Timing of invasive treatment after fibrinolysis in ST elevation myocardial infarction: a meta-analysis of immediate or early routine versus deferred or ischemia-guided randomised controlled trials

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CRD summary
This review concluded that significant reductions in re-infarction and recurrent ischaemia were observed with early initiation of angiographic treatment in patients with ST-segment elevated myocardial infarction. The review was generally well conducted and the authors' conclusions are likely to be reliable.

Authors' objectives
To evaluate the risks and benefits of the timing of invasive treatment after fibrinolysis in patients with ST-segment myocardial infarction (STEMI).

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Clinical Trials (CENTRAL) were searched without language restrictions for relevant studies published between 1995 and 2009; search terms were reported. Conference abstracts from the annual meetings of the American Heart Association (1995 to 2009), American College of Cardiology (1995 to 2010), Transcatheter Cardiovascular Therapeutics (2006 to 2009) and European Society of Cardiology (1995 to 2009) were searched. Reference lists of the retrieved articles and reviews were checked to identify additional articles.

Study selection
Randomised Controlled Trials (RCTs) in which immediate or early (within 24 hours of symptom onset) angiography was compared to planned deferred angiography or medical treatment in patients who presented with STEMI were eligible for inclusion. Stents needed to be in routine use and patients needed to be receiving aspirin and thienopyridines. Patients in the deferred treatment group received angiography only in rescue situations or recurrent ischaemia.

Mean/median ages of the included patients ranged from 56 to 63 years. Immediate/early initiation of treatment commenced from 1.1 hours to 16.7 hours from the start of fibrinolysis. In the trials where deferred angiography was used, onset of treatment ranged from 32.5 hours to 5.5 days after the onset of symptoms. Most studies used full-dose regimens of fibrinolytic agents; the other studies used half-dose fibrinolytics combined with full-dose glycoprotein IIb/IIIa inhibitors. Outcomes evaluated were death, recurrent non-fatal myocardial infarction, recurrent ischaemic events, stroke and in-hospital major bleeding.

Two reviewers independently screened abstracts from the electronic database searches and selected articles for inclusion. Conference abstracts were screened by one investigator. Potentially relevant abstracts were reviewed independently by a second abstractor.

Assessment of study quality
Two reviewers independently assessed methodological quality in terms of randomisation methods, allocation concealment, blinding of outcome assessors, description of incomplete data and risk of selective outcome reporting. The reviewers generated a risk of bias summary graph using recommendations from the Cochrane Collaboration.

Data extraction
Two reviewers independently extracted data to calculate risk ratios (RR) and 95% confidence intervals for the endpoints. The reviewers used a standard form and the results were cross-checked. The reviewers contacted the trial authors to locate any missing data.

Methods of synthesis
Statistical heterogeneity across the trials for the results was evaluated using $X^2$. In the absence of statistical
heterogeneity, pooled risk ratios and 95% CIs were calculated using a Mantel-Haenszel fixed-effect model. Subgroup analyses were performed on the basis of delay in the early angiography group of 3.5 hours or less and 13.2 hours or more and low and high rates of rescue percutaneous coronary intervention. Results at 30 days were assessed to evaluate short-term effects.

**Results of the review**

Nine RCTs (n=3,325 participants, range 163 to 1,059) were included in the review. Seven trials reported adequate sequence generation and allocation concealment. All nine trials blinded outcome assessors. Seven trials used intention-to-treat analyses and five avoided outcome reporting bias.

Significant reductions were observed for patients who were treated with immediate or early angiography in recurrent non-fatal myocardial infarction (RR 0.55, 95% CI 0.41 to 0.75, I²=0%) and recurrent ischaemia (RR 0.35, 95% CI 0.25 to 0.49, I² 76%). There was a non-significant reduction in total mortality (RR 0.76, 95% CI 0.58 to 1.01, I²=0%). There was some evidence that the benefit of early angiography on mortality and ischaemia was greater in studies with lower rates of rescue PCI. No differences between the treatment groups were observed in rates of stroke or major in-hospital bleeding.

At short-term (30-day) follow-up, reductions in the risk of recurrent non-fatal myocardial infarction (RR 0.55, 95% CI 0.39 to 0.78) and recurrent ischaemia (RR 0.35, 95% CI 0.25 to 0.49) were observed for patients who underwent immediate or early angiography. There were no significant reductions in risk observed between immediate/early angiography and deferred/no angiography for mortality, stroke and major bleeding.

**Authors' conclusions**

Compared to deferred PCI or standard ischaemia-guided treatment, planned immediate or early invasive angiography after fibrinolytic therapy was associated with a significant reduction in reinfarction and recurrent ischaemia. There was a trend for improved survival without evidence for an excess in bleeding complications or stroke.

**CRD commentary**

The review addressed a well-defined question. Criteria for inclusion of studies were clearly stipulated. Appropriate electronic databases were searched without language restrictions to identify studies. Attempts were made to identify unpublished studies and the authors sought contact with trial authors to gain missing data. Steps were taken by the reviewers to minimise errors and biases throughout the review process. The authors' decision to pool the results of the studies appeared justified, although the results for recurrent ischaemia were subject to significant statistical heterogeneity. The authors reported that this was due to the influence of a trial of unknown quality but was not investigated further.

This review was well conducted and the authors' conclusions are likely to be reliable.

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

**Practice**: The authors stated that the results supported recommendations of routine early invasive angiographic treatment in patients with STEMI after successful fibrinolysis.

**Research**: The authors stated that more research was required to find the optimal timing of early invasive strategies within the range of 24 hours after successful fibrinolysis.

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None stated.

**Bibliographic details**

Record Status
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.