org, www.clinicaltrialresults.org, industry supported websites). Subject experts were contacted.

Study selection
Randomised controlled trials (RCTs) (at least single blind) that compared drug-eluting stents (sirolimus, paclitaxel or zotarolimus) with bare metal stents in adult patients with coronary artery disease were eligible for inclusion. Open trials, trials that reported per-protocol analyses, trials of non-native coronary arteries and trials where drug-eluting stents were compared with each other or where stenting was compared with other percutaneous coronary interventions (PCIs) were excluded. The primary outcome was late and very late thrombosis. The secondary outcome was early thrombosis. Definitions of outcome measures were reported in the paper.

Most trials assessed paclitaxel stents. Regimens and durations of antiplatelet therapies varied: aspirin (at least 75mg to 325mg daily) and clopidogrel (mostly 75mg daily or ticlopidine 250mg twice daily).

Two reviewers independently selected studies for inclusion. A third reviewer resolved disagreements.

Assessment of study quality
Two reviewers independently assessed the quality of included studies using a modified Jadad scale (maximum score 5). Key criteria assessed were allocation concealment, blinding (patients and caregivers), intention-to-treat analysis and withdrawals and losses to follow-up. A third reviewer resolved disagreements.

Data extraction
Two reviewers independently extracted data to enable calculation of odds ratios (ORs) and 95% confidence intervals (CIs). A third reviewer resolved disagreements.

Methods of synthesis
Pooled odds ratios and 95% CIs were calculated using Mantel-Haenszel fixed-effects model. Where no events were reported, zero cell correction method was applied. Heterogeneity was assessed using $X^2$ and $I^2$ statistics. Publication bias was assessed using a funnel plot.

Results of the review
Fourteen RCTs (n=8,122 participants) were included. All trials scored 4 or 5 on the Jadad scale. Allocation concealment and blinding of both patients and caregivers were reported in all trials except two. Intention-to-treat analysis was reported in all trials. Reasons for withdrawals and losses to follow-up were not adequately reported in three trials. All trials reported losses of follow-ups below 10%.
There was no difference in the incidence of late and very late stent thrombosis in patients treated with drug-eluting stents compared with patients treated with bare metal stents (14 RCTs). No evidence of heterogeneity was found. Results of funnel plots suggested little evidence of publication bias.

**Authors’ conclusions**
The safety profile of drug-eluting stents was similar to bare metal stents in terms of stent thrombosis. There was no evidence of increased risk of late and very late thrombosis for drug-eluting stents.

**CRD commentary**
The review question was clearly stated. Two major databases were searched and efforts were made to identify unpublished studies, which minimised potential for publication bias. Language bias was likely since searches were restricted to papers published in English. Review processes were conducted in duplicate, which minimised risks of error and bias. Study quality was assessed using a modified Jadad scale and results were reported. The decision to combine results in a meta-analysis was justified given absence of evidence of heterogeneity.

The conclusions appear reliable but should be viewed with caution given possible language bias.

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

**Research:** The authors stated that comparative analysis of the safety profile of drug-eluting stents in RCTs versus observational studies were needed to generate more accurate information on the safety of interventions over a longer time period.

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