Early routine percutaneous coronary intervention after fibrinolysis vs standard therapy in ST-segment elevation myocardial infarction: a meta-analysis


CRD summary
This review concluded that patients with ST-segment elevation myocardial infarction had reduced reinfarction and recurrent ischaemia, without increasing bleeding events, with early routine percutaneous coronary intervention after fibrinolysis compared with standard therapy. Given the possibility of missed trials and the lack of reporting on the quality of included trials, the authors' conclusions should be treated with caution.

Authors' objectives
To compare early routine percutaneous coronary intervention (PCI) after fibrinolysis with standard therapy in patients with ST-segment elevation myocardial infarction (STEMI).

Searching
MEDLINE and the Cochrane Library were searched for studies published since 1999. Search terms were reported. Only English language papers from peer reviewed journals were sought. Reference lists of identified studies were checked.

Study selection
Randomised controlled trials (RCTs) that compared early percutaneous coronary intervention (PCI) with standard therapy in patients with ST-segment elevation myocardial infarction (STEMI) presenting in non-PCI centres were eligible for inclusion. Early PCI was defined as that performed within 24 hours of fibrin-specific lytic therapy. Trials involving facilitated angioplasty and balloon percutaneous transluminal coronary angioplasty were excluded.

The outcomes of interest were all-cause mortality, reinfarction, combined death/reinfarction, recurrent ischaemia, revascularisation, stroke, and major bleeding at 30 days or longer follow-up.

In the included trials, patients had STEMI or high risk STEMI, presenting within below six up to 12 hours from symptom onset. Fibrinolytic agents used were reteplase, alteplase and tenecteplase. Most participants received fibrinolysis in non-PCI capable hospitals; some were in pre-hospital ambulance settings. Time from symptoms to fibrinolytic therapy was between 113 and 216 minutes; time from fibrinolytic therapy to PCI was 84 to 1,002 minutes. All included trials used dual antiplatelet therapy (aspirin and clopidogrel) for at least one month after PCI; some participants received either unfractionated heparin or enoxaparin during PCI. PCI was achieved in between 80 and 100% of those in the early PCI group; the rate of rescue PCI in the standard therapy group was 12% in older trials to 27.4% in more recent trials.

Two authors independently assessed studies for inclusion.

Assessment of study quality
Quality was assessed using the Jadad scale; items included method of randomisation and evidence of blinded outcome assessment.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted for the relevant outcomes and used to calculate odds ratio (OR) and 95% confidence intervals (CI). Authors were contacted for additional information.

Data were extracted by two authors independently and checked by the main investigators of individual trials.
Methods of synthesis
Data were analysed on an intention-to-treat basis. Pooled odds ratios and 95% confidence intervals were calculated using a random-effects model. Where there were no events in a treatment group, 0.5 was added to each cell to facilitate analyses. Numbers needed to treat (NNT) and 95% confidence intervals were calculated for those outcomes where statistically significant differences were identified. Heterogeneity was assessed using the Q statistic and $I^2$ Index.

Sensitivity analyses were conducted removing each trial individually from the analyses. Weighted random-effect meta-regression was performed to explore the relationship between risk profile of participants, reinfarction and death/reinfarction.

Publication bias was investigated using Egger's regression test.

Results of the review
Seven RCTs were included in the review (2,961 participants). Trial size ranged from 163 to 1,059 participants.

In patients with ST-segment elevation myocardial infarction (STEMI), there was no difference in mortality between the standard therapy group and the early percutaneous coronary intervention (PCI) group at either 30 days or six to 12 months follow-up.

Endpoints at 30 days: Compared with standard therapy at 30 days, early PCI after fibrinolysis was associated with a reduction in reinfarction (OR 0.55, 95% CI 0.36 to 0.82; $I^2=0%$; NNT 48), combined death/reinfarction (OR 0.65, 95% CI 0.49 to 0.88; $I^2=0%$; NNT 37), and recurrent ischaemia (OR 0.25, 95% CI 0.13 to 0.49; $I^2=45%$; NNT 19). There was no difference between the two groups for stroke and major bleeding at 30 days. For revascularisation at 30 days, heterogeneity was too high to consider the results conclusive.

Endpoints at six to 12 months: Compared with standard therapy at six to 12 months, early PCI after fibrinolysis was associated with a reduction in reinfarction (OR 0.64, 95% CI 0.40 to 0.98; $I^2=21%$; NNT 46) and combined death/reinfarction (OR 0.71, 95% CI 0.52 to 0.97; $I^2=23%$; NNT 37). Heterogeneity was too high to consider results conclusive for revascularisation and recurrent ischaemic events at six to 12 months follow-up.

Meta-regression showed a trend towards a reduction in reinfarction and death/reinfarction in higher risk patients.

Sensitivity analyses, removing trials individually, showed similar results to the main analyses.

Authors' conclusions
In patients with ST-segment elevation myocardial infarction, early routine percutaneous coronary intervention after fibrinolysis significantly reduced reinfarction and recurrent ischaemia at 30 days compared with standard therapy; it was not associated with any significant increase in bleeding events. The benefits persisted at six to 12 month follow-up.

CRD commentary
The aims of the review were clearly stated for participants, study design and treatment. Two databases were searched, but the search was limited to English language peer reviewed papers. Therefore, it was possible that language bias or publication bias could have affected the review. The authors stated that they tested for publication bias, but the results were not reported. The methods of study selection and data extraction were aimed at reducing reviewer error and/or bias.

The authors stated that they assessed quality of included trials, but the results were not reported or used in the analyses. The methods of synthesis were appropriate; heterogeneity was investigated.

Given the possibility of missed trials and the lack of reporting on the quality of included trials, the authors' conclusions should be treated with caution.

Nine of the authors disclosed that they were also investigators in the included trials involving some sponsorship from pharmaceutical companies (Hoffman La Roche, Abbott Vascular, Boehringer Ingelheim, Eli Lilly and Sanofi-Aventis).
Implications of the review for practice and research

**Practice**: The authors stated that data supported the routine implementation of an early invasive strategy, after successful fibrinolysis, in patients with STEMI.

**Research**: The authors stated that an ongoing individual patient meta-analysis is underway, but that there is still a need for additional larger RCTs, with broader inclusion criteria to assess the effects of routine PCI after fibrinolysis in people with STEMI who do not have initial access to PCI facilities.

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