Early versus delayed percutaneous coronary intervention for patients with non-ST segment elevation acute coronary syndrome: a meta-analysis of randomized controlled clinical trials


CRD summary
The authors concluded that early percutaneous intervention did not reduce the odds of the composite outcome of death or non-fatal myocardial infarction at 30 days in patients with non-ST elevation acute coronary syndrome. Although these conclusions appear reliable, the possible flaws in the review methods should be borne in mind.

Authors' objectives
To compare the incidence of death or non-fatal myocardial infarction at 30 days in patients with non-ST segment elevation acute coronary syndromes who received percutaneous coronary intervention (PCI) within 24 hours of presentation (early PCI) with those receiving it more than 24 hours after presentation (delayed PCI).

Searching
MEDLINE was searched from 1990 to June 2010; search terms were reported. Reference lists of retrieved articles, Google Scholar, and abstracts or presentations from major cardiology meetings (1990-2010) were also searched.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared early PCI with delayed PCI in patients with unstable angina pectoris and/or non-ST segment elevation myocardial infarction. The primary outcome was the composite of death or non-fatal myocardial infarction at 30 days. Separate secondary outcomes included death, myocardial infarction, repeat revascularisation, and bleeding (all defined in paper).

The mean age of patients in the included trial ranged from 60 to 70 years; the proportions of women ranged from 26% to 35%. Baseline proportions were also reported for patients who were smokers (range 18% to 39%) or those who had been diagnosed with diabetes mellitus (range 14% to 32%), previous myocardial infarction (range 13% to 32%), and hypertension (33% to 87%). Mean time to early PCI ranged from 1.2 to 14 hours; that for delayed PCI ranged from 21 to 86 hours. Use of medical therapies and revascularisation strategies varied across the included trials (reported fully in paper).

The authors did not state the number of reviewers involved in study selection.

Assessment of study quality
The authors did not report whether any quality assessment was undertaken.

Data extraction
Data (number of events for each of the outcomes assessed) per treatment group were extracted to calculate odds ratios and 95% confidence intervals. The authors did not state the number of reviewers who extracted the data, although they did state that two reviewers cross checked the data extraction for accuracy.

Methods of synthesis
Odds ratios and 95% confidence intervals from individual trials were pooled using the random-effects Mantel Haenszel method. Statistical heterogeneity was assessed using $I^2$. Publication bias was assessed using a funnel plot.

Results of the review
Seven RCTs were included in the review (13,762 patients).

Compared with patients undergoing delayed percutaneous coronary intervention (PCI), lower odds for the composite outcome of death or non-fatal myocardial infarction was found among patients undergoing early PCI, but the result was not statistically significant (OR 0.83, 95% CI 0.62 to 1.10; seven trials). Significant statistical heterogeneity was shown between the trials ($I^2=74\%$).
The early PCI group had lower odds for the separate outcomes of 30-day death (OR 0.57, 95% CI 0.23 to 1.38; five trials; $I^2=78\%$) and non-fatal myocardial infarction (OR 0.93, 95% CI 0.64 to 1.34; six trials; $I^2=64\%$), although these differences were not statistically significant. Further comparisons revealed that the delayed PCI group had statistically significantly lower odds (33% reduction) of repeat revascularisation than the early PCI group (OR 1.33, 95% CI 1.14 to 1.56; five trials; $I^2=0\%$). Significantly lower odds (24% reduction) of bleeding were found for the early PCI group over the delayed PCI group (OR 0.76, 95% CI 0.63 to 0.91; five trials; $I^2=0\%$).

A post hoc sensitivity analysis was conducted, by removing a trial that was completed before widespread use of oral thienopyridines in the trial population. Results for this sensitivity analysis were not substantially different from the initial findings. No evidence of publication bias was found.

**Authors’ conclusions**

In patients with non-ST elevation acute coronary syndrome, early percutaneous coronary intervention did not reduce the odds of the composite outcome of death or non-fatal myocardial infarction at 30 days. This strategy was associated with lower odds of bleeding and higher odds of repeat revascularization at 30 days than delayed percutaneous coronary intervention.

**CRD commentary**

The review question and inclusion criteria were clearly defined. Relevant data sources were accessed and an attempt was made to locate unpublished studies, although the search of only one database may mean that relevant studies were missed. No evidence of publication bias was found, but funnel plots for less than 10 studies are not very meaningful, so publication bias could not be fully ruled out. Limited information was reported for the review processes of study selection and data extraction, which meant that there may have been potential for reviewer error and bias.

No quality assessment was reported, which made it difficult to ascertain possible levels of bias within individual trials. Trial details were presented and the methods of synthesis seemed appropriate. Differences between the trials were evident, although the authors attempted to explore this heterogeneity through a post hoc sensitivity analysis. The authors acknowledged that two of the included trials were post hoc analyses with large sample sizes, and that the rest of the RCTs included had relatively small sample sizes. They also acknowledged that insufficient data meant that they were unable to analyse high-risk patients separately from other patients.

Although the authors’ conclusions appear reliable, the possible flaws in the review methods should be borne in mind.

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

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

**Research:** The authors stated that the issue of optimal timing of percutaneous coronary intervention in the study population required further investigation through large RCTs, that focused specifically on the effects of early and delayed PCI on death, myocardial infarction, and other key outcomes.

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