Percutaneous coronary intervention for late reperfusion after myocardial infarction in stable patients
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CRD summary
The authors conclude that the use of percutaneous coronary artery revascularisation of occluded arteries after myocardial infarction in stable patients does not appear to be of benefit. Despite some limitations in the reporting of methods, the review was well-conducted and these conclusions are likely to be reliable.

Authors' objectives
To evaluate the effect on clinical end points and left ventricular ejection fraction (LVEF) of percutaneous coronary artery revascularisation for late reperfusion after myocardial infarction (MI) in stable patients.

Searching
PubMed and the Cochrane CENTRAL Register were searched to April 2007; the search terms were reported. Conference proceedings from major meetings of the American College of Cardiology, the American Heart Association and the European Society of Cardiology were also searched, as were the reference lists of retrieved articles and relevant reviews.

Study selection
Randomised controlled trials (RCTs) that compared late coronary revascularisation by percutaneous coronary intervention (PCI) with medical therapy were eligible for inclusion, provided that at least 80% of the participants in the intervention arm had PCI performed between 1 and 45 days from symptom onset. Studies were excluded if PCI was conducted within the first 24 hours of symptom onset. Where reported, the included studies used stents in 0 to 100% of the patients; stents were typically bare metal, though a small minority were drug eluting. The participants in eligible studies were stable patients with a previous MI and angiographic evidence of persistent occlusion in the affected blood vessel. Their mean age was 54 to 62 years. At least 70% were male and a minority (range: 14 to 37%, where reported) had diabetes. Studies of patients requiring urgent intervention for acute coronary syndrome (e.g. due to reinfarction) were excluded. In most studies the participants had a mean baseline EF of 44 to 53%. Eligible studies reported all-cause death and/or MI, congestive heart failure (CHF) and LVEF. When available, the review reported centrally-adjudicated outcomes in preference to site-determined ones. MI was defined in terms of symptoms, electrocardiography and enzymes. CHF was defined according to the criteria used in primary studies. LVEF outcomes used the latest follow-up evaluation. Follow-up in the included studies varied from 4 months to a mean of 50 months. LVEF was measured in the included studies by magnetic resonance imaging, echocardiography or left ventricular angiography.

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 following quality criteria were considered: blinding, generation of randomisation sequence, allocation concealment and description of withdrawals. The authors did not state how the validity assessment was performed.

Data extraction
For binary outcomes, risk ratios and 95% confidence intervals (CIs) were calculated. For the continuous outcome of LVEF, the mean change in each group and standard deviation (SD) were reported. Where the SD was not reported for each group, the SD of the mean difference in change between the groups was calculated from the reported p-value for the comparison between the groups.

Two reviewers independently extracted the data, with any discrepancies resolved by discussion.
Methods of synthesis
The data were combined using fixed-effect and random-effects (DerSimonian and Laird) models. The z statistic was used to calculate whether the results of the largest study differed significantly from the pooled results of the earlier smaller studies. Heterogeneity was investigated using the $\chi^2$ test (level of significance $p<0.10$) and the $I^2$ statistic (50% indicating large heterogeneity).

Results of the review
Six RCTs ($n=2,607$) were included. The largest of these (OAT/TOSCA study, $n=2,166$) provided data for clinical outcomes and incorporated a substudy ($n=381$) which provided data for EF. The other 5 RCTs were much smaller (total $n=441$).

In the largest study, methods for randomisation and allocation concealment were described. Only one other study reported on randomisation procedures and no others adequately described allocation concealment. The outcome assessment was adjudicated centrally in the largest study and one other study. Assessors were described as blinded to the outcome of EF in all but one study, and all studies provided some information on withdrawals and clearly reported rates of follow-up.

Clinical outcomes of death, MI, death and MI combined, and CHF (6 RCTs, $n=2,607$): there was no statistically significant difference between the groups for any of these outcomes. No statistically significant heterogeneity was found.

LVEF (6 RCTs, $n=653$): there was a small statistically significant difference between the groups for this outcome, favouring the PCI group (absolute mean difference 1.4%, 95% confidence interval: 0.1, 2.8, fixed-effect model). There was no statistically significant heterogeneity ($\chi^2$ test, $p=0.13$), but some heterogeneity could not be excluded as the $I^2$ statistic was 41%. When a random-effects model was used, this result was no longer statistically significant.

Early studies versus OAT/TOSCA study: for clinical outcomes, the OAT/TOSCA study found no benefit and a trend for harm associated with PCI. These findings differed significantly from the findings of earlier studies (z statistic, $p=0.02$), which had found a statistically significant benefit associated with PCI. Similarly, for the outcome of change in EF, the TOSCA study found no benefit associated with PCI, whereas the earlier studies had found a 2% benefit.

Authors’ conclusions
PCI for late revascularisation of occluded arteries after MI in stable patients does not appear to be of benefit.

CRD commentary
The study objectives and inclusion criteria were clear, the search was adequate, and relevant criteria were assessed for risk of bias. However, it was not reported whether steps were taken to minimise reviewer error and bias in the selection of studies and assessment of risk of bias (such as an independent assessment by more than one reviewer). The meta-analysis appears justified and potential sources of clinical, methodological and statistical heterogeneity were discussed and evaluated appropriately. Despite some limitations in the reporting of review methods, the review was well conducted and the conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that late reperfusion for blocked coronary arteries is not justified since it does not improve major clinical outcomes and involves costs and high radiation times for both physicians and patients. These issues should be considered when updating cardiology guidelines.

Research: The authors state that further large studies on this topic are not warranted, but it may be worthwhile to conduct additional follow-up of patients already randomised. Any future research in this area should have CHF and EF as outcomes with blinded arbitration.

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