Rescue angioplasty or repeat fibrinolysis after failed fibrinolytic therapy for ST-segment myocardial infarction: a meta-analysis of randomized trials


CRD summary
The authors concluded that rescue percutaneous coronary intervention is associated with improved clinical outcomes for ST-segment myocardial infarction patients after failed fibrinolytic therapy, but there are potential risks. No significant clinical improvements were shown for fibrinolytic therapy and it may be associated with increased harm. Overall, the conclusions appear reliable.

Authors' objectives
To evaluate the effectiveness and safety of rescue percutaneous coronary intervention (PCI) and repeat fibrinolytic therapy, compared with conservative management, in patients with failed fibrinolytic therapy for ST-segment myocardial infarction (STEMI).

Searching
MEDLINE, EMBASE and the Cochrane Library were searched to February 2006 without language restrictions; the search terms were reported. Bibliographies of articles and reviews were also searched.

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 rescue PCI or repeat fibrinolytic therapy with conservative therapy were eligible for inclusion. Conservative therapy was defined as no further immediate reperfusion therapy. In the included studies, the average time from administration of initial fibrinolytic therapy to rescue PCI ranged from 77 to 274 minutes. The average time from onset of initial symptoms to repeat fibrinolytic therapy ranged from 332 to 360 minutes where specified; the agent used was tissue plasminogen activator.

Participants included in the review
Studies enrolling STEMI patients who failed initial fibrinolytic therapy were eligible. Studies not restricted to STEMI patients were excluded. The reviewers accepted angiographic and clinical definitions for failed fibrinolytic therapy. The mean age of the patients in the included studies ranged from 56 to 63 years. Anterior wall infarction was present in between 41% and 100% of patients.

Outcomes assessed in the review
Clinical outcomes of interest included all-cause mortality, heart failure and reinfarction, while safety outcomes included stroke, major and minor bleeding; the original study definitions were used. The duration of follow-up ranged from the time of hospital discharge to 6 months.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the eligibility of studies for inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed using the 5-point Jadad scale, which evaluates the reporting of randomisation, blinding and withdrawals. The authors did not state how the validity assessment was performed.
Data extraction

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

The results from the primary studies were expressed as relative risks (RRs) together with 95% confidence intervals (CIs).

Methods of synthesis

How were the studies combined?
A Mantel-Haenszel fixed-effect model was used to estimate the pooled RRs and absolute risk reduction. From these the number-needed-to-treat and number-needed-to-harm were derived.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test and the I-squared statistic.

Results of the review

Eight trials (n=1,177) were included. Six trials provided data for the rescue PCI analysis (n=908); 3 trials randomised 420 patients to repeat fibrinolysis or conservative therapy.

Among the rescue PCI trials, only one had a Jadad score of 4, three had a score of 3 and two had scores of 2. All trials which compared repeat fibrinolysis with conservative management had a Jadad score of 4.

Rescue PCI was not associated with a significant reduction in all-cause mortality compared with no additional immediate reperfusion treatment (RR 0.69, 95% CI: 0.46, 1.05, p=0.09; 6 trials). It showed an RR of 0.73 for heart failure (95% CI: 0.54, 1.00, p=0.05; 4 trials) and was associated with a significant reduction in reinfarction (RR 0.58, 95% CI: 0.35, 0.97, p=0.04; 3 trials).

Rescue PCI was associated with an increased risk of stroke compared with conservative therapy (RR 4.98, 95% CI: 1.10, 22.48, p=0.04; 2 trials) and minor bleeding (RR 4.58, 95% CI: 2.46, 8.55, p<0.001; 3 trials).

Repeat fibrinolytic therapy was not associated with a significant reduction in all-cause mortality (RR 0.68, 95% CI: 0.41, 1.14, p=0.14; 3 trials) or reinfarction (RR 1.79, 95% CI: 0.92, 3.48, p=0.09; 2 trials) compared with conservative therapy.

CRD commentary

The review addressed a clear question with well-defined inclusion criteria. No language restrictions were applied, thus reducing the possibility of language bias. No explicit attempt to identify unpublished studies was described, which raises the possibility that publication bias might have been introduced in the review. The authors attempted to minimise bias and error during the review process by carrying out the study selection in duplicate. It was unclear whether the study quality assessment and data extraction were also performed in duplicate, therefore reviewer error and bias might have been introduced at these stages. Study quality was assessed but details of the individual components were not given...
and pertinent issues such as allocation concealment were not assessed. The inclusion of results from trials with very low Jadad scores could have affected the pooled estimates in the meta-analysis, but this was not further explored. Some sensitivity analyses were performed. Most analyses were based on a small number of studies. It should be noted that only selected clinical outcomes showed a statistically significant benefit for rescue PCI. Overall, the conclusions appear reliable.

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

**Practice:** The authors stated that repeat fibrinolytic therapy in patients with STEMI cannot be recommended.

**Research:** The authors stated that randomised trials are needed to determine the most appropriate adjunctive pharmacotherapy in patients undergoing rescue PCI.

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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.