Percutaneous coronary intervention versus conservative therapy in nonacute coronary artery disease: a meta-analysis
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CRD summary
The review compared percutaneous coronary intervention with conservative treatment for chronic coronary artery disease. The authors concluded that patients who have not had a recent myocardial infarction do not benefit more from percutaneous coronary intervention than from conservative treatment. The review was generally well conducted and the conclusions are likely to be reliable.

Authors' objectives
To assess the effectiveness of percutaneous coronary intervention (PCI) compared with conservative therapy in patients with nonacute coronary artery disease (CAD).

Searching
PubMed and the Cochrane Controlled Trials Register were searched up to October 2004; the search terms were reported. Trials reported at meetings of the American College of Cardiology and American Heart Association, as well as references cited in retrieved articles and reviews, were screened for additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared coronary revascularisation by PCI with conservative medical therapy were eligible for inclusion. Comparisons of PCI versus conservative therapy within 3-arm trials of conservative therapy versus PCI versus coronary artery bypass grafting (CABG) were included. Studies that compared conservative therapy with any type of revascularisation including both PCI and CABG in the same treatment group were excluded. Stents were used to a varying extent in about half of the included studies (none used drug-eluting stents). The characteristics of conservative therapy differed, although all trials used anti-anginal and anti-ischaemic treatments and the more recent trials made use of statins.

Participants included in the review
Studies in patients with nonacute CAD and angiographically documented stenosis in one or more coronary vessels were eligible for inclusion. Additional documentation for the functional impact of the stenoses did not affect eligibility. Studies that involved patients who had an acute coronary syndrome within 1 week of study entry, but included patients who had myocardial infarction (MI) or unstable angina in the more distant past, were excluded. The mean age range in the included studies was 53 to 61 years and most of the participants were men. The proportion of patients with diabetes ranged from zero to 30% across the trials, and the proportion with a history of MI ranged from zero to 100%. Most patients had single- or two-vessel CAD, apart from one trial in which almost 60% had three-vessel disease. Where reported, the proportion of patients with angina symptoms ranged from 80 to 100% and the mean ejection fraction ranged from 46 to 76%.

Outcomes assessed in the review
The outcomes of interest were death, cardiac death or MI (fatal or nonfatal), nonfatal MI, CABG and PCI in the target vessel or other vessel or segment during follow-up. Death included all-cause mortality unless only cardiac deaths were reported. The diagnosis of MI was based on standard electrocardiogram and enzyme criteria. The mean duration of follow-up ranged from 1 to 7 years.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

**Assessment of study quality**
The criteria used to assess study quality were blinding, generation of the randomisation sequence, allocation concealment and withdrawals. Two reviewers applied the criteria independently and reached consensus on disagreements.

**Data extraction**
Two reviewers extracted the data independently and reached consensus on disagreements. The number of patients in each group who experienced each outcome event was extracted. The longest available follow-up data were used in the analysis.

**Methods of synthesis**
How were the studies combined?
The studies were combined using fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) meta-analyses to calculate pooled relative risks (RRs) with 95% confidence intervals (CIs). The random-effects estimates were reported. A Bayesian model was also used.

How were differences between studies investigated?
Statistical heterogeneity in the meta-analysis was assessed using the chi-squared statistic (p<0.1 indicated statistical significance) and the I-squared statistic (I2 >= 75% indicated a large amount of heterogeneity).

A sensitivity analysis was conducted to examine the difference in effect size estimates between studies with small (fewer events) and large (more events) variance.

The following subgroup analyses were conducted: studies in which stents were available versus those in which stents were not placed in the initial intervention in the PCI arm; mean follow-up exceeding 2 years versus up to 2 years; studies in which all enrolled patients had a recent history of MI (8 days to 3 months before enrolment) versus others; studies in which more than 80% of patients had a positive exercise test or scintigraphy versus others. General variance methods were used to compare subgroup estimates of effect.

**Results of the review**
Eleven studies, including 2,950 patients, were included.

The trial reports provided inadequate information on the method of randomisation. The outcome assessors were blinded for some or all outcomes in four trials. All the trials provided some information on withdrawals.

The meta-analysis showed no statistically significant difference between PCI and conservative therapy for death, cardiac death or MI, nonfatal MI, CABG or PCI during follow-up. There was generally no statistically significant heterogeneity between the studies; the exception was in the analysis of PCI during follow-up. The Bayesian analysis gave similar results.

In the sensitivity analysis, smaller trials with fewer events showed significantly less favourable effects with PCI compared to conservative therapy than larger trials with more events for the outcomes cardiac deaths and MI and nonfatal MI (p=0.024).

The subgroup analysis showed a statistically significant difference in the risk of death and subsequent PCI between trials that enrolled patients with a recent history of MI versus the other trials (p<0.05). In the subgroup of two trials that enrolled patients with relatively recent MI there was a statistically significant reduction in the risk of death (RR 0.40, 95% CI: 0.17, 0.95, p=0.037) and subsequent PCI (RR 0.42, 95% CI: 0.20, 0.91, p=0.029).
Authors' conclusions
Compared with conservative medical treatment, PCI did not offer any benefit to patients with chronic stable CAD without recent MI in terms of death, MI or the need for subsequent revascularisation.

CRD commentary
The review addressed a well-defined question. The search was probably sufficient to identify most of the relevant trials, although methods used to minimise bias in the selection of studies were not reported. Robust methods were used to extract the data and assess study quality. The analysis was generally well conducted, although the handling of withdrawals and other losses to follow-up was not clear. Poor reporting of study quality in the original trial reports limited the extent to which it could be taken into account in the analysis. On the basis of the evidence presented, the authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that PCI may be indicated in special circumstances such as relatively early after MI (see research implication below). With regard to stents, they found no evidence of superiority for PCI even when the analysis was limited to studies that used stents.

Research: The authors stated that longer follow-up data are needed to support a recommendation to use PCI in patients who have had a relatively recent MI. In addition, individual patient data are required to assess whether the intensity of angina symptoms, functional demonstration of ischaemia and the angiographic extent of CAD affect the outcome of interventional versus conservative strategies.

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