Facilitated angioplasty with combo therapy among patients with ST-segment elevation myocardial infarction: a meta-analysis of randomized trials

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CRD summary
The authors concluded that in patients with ST-segment elevation myocardial infarction who underwent primary angioplasty, glycoprotein (Gp) IIb-IIIa inhibitors plus reduced lytic therapy was not superior to Gp IIb-IIIa inhibitors alone and could not be routinely recommended. These conclusions appeared to reflect the evidence, but incomplete reporting of review methods and absence of validity assessment means their reliability is unclear.

Authors’ objectives
To compare adjunctive glycoprotein (GP) IIb-IIIa inhibitors plus reduced lytic therapy with adjunctive Gp IIb-IIIa inhibitors in patients with ST-segment elevation myocardial infarction (STEMI) who are undergoing angioplasty.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) and abstracts from scientific sessions in Circulation, Journal of the American College of Cardiology, European Heart Journal and American Journal of Cardiology were searched from 1990 to December 2007. Oral presentations and/or expert slide presentations were searched on www.tctmd.com, www.europcr.com, American College of Cardiology (www.acc.org), American Hospital Association (www.aha.org) and European Society of Cardiology (www.escardio.org) websites from 2002 to December 2007. Search terms were reported. No language restrictions were applied.

Study selection
Completed randomised controlled trials (RCTs) were included if they compared adjunctive Gp IIb-IIIa inhibitors plus half-dose lytic therapy with adjunctive Gp IIb-IIIa inhibitors in patients with STEMI who underwent primary angioplasty. Studies had to have follow-up of 90% or more of patients.

The review assessed angiographic end points (preprocedural and postprocedural thrombolysis in myocardial infarction (TIMI) 3 flow, clinical end points (mortality and reinfarction) and safety end points (major bleeding and intracranial bleeding).

The included studies evaluated various Gp IIb-IIIa inhibitors (mostly abciximab; eptifibatide and tirofiban were each used in a single study) and lytic therapy (mostly reteplase or alteplase; tenecteplase was used in a single study). In most studies STEMI had to have occurred less than six hours before; in two studies patients with STEMI less than 12 hours before were included. Where reported, mean time from symptom onset to administration of drugs ranged from 138 to 259 minutes across treatment groups.

The authors state neither how papers were selected for the review nor how many reviewers performed the selection.

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

Data extraction
Two reviewers independently extracted odds ratios (OR) and 95% confidence intervals (CI) on an intention-to-treat basis. Disagreements were resolved by consensus. Authors of studies with incomplete or missing information were contacted for additional data.

Methods of synthesis
Pooled odds ratios and 95% CI were calculated using the fixed-effect Mantel-Haenszel method; DerSimonian and Laird random-effects model was used in the presence of significant heterogeneity. Heterogeneity was assessed using $X^2$ and $I^2$. The possibility of publication bias was assessed using a funnel plot and Egger's linear regression test.
Results of the review
Six RCTs were included (n=2,684 patients).

Adjunctive Gp IIb-IIIa inhibitors plus reduced lytic therapy was associated with a statistically significant improvement in preprocedural TIMI 3 flow (44.3% versus 15.2%, OR 4.14, 95% CI 3.44 to 4.99) compared to compared adjunctive Gp IIb-IIIa inhibitors alone. There was no significant difference in postprocedural TIMI 3 flow (91.5% versus 91.2%). Significant heterogeneity was found for preprocedural (p<0.0001) but not postprocedural TIMI 3 flow.

There was no significant difference between treatments in 30-day mortality (4.2% versus 4.6%) or 30-day reinfarction (1.3% versus 1.3%).

Adjunctive Gp IIb-IIIa inhibitors plus reduced lytic therapy was associated with a statistically significant increase in risk of bleeding complications (5.8% versus 3.9%, OR 1.50, 95% CI 1.04 to 2.18).

No significant heterogeneity was found for mortality, reinfarction or bleeding outcomes.

There was no evidence of publication bias from Egger’s test.

Authors' conclusions
Among patients with STEMI who underwent primary angioplasty the combination of adjunctive Gp IIb-IIIa inhibitors plus reduced lytic therapy was not superior to adjunctive Gp IIb-IIIa inhibitors alone and thus may not be routinely recommended.

CRD commentary
The review question was clearly stated and inclusion criteria appropriately defined. Several relevant sources were searched and attempts were made to minimise publication and language bias. Methods were used to minimise reviewer errors and bias in extraction of data; it was unclear whether similar steps were taken in study selection. Only RCTs were included, but study validity was not assessed and so results from these studies and any synthesis may not be reliable. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. Although heterogeneity was found for some outcomes, forest plots showed that all studies had the same direction of treatment effect. Evidence appeared to support the authors’ conclusions, but incomplete reporting of review methods and a lack of assessment of study quality means that the reliability of the findings is unclear.

Implications of the review for practice and research
Practice: The authors stated that combination of adjunctive Gp IIb-IIIa inhibitors plus reduced lytic therapy could not be routinely recommended for patients with STEMI who underwent primary angioplasty.

Research: The authors stated that future studies should evaluate combination therapy with adjunctive Gp IIb-IIIa inhibitors plus reduced lytic therapy given within the first few hours from symptom onset, especially in patients who were being transferred for primary angioplasty.

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