Abciximab as adjunctive therapy to reperfusion in acute ST-segment elevation myocardial infarction: a meta-analysis of randomized trials

CRD summary
This review assessed the efficacy and safety of adjunctive treatment with abciximab in patients with ST-segment elevation myocardial infarction. The authors concluded that abciximab significantly reduces 30-day and long-term mortality when combined with primary angioplasty (but not fibrinolysis), but increases major bleeding complications when used with fibrinolysis. The authors’ conclusions are likely to be reliable.

Authors’ objectives
To assess the efficacy and safety of abciximab as adjunctive treatment to reperfusion in patients with ST-segment elevation myocardial infarction (STEMI).

Searching
MEDLINE and PubMed were searched from 1990 to December 2004; the key search words were reported. Scientific session abstracts were searched in Circulation - Journal of the American College of Cardiology, and European Heart Journal from January 1999 to December 2004. Only completed, published studies were eligible.

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 of abciximab were eligible for inclusion if the same primary reperfusion treatment (fibrinolysis or primary angioplasty) was used in the treatment and control groups. All studies of fibrinolysis used full-dose abciximab plus half-dose fibrinolysis.

Participants included in the review
Studies of participants with STEMI were eligible for inclusion.

Outcomes assessed in the review
The primary outcomes in the review were mortality at 30 days and at long-term follow-up (6 to 12 months). The secondary outcomes were reinfarction at 30 days, intracranial bleeding and other major bleeding complications (defined by Thrombolysis in Myocardial Infarction or Global Utilisation of Strategies to Open Occluded Arteries criteria).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers extracted the data and resolved any disagreements through reaching consensus. The authors of reports with unclear or incomplete data were contacted for further details. Data on clinical outcomes were extracted on an intention-to-treat basis.
Methods of synthesis

How were the studies combined?
Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using a fixed-effect model (Mantel-Haenszel) in the absence of significant statistical heterogeneity and a random-effects model (DerSimonian and Laird) when significant heterogeneity was found.

Where a statistically significant difference between treatments was found, either the number-needed-to-treat (NNT) or the number-needed-to-harm (NNH) was calculated. Publication bias was assessed using a funnel plot, with linear regression used to measure funnel plot asymmetry.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Breslow-Day test (significance level P<0.10). Pre-specified subgroup analyses were conducted according to reperfusion treatment. The influence of each study on the pooled OR was examined.

Results of the review

Eleven RCTs (n=27,115) were included, of which eight used primary angioplasty (n=3,949) and three used fibrinolysis (n=23,166).

Mortality at 30 days: there was no significant difference between abciximab and no abciximab in 30-day mortality for all studies combined (5.2% versus 5.5%; OR 0.97, 95% CI: 0.87, 1.08, P=0.61), or for studies using fibrinolysis (5.8% versus 3.8%; OR 1.0, 95% CI: 0.9, 1.12, P=0.95). Abciximab significantly reduced 30-day mortality in studies using angioplasty (2.4% versus 3.4%; OR 0.68, 95% CI: 0.47, 0.99, P=0.047). The NNT to prevent one death was estimated as 100. There was no evidence of statistically significant heterogeneity in any of these analyses.

Long-term mortality: there was no significant difference between abciximab and no abciximab in long-term mortality for all studies combined (7.9% versus 8.0%; OR using random-effects model 0.88, 95% CI: 0.71, 1.09, P=0.25; heterogeneity significant, P=0.03), or for studies using fibrinolysis (8.6% versus 8.3%; OR 1.04, 95% CI: 0.95, 1.15, P=0.41; heterogeneity not significant, P=0.15). Abciximab significantly reduced long-term mortality in studies using angioplasty (4.4% versus 6.2%; OR 0.69, 95% CI: 0.52, 0.92, P=0.01; heterogeneity not significant, P=0.15). The NNT was 55.6.

Reinfarction at 30 days: abciximab significantly reduced reinfarction at 30 days compared with no abciximab for all studies combined (2.1% versus 3.3%; OR 0.63, 95% CI: 0.54, 0.73, P<0.001; heterogeneity not significant, P=0.66; NNT 83.3), for studies using primary angioplasty (NNT 111.1) and for studies using fibrinolysis (NNT 76.9).

Bleeding: there was no significant difference between abciximab and no abciximab for intracranial bleeding for all studies combined, for studies using primary angioplasty, or for studies using fibrinolysis. Bleeding complications: abciximab significantly increased bleeding complications for all studies combined (5.2% versus 3.2%; OR using random-effects model 1.51, 95% CI: 1.15, 1.98, P<0.001; heterogeneity significant, P=0.02; NNH 50) and for studies using fibrinolysis (5.2% versus 3.1 %; OR 1.77, 95% CI: 1.55, 2.03, P<0.001; heterogeneity not significant, P=0.15; NNT 47.6). There was no significant difference between abciximab and no abciximab in terms of bleeding complications for studies using primary angioplasty.

There was no evidence for publication bias using the funnel plot or linear regression (P=0.40). Individual studies did not influence results.

Authors' conclusions

Adjunctive treatment with abciximab for STEMI significantly reduced 30-day and long-term mortality when used with primary angioplasty, but not when combined with fibrinolysis. Abciximab significantly reduced the 30-day reinfarction rate when used with either primary angioplasty or fibrinolysis. Abciximab increased major bleeding complications when used with fibrinolysis.
CRD commentary
The review addressed a clear question in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched and the search terms were stated, but it was unclear whether any language limitations had been applied. Only published studies were included, thus raising the possibility of publication bias, although the authors found no evidence for such bias. The methods used to select the studies were not described, so it is not known whether any efforts were made to reduce errors and bias. However, methods were used to minimise bias when extracting the data and the data were extracted on an intention-to-treat basis. Only RCTs were included but their validity was assessed.

Statistical heterogeneity was assessed and the data were appropriately combined in meta-analyses. Subgroup analyses were pre-specified and no significant heterogeneity among subgroups was found. The authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that until the results from large RCTs are available abciximab should be strongly considered in primary angioplasty for STEMI, especially in high-risk patients. However, the combination of abciximab and fibrinolysis should be avoided because of the risk of bleeding, especially in elderly patients.

Research: The authors stated that future RCTs should examine the interaction between age and the risk of intracranial bleeding.

Bibliographic details

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Other publications of related interest
This additional published commentary may also be of interest. Abciximab in the treatment of ST-segment elevation myocardial infarction [letters]. JAMA 2005;294:1760-1.

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Subject indexing assigned by NLM

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Angioplasty, Balloon, Coronary; Antibodies, Monoclonal /therapeutic use; Chemotherapy, Adjuvant; Humans; Immunoglobulin Fab Fragments /therapeutic use; Myocardial Infarction /drug therapy /therapy; Platelet Aggregation Inhibitors /therapeutic use; Platelet Glycoprotein GPIIb-IIIa Complex /antagonists & inhibitors; Randomized Controlled Trials as Topic; Survival Analysis

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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.