Role of adjunctive thrombectomy and embolic protection devices in acute myocardial infarction: a comprehensive meta-analysis of randomized trials

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CRD summary
This review concluded that catheter thrombus aspiration devices are beneficial in reducing mortality in acute ST-segment-elevation myocardial infarction, compared to percutaneous coronary intervention alone. However, mechanical thrombectomy devices appeared to increase mortality, and embolic protection devices had a neutral effect. Despite some uncertainties surrounding review methodology, the authors’ conclusions appear to be reasonable.

Authors' objectives
To assess the clinical effects of adjunctive thrombectomy and embolic protection devices during revascularisation for acute myocardial infarction.

Searching
MEDLINE and the Cochrane Library were searched from 1996 to June 2008. Search terms were reported. Two websites (Clinicaltrials.gov and tctmd.com) and supplements from four relevant journals were also searched. Reference lists of identified reviews were checked. The Science Citation Index was used to identify further references through identified studies. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that randomised participants within 12 hours of acute myocardial infarction, that had used one of three specified interventions to protect against embolisation, were eligible for inclusion. The interventions of interest were thrombus aspiration, mechanical thrombectomy and embolic protection, prior to percutaneous coronary intervention. The comparator was percutaneous coronary intervention alone. Trials that compared one type of device against another were excluded, as were trials on thrombectomy on saphenous vein grafts. More details on the devices were given in the paper.

Clinical outcomes or markers of myocardial perfusion (myocardial blush and ST-segment resolution) had to be reported. The primary outcome of interest was all-cause mortality. Secondary outcomes were major adverse cardiac events, myocardial infarction, target vessel revascularisation and stroke. A major adverse cardiac event was defined as a composite of death, myocardial infarction and target vessel revascularisation. Definitions of myocardial infarction and stroke were given. Target vessel revascularisation was defined as repeat percutaneous coronary intervention or surgical revascularisation.

In the included trials mean ages of participants ranged from 28 to 67 years, and between 39 to 90% were men. Between 55 and 100% had TIMI (Thrombolysis In Myocardial Infarction) flow grade 0/1 and, where stated, 44 to 100% had visible thrombus. All participants received aspirin and intravenous heparin; in most trials clopidogrel was used. Some participants also received glycoprotein IIb/IIIa inhibitors. Where stated, stents were used in 66 to 100% of participants. Time between onset of ischaemia symptoms and percutaneous coronary intervention ranged from 2.4 to 7.9 hours. Nearly half of all included trials used thrombus aspiration interventions, 38% used embolic aspiration, and 15% used mechanical aspiration devices (see paper for more detail on devices).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Quality was assessed based on: adequate description of treatment allocation; blinding of outcome assessors; and description of losses to follow-up.

The authors did not state how the validity assessment was performed.
Data extraction

All outcomes were assessed according to maximal follow-up time in individual trials. Additionally, mortality was assessed at 30 days or less. Weighted mean follow-up times were calculated using each trial's sample size and length of follow-up. Events reported to hospital discharge were taken as three days. The authors assessed myocardial perfusion at 60 minutes after the intervention or, if this was unavailable, immediately after reperfusion up to 90 minutes or, if multiple time points reported, the time point closest to 60 minutes. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated for clinical outcomes.

Data were extracted by two reviewers independently. Discrepancies were resolved by discussion and, where necessary, with a third reviewer. Some study investigators were contacted to clarify data.

Methods of synthesis

Data were pooled using Mantel-Haenszel fixed-effect model and DerSimonian-Laird random-effects model. Fixed-effect results were reported unless there was significant heterogeneity, then random-effects were reported. Pooled risk ratios together with 95% confidence intervals were presented. Heterogeneity was assessed using the $I^2$ statistic. Sensitivity analyses were conducted according to type of trial (published and unpublished). Overall results were presented, as well as those for trials, grouped according to category of device. Intention-to-treat analyses were performed for clinical outcomes. Treatment received analysis was used for myocardial blush and ST-segment resolution outcomes. Automatic ‘zero cell’ corrections were used for trials with no events in individual outcomes. Publication bias was assessed using Begg’s method.

Results of the review

Thirty randomised controlled trials (RCTs) were included in the review (6,402 participants). Thirteen RCTs (3,026 participants) reported on catheter aspiration devices, five RCTs (934 participants) on mechanical thrombectomy devices and 12 RCTs (2442 participants) on embolic protection. Most trials were small; trial size ranged from 40 to 1071 participants. Follow-up from hospital discharge ranged from one to 12 months (12 RCTs had a follow-up of six months or longer). Eight RCTs provided a description of treatment allocation. The outcome assessor was blinded in 14 RCTs; it was unclear in the remainder. Thirteen studies did not provide information of loss to follow-up; the remainder reported losses of between 0% and 10%.

**Mortality:** There was no difference between adjunctive devices as compared to percutaneous coronary intervention alone, with a mortality incidence of 3.2% versus 3.7% (RR 0.87, 95% CI 0.67 to 1.13; $I^2$=0%; mean follow-up 5.0 months). When categories of device were analysed separately; there was a reduction with catheter aspiration devices (RR 0.63, 95% CI 0.43 to 0.93; mean follow-up 6.2 months); there was a trend towards an increase with mechanical thrombectomy devices (RR 1.93, 95% CI 1.00 to 3.72; mean follow-up 4.6 months); there was no difference with embolic protection devices (RR 0.92, 95% CI 0.60 to 1.40; mean follow-up 3.7 months).

**Clinical events:** Pooled data (for all devices) showed no statistical significant differences between adjunctive devices and percutaneous coronary intervention alone for myocardial infarction, target vessel revascularisation, stroke and major adverse cardiac events. However, there were trends favouring adjunctive devices for myocardial infarction (RR 0.71, 95% CI 0.48 to 1.05) and major adverse cardiac events (risk ratio 0.88, 95% CI: 0.74 to 1.04), and favouring percutaneous coronary intervention for stroke (RR 1.92, 95% CI 0.96 to 3.83). See paper for details of results by category.

**Myocardial perfusion:** Use of devices increased the incidence of TIMI (Thrombolysis In Myocardial Infarction) blush grade 3 after revascularisation and of complete ST-segment elevation resolution, although there was heterogeneity between trials. See paper for full details.

Tests showed no evidence of publication bias for clinical outcomes, but it was present for markers of perfusion.

Authors' conclusions

Catheter thrombus aspiration devices were beneficial in reducing mortality, compared to percutaneous coronary intervention alone, during acute myocardial infarction. However, mechanical thrombectomy appeared to increase
mortality, and embolic protection devices had a neutral effect.

**CRD commentary**

The inclusion criteria, in terms of study design, participants and interventions, were clearly stated. The search covered a number of appropriate sources, and included unpublished studies, which is likely to have reduced the risk of publication bias. Methods of study selection and quality assessment were not described, so it is not possible to assess how appropriate these were. However, methods of data extraction were designed to reduce the risk of reviewer error and bias. Appropriate methods were used to assess the quality of included trials, although the results were not used to inform any differences between results in individual trials. Data were pooled appropriately and heterogeneity was investigated. The authors commented that the results may not be generalisable to people who fall outside the specific inclusion criteria for the included trials. Despite some uncertainties surrounding the methodology used to select and validate trials, overall the authors' conclusions appear to be reasonable.

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

**Practice:** The authors stated that the routine use of mechanical thrombectomy devices should be avoided in acute ST-elevation myocardial infarction until further data becomes available.

**Research:** The authors stated that TIMI (Thrombolysis In Myocardial Infarction) blush grade and ST-segment resolution should not be used as sole outcome measures, in place of clinical outcomes, when designing studies on acute myocardial infarction.

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