Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials

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CRD summary
This review compared facilitated regimens and primary approaches of percutaneous coronary intervention in patients with ST-segment-elevation myocardial infarction. The authors concluded that no additional benefit arose from the facilitated intervention. Due to adverse events, facilitated regimens (especially using thrombolytic therapy) were not recommended for practice. Despite some limitations in the review process, the authors' conclusions appear justified.

Authors' objectives
To compare facilitated regimens and primary approaches of percutaneous coronary intervention (PCI).

Searching
MEDLINE and the Cochrane Controlled Trials Register were searched from January 1990 to September 2005; the search terms were reported. Conference proceedings were handsearched for further relevant trials, including those of the American Heart Association, American College of Cardiology, European Society of Cardiology and Transcatheter Cardiovascular Therapeutics meetings (1990 to 2005). References of relevant journal articles and reviews were also checked. The principal investigators of all trials were contacted to clarify data and to gain additional information (including unpublished data), where necessary.

Study selection
Study designs of evaluations included in the review
Randomised-controlled trials (RCTs) were eligible for inclusion in the review. The included trials were a mixture of open-label and double-blind placebo-controlled designs.

Specific interventions included in the review
Studies of facilitated PCI (administered at the pre-hospital and pre-transfer stage, or in an emergency centre) were eligible for inclusion in the review. The drugs of interest were high-dose heparin, platelet glycoprotein IIb/IIIa inhibitors, full-dose thrombolytic therapy, reduced-dose thrombolytic therapy, or a combination of both platelet glycoprotein IIb/IIIa inhibitors and reduced-dose thrombolytic therapy. The interventions were compared with non-facilitated (primary) percutaneous intervention.

Participants included in the review
Studies of patients with ST-segment-elevation myocardial infarction (STEMI) were eligible for inclusion in the review.

Outcomes assessed in the review
Short-term (up to 42 days post procedure) clinical and angiographic outcomes were eligible for inclusion. The primary clinical outcomes of interest were death, stroke, nonfatal myocardial infarction, urgent target vessel revascularisation, and major bleeding. The primary angiographic outcomes were TIMI (pre-thrombosis and post-thrombosis in myocardial infarction) grade 3 flow, and pre- and post-myocardial perfusion grade 3 flow. ST-segment resolution was also reported.

How were decisions on the relevance of primary studies made?
Two investigators independently assessed the relevance of trials for inclusion in the review.

Assessment of study quality
The validity of the trials was assessed in terms of blinding, allocation concealment and whether enrolment was
terminated early. The authors did not state who performed the validity assessment.

**Data extraction**
The authors did not state how many investigators performed the data extraction. Outcome data were extracted using actual counts in each trial, based on intention-to-treat and according to randomisation. These were extracted for all studies together, as well as for the pharmacological pre-treatment subgroups. Data were collected prior to using chi-squared and Fisher’s exact tests to compare the treatment regimens, and odd ratios (ORs) and 95% confidence intervals (CI) were calculated.

**Methods of synthesis**

How were the studies combined?
The studies were combined in a meta-analysis using a random-effects model.

How were differences between studies investigated?
Heterogeneity was examined using the I-squared statistic. High heterogeneity was regarded as a value of more than 75%, while low heterogeneity was a value below 25%.

**Results of the review**

Seventeen RCTs were included to compare facilitated (n=2,237) and primary (n=2,267) PCI.

The authors reported that most trials fulfilled their validity criteria. All trials used a concealed allocation method. Four of the 17 trials were double-blinded and placebo-controlled. Three trials were stopped early.

**Clinical outcomes.**
Mortality was significantly increased (5% versus 3%) as a result of the facilitated intervention compared with the primary PCI (OR 1.38, 95% CI: 1.01, 1.87, P=0.04). The effect was largely in trials using thrombolytic therapy alone (6% versus 4%) (OR 1.43, 95% CI: 1.01, 2.02, P=0.04). There was no evidence of heterogeneity amongst the studies.

Nonfatal reinfarction was significantly increased in those receiving a facilitated intervention (3% versus 2%) (OR 1.71, 95% CI: 1.16, 2.51, P=0.006). Again, this was largely in those regimens employing thrombolytic therapy alone (4% versus 2%) (OR 1.81, 95% CI: 1.19, 2.77, P=0.006). There was no evidence of heterogeneity amongst the studies.

Urgent target vessel revascularisation rates were higher in patients receiving the facilitated intervention (4% versus 1%) (OR 2.39, 95% CI: 1.23, 4.66, P=0.010). Thrombolytic therapy alone represented a large contributor to this finding (5% versus 1%) (OR 4.81, 95% CI: 2.47, 9.37, P<0.0001). There was no evidence of heterogeneity amongst the studies.

Major bleeding rates were higher in those receiving the facilitated intervention (7% versus 5%) (OR 1.51, 95% CI: 1.10, 2.08, P=0.010). Rates of haemorrhage (0.7% versus 0.1%, P=0.0014) and total stroke (1.1% versus 0.3%, P=0.0008) were higher in those receiving thrombolytic therapy as part of the intervention.

**Angiographic outcomes.**
The facilitated PCI was associated with a two-fold increase (37% versus 15%) in those with initial TIMI grade 3 flow compared with those receiving the primary intervention (OR 3.18, 95% CI: 2.22, 4.55, P=0.0001); there was substantial heterogeneity amongst these studies (I-squared 74%). There was no significant difference between the final flow rates (OR 1.19, 95% CI: 0.86, 1.64, P=0.30); no heterogeneity was found between these studies.

In 8 trials using single or combination therapy, initial rates of myocardial perfusion grade 3 flow were significantly higher in studies of facilitated intervention with platelet glycoprotein IIb/IIIa inhibitors than in those with the primary intervention (31% versus 19%) (OR 2.60, 95% CI: 1.36, 4.95, P=0.04). However, there was no difference in the final rates (OR 1.79, 95% CI: 0.93, 3.44, P=0.08). In one small trial that compared the facilitated approach using thrombolytic therapy, a significant improvement in initial and final rates of myocardial perfusion grade 3 flow was
A significant difference (P<0.03) was noted in favour of the facilitated intervention in 4 of the 9 trials reporting ST-segment resolution data.

**Cost information**
No

**Authors’ conclusions**
Facilitated PCI does not offer any additional benefit compared with primary percutaneous intervention in patients with STEMI.

**CRD commentary**
The review addressed a clear research question and contained explicit inclusion criteria for the participants, intervention, outcomes and study design. A thorough search strategy was conducted, which included attempts to retrieve unpublished data. However, publication bias was not explored and could not, therefore, be ruled out. Most studies were deemed to meet the specified validity criteria, although full details were not provided. Heterogeneity was explored, and the method of study synthesis appeared appropriate. Biases on some aspects of the review process could not be ruled out. Despite this limitation, the authors' conclusions are an accurate reflection of the evidence presented. Given the high incidence of adverse events, their recommendations for practice are justified.

**Implications of the review for practice and research**
Practice: The authors stated that facilitated PCI (especially those using thrombolytic therapy alone) should not be used outside the context of RCTs.

Research: The authors did not state any recommendations for research.

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