Comparison of primary percutaneous coronary intervention and fibrinolytic therapy in ST-segment-elevation myocardial infarction: Bayesian hierarchical meta-analyses of randomized controlled trials and observational studies

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CRD summary
The authors concluded that compared with fibrinolysis, primary percutaneous coronary intervention (PCI) was associated with short-term reductions in mortality, reinfarction and stroke in ST-segment elevation myocardial infarction. PCI was associated with long-term reductions in mortality and reinfarction in randomised controlled trials, but not in observational studies. This was a well-conducted review and the authors' conclusions are likely to be reliable.

Authors' objectives
To compare primary percutaneous coronary intervention (PCI) with fibrinolytic therapy in patients with ST-segment elevation myocardial infarction (STEMI) using data from randomised controlled trials (RCTs) and observational studies.

Searching
BIOSIS Previews, CINAHL, EMBASE, PubMed, Web of Science, Current Contents, Cochrane Library and health technology assessment agencies were searched without language restrictions to May 2008. Search terms were reported. In addition, reference lists of published reports were screened. Studies were excluded if they had been presented at conferences or published only as abstracts or conference proceedings.

Study selection
Studies (RCTs and observational studies) that compared full-dose commercially approved fibrinolytic therapy (such as streptokinase, urokinase and fibrin-specific tissue plasminogen activators such as tenecteplase and reteplase with PCI in patients with STEMI were eligible for inclusion. Observational studies had to meet minimum quality criteria described by Concato et al (see under validity for details). Studies that evaluated facilitated PCI, experimental fibrinolytic agents or intracoronary fibrinolytic therapy or that enrolled patients with contraindications to either fibrinolytic therapy or PCI were excluded. The review assessed mortality, stroke (incorporating intracranial bleeding), reinfarction, and major bleeding. Short-term (up to six weeks post STEMI) and long-term (at least one year post STEMI) complications were assessed.

In the included studies, the mean age of patients ranged from 57 to 91 years. In a minority of studies pre-hospital fibrinolysis was used (two RCTs and seven observational studies). Some studies used fibrin-specific agents (16 RCTs and 11 observational studies). Several of the RCTs excluded high-risk patients (elderly, renal disease, cardiogenic shock, left bundle branch block and Killip class of two or more).

Two reviewers independently selected studies and resolved disagreements by consensus.

Assessment of study quality
Observation studies had to use concurrent controls, clearly define inclusion criteria and specify study entry time. The assessment of the validity of RCTs and observational studies was based on the CONSORT and MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines.

Two reviewers independently assessed validity and resolved disagreements by consensus.

Data extraction
Two reviewers independently extracted data and resolved disagreements by consensus.

Methods of synthesis
Data from RCTs and observational studies were analysed separately. Pooled odds ratios (OR) and 95% credibility intervals (CrI) were calculated using a Bayesian hierarchical random effects model. Non-informative prior distributions were selected for all parameters (details were reported). Sensitivity analyses were conducted by varying prior distributions for a sigma and gamma prior distribution, and by repeating the analysis using non-Bayesian methods, random effects restricted-maximum-likelihood methods and random effects DerSimonian and Laird models. Studies that used pre-hospital fibrinolysis were also analysed separately as were studies with optimal follow-up. Absolute risk reductions and numbers needed to treat were also reported. Publication bias was assessed using funnel plots, fail-safe N and trim and the fill method.

Results of the review

Twenty-three RCTs (n=8,140) and 32 observational studies (n=185,900) were included. Ten RCTs reported use of central randomisation and 10 RCTs reported blinded outcome assessment. In all but one RCT, almost all patients were followed-up long term. Five observational studies reported at least 95% long-term follow-up. Differences between treatment groups in observational studies were discussed.

Results from sensitivity analyses using varying values for prior distributions and non-Bayesian models were similar to results for Bayesian analyses. Results below are for Bayesian analysis.

Compared to fibrinolysis, PCI interventions were associated with a statistically significant reduction in short-term mortality in RCTs and observational studies (OR for RCTs 0.66, 95% CrI 0.51 to 0.82; 23 studies. OR for observational studies 0.77, 95% CrI 0.62 to 0.95; 29 studies).

Compared to fibrinolysis, PCI interventions were associated with a statistically significant reduction in stroke in RCTs and observational studies (OR for RCTs 0.37, 95% CrI 0.21 to 0.60; 21 studies. OR for observational studies 0.39, 95% CrI 0.29 to 0.61; 15 studies).

At long-term follow-up, PCI interventions were associated with a statistically significant reduction in mortality and short- and long-term reinfarction in RCTs (OR for mortality in RCTs 0.76, 95% CrI 0.58 to 0.95; 11 studies. OR for short-term reinfarction in RCTs 0.35, 95% CrI 0.24 to 0.51; 22 studies. OR for long-term reinfarction in RCTs 0.49, 95% CrI 0.32 to 0.66; nine studies).

There was no significant difference between PCI and fibrinolysis in long-term mortality (12 studies) or reinfarction (four studies) in observational studies.

Funnel plots were symmetrical suggesting the absence of publication bias.

Authors’ conclusions

Compared with fibrinolysis, PCI was associated with short-term reductions in mortality, re-infarction and stroke in STEMI. PCI was also associated with long-term reductions in mortality and reinfarction in RCTs, but there was no conclusive evidence for a long-term benefit in mortality or reinfarction in observational studies.

CRD commentary

The review question was clearly stated and inclusion criteria were defined. Several relevant sources were searched and no language restrictions were applied. No attempts were made to minimise publication bias; potential for publication bias was assessed and no evidence was found. Appropriate methods were used to minimise reviewer error and bias during the review process. Only observational studies that met minimum quality criteria were included. Validity was assessed and results were reported albeit in the discussion. Appropriate methods were used for the meta-analyses and sensitivity analyses were conducted. However, some analysis of observational studies showed non-overlapping credibility intervals, which suggested presence of heterogeneity. Overall, this was a well-conducted review and the authors’ conclusions are likely to be reliable.

Implications of the review for practice and research

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

Research: The authors stated that further large studies were required to compare the efficacy and safety of pre-hospital
fibrinolysis with primary PCI.

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