Is bare-metal stenting superior to balloon angioplasty for small vessel coronary artery disease: evidence from a meta-analysis of randomized trials

CRD summary
This review compared stenting with percutaneous transluminal coronary angioplasty (PTCA) for small vessel coronary artery disease. The authors concluded that stenting was superior to PTCA, especially after suboptimal PTCA, but that optimal PTCA (with provisional stenting) may be no worse than routine stenting. This was a well-conducted review and the authors’ conclusions are likely to be robust.

Authors’ objectives
To compare bare-metal stenting with percutaneous transluminal coronary angioplasty (PTCA) for the treatment of lesions in small coronary arteries.

Searching
MEDLINE and the CENTRAL Register were searched from January 1994 to August 2004; the search terms were reported. Conference proceedings from four named societies were also searched (2000 to 2004).

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that used intention-to-treat analysis and had at least 6 months’ follow-up were eligible for inclusion. The included studies followed up patients for up to 16 months (median 8).

Specific interventions included in the review
Studies that compared stenting with PTCA were eligible for inclusion. Studies that used drug-eluting stents, devices other than stents, or anti-platelet drugs other than acetylsalicylic acid or thienopyridines, were excluded. Most of the included studies used bare metal stents; other studies used stents coated with heparin, silicon carbide or phosphorylcholine. Eleven studies are reported to have used double antiplatelet therapy (acetylsalicylic acid or thienopyridines) for one month in patients allocated to stenting. Most studies used only acetylsalicylic acid for patients allocated to PTCA. Other cointerventions included glycoprotein IIb/IIa inhibitors (6 studies) in varying proportions of patients (details were reported).

Participants included in the review
Studies of patients with a coronary artery reference vessel diameter (RVD) of less than 3 mm were eligible for inclusion. The mean age of the patients in the included studies was 62 years, 73% were male, 29% had diabetes and 31.5% of patients received treatment for unstable angina. The mean RDV was 2.33 mm in the stent group and 2.31 mm in the PTCA group.

Outcomes assessed in the review
The primary review outcome was the incidence of major adverse cardiovascular events (MACE), defined as the composite outcome of death, myocardial infarction (MI) and repeat revascularisation (RR) of the target lesion at the longest follow-up reported. The reviewers accepted the definitions used in the primary studies. The review also assessed death, MI, RR, crossover from PTCA to stent (defined only as bail-out), crossover from stent to PTCA (defined as failure to implant the stent), angiographic restenosis, minimal luminal diameter (MLD) and diameter stenosis (DS) immediately after the intervention and at follow-up, and acute gain and late loss.

How were decisions on the relevance of primary studies made?
Two reviewers independently conducted searches and selected studies.
Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers the reporting and handling of randomisation, blinding and handling of withdrawals. The maximum possible score was 5 points.

Two reviewers independently assessed validity and resolved any disagreements by consensus.

Data extraction
Two reviewers independently extracted the data using predefined forms and resolved any disagreements by consensus. The authors of the primary studies were contacted for missing data. Data extracted included baseline angiographic characteristics and outcomes data. In addition, for each treatment group, the reviewers calculated the mean crossover rate, the post-procedural mean DS and MLD, and the weighted mean difference (WMD) for the DS, MLD and acute gain.

Methods of synthesis
How were the studies combined?
Baseline characteristics were compared between treatment groups. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for dichotomous data, using both fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) models; the pooled WMD and 95% CI were calculated for continuous data using a random-effects model (DerSimonian and Laird model). The number-needed-to-treat (NNT) with 95% CI was also calculated. The reviewers calculated the power of the meta-analysis. The possibility of publication bias was explored using a funnel plot and tested using the Egger statistic.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. A predefined subgroup analysis was used to assess the effects of studies performing optimal PTCA (mean residual DS less than 20% with PTCA) and studies achieving suboptimal PTCA (DS more than 20% with PTCA). Subgroup analyses were also used to calculate results from high-quality studies that were published in full, studies of smaller vessels with maximum RVD less than 2.8 mm, studies including coated or bare metal stents, and studies using stents designed specifically for small vessels.

Results of the review
Thirteen RCTs (n=4,383) were included.

Crossovers: the overall crossover rate was 22.2% in patients allocated to PTCA and 2.4% in patients allocated to stents.

Death and MI (13 RCTs): there was no significant difference between stents and PTCA for death (OR 0.81, 95% CI: 0.48, 1.36) or MI (OR 0.80, 95% CI: 0.58, 1.11). RR (13 RCTs): stenting significantly reduced the risk of RR compared with PTCA (14.9% versus 18.7%; OR 0.76, 95% CI: 0.61, 0.95), but statistically significant heterogeneity was found (P=0.04). Studies of optimal PTCA were statistically homogeneous (P=0.62), and for this subgroup there was no significant difference in RR between treatments (OR, 0.93 95% CI: 0.73, 1.18). Studies of suboptimal PTCA found a significant reduction in RR compared with stenting (OR 0.64, 95% CI: 0.45, 0.92).

MACE (13 RCTs): MACE were significantly less frequent with stents than with PTCA (17.6% versus 22.7%; OR 0.71, 95% CI: 0.57, 0.90; NNT 20, 95% CI: 11, 50), but statistically significant heterogeneity was found (P=0.01). Studies of optimal PTCA were statistically homogeneous (P=0.27), and for this subgroup there was no significant difference in RR between treatments (OR 0.86, 95% CI: 0.66, 1.11). Studies of suboptimal PTCA found a significant reduction in RR with stenting (OR 0.62, 95% CI: 0.44, 0.88).

Angiographic follow-up (12 RCTs): restenosis was significantly more common with PTCA than with stenting (OR 0.67, 95% CI: 0.52, 0.87), but statistically significant heterogeneity was found (P=0.01). For studies with optimal PTCA, there was no significant difference in restenosis between PTCA and stenting. However, studies of suboptimal PTCA found a significant reduction in restenosis with stenting.
There was no evidence of publication bias, either from the funnel plot or when using Egger's test (P=0.22).

**Authors' conclusions**
Stenting was more effective than PTCA for the treatment of small coronary vessels, especially after suboptimal PTCA. There may be little difference between optimal PTCA (with provisional stenting) and routine stenting.

**CRD commentary**
The review question was clear in terms of the study design, intervention and participants. Several relevant sources were searched and attempts were made to locate unpublished studies, thereby limiting the possibility of publication bias. Appropriate methods were used to assess the presence of such bias, but no evidence of it was found. It was not clear whether any language restrictions had been applied. Two reviewers independently selected studies, assessed validity and extracted the data, thus reducing the potential for bias and errors. Only RCTs that used intention-to-treat analysis were included, and validity was assessed using the specified established criteria.

The text and tables contained adequate information on the included studies. Pooling studies by meta-analysis and exploring potential sources of heterogeneity was an appropriate method of combining the studies. The influence of various factors on the results was examined. This was a well-conducted review and the authors' conclusions are likely to be robust.

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

Research: The authors stated that there is a need for devices that reduce the rates of MACE, repeat percutaneous coronary intervention and restenosis after stenting of small vessels. They also stated that the cost-effectiveness of systematic drug-eluting stents compared with optimal PTCA (with provision stenting) could be examined.

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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.