Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials

CRD summary
This review compared routine versus selective invasive strategies for unstable angina and non-ST-segment elevation myocardial infarction. The authors concluded that the routine invasive strategy reduced long-term myocardial infarction, angina and rehospitalisation. Incomplete reporting of the review methods and the lack of a validity assessment make it difficult to comment on the strength of the evidence for the authors' conclusions.

Authors' objectives
To evaluate the early and late effects of a routine invasive strategy versus a selective invasive strategy on major cardiovascular outcomes in patients with unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI).

Searching
MEDLINE and the Cochrane CENTRAL Register were searched from 1970 to June 2004. Abstracts from major cardiology meetings were also searched, as were the reference lists of original articles and reviews.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Studies with inadequate allocation concealment (e.g. allocation by day of the week) were excluded, as were those in which participant inclusion was determined after coronary angiography had been performed.

Specific interventions included in the review
Studies that compared a routine invasive strategy with a selective invasive strategy were eligible for inclusion. A routine invasive strategy was defined as the referral of all patients with unstable angina or NSTEMI for coronary angiography, followed by revascularisation in those with suitable coronary anatomy. A selective invasive strategy was defined as an approach in which patients were initially treated with pharmacological therapy, after which cardiac catheterisation and revascularisation were performed only for those with recurrent symptoms or objective evidence of inducible ischaemia on noninvasive testing.

Participants included in the review
Studies of patients with unstable angina or NSTEMI were eligible for inclusion. Studies were excluded if the majority of its patients had stable angina pectoris or acute ST-segment elevation myocardial infarction (MI). The included studies involved higher-risk patients (elevated cardiac biomarkers at baseline) and lower-risk patients (negative cardiac biomarkers at baseline).

Outcomes assessed in the review
Studies assessing the major outcomes of death and MI occurring from initial hospitalisation to the end of follow-up were eligible for inclusion. The review assessed in-hospital and longer-term death, nonfatal MI, the composite of death or nonfatal MI, Canadian Cardiovascular Society class III or IV angina, and rehospitalisation. The weighted mean duration of follow-up was 17.3 months (range: 6 to 24).

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 independently extracted the data, which were then sent to the principal investigators of the included studies for verification. Verification of the data was achieved for all of the included studies. The number of events in the treatment group minus the expected events was calculated for each study, along with the variance, and used to calculate the odds ratio (OR) and 95% confidence interval (CI).

Methods of synthesis
How were the studies combined?
A pooled OR and 95% CI were calculated for each outcome. Pooled relative risks and 95% CIs were also calculated using a random-effects model.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test. Sensitivity analyses were performed to explore the influence on the results of the year of publication, the timing of the outcome assessment and the risk status of the patients. Where significant heterogeneity was found, attempts were made to identify the studies responsible and the characteristics of these studies were examined.

Results of the review
Seven RCTs (n=9,208) were included.

Over all time periods, the routine invasive strategy significantly reduced death or MI in comparison with the selective invasive strategy (12.2% versus 14.4%; OR 0.82, 95% CI: 0.72, 0.93, P=0.001) and also MI alone (OR 0.75, 95% CI: 0.65, 0.88, P<0.001). There was a non statistically significant trend towards a reduction in death with the routine invasive strategy (OR 0.92, 95% CI: 0.77, 1.09, P=0.33).

In terms of time period, the routine invasive strategy significantly increased early mortality (OR 1.6, 95% CI: 1.14, 2.25, P=0.007) and the combined outcome of death or MI (OR 1.36, 95% CI: 1.12, 1.66, P=0.002), but reduced mortality (OR 0.76, 95% CI: 0.62, 0.94, P=0.01) and the combined outcome of death or MI (OR 0.64, 95% CI: 0.56, 0.75, P<0.001) after discharge.

In terms of risk status, the routine intervention had a greater effect on higher-risk patients, but there was no apparent benefit in lower-risk patients.

There was evidence of heterogeneity among the studies pooled for in-hospital MI (P=0.001) and the composite of death or MI (P=0.001). Two studies appeared responsible.

The routine invasive strategy also reduced severe angina (OR 0.77, 95% CI: 0.68, 0.87, P<0.001) and rehospitalisation (OR 0.66, 95% CI: 0.60, 0.72, P<0.001) in comparison with the selective strategy.

Authors' conclusions
Compared with the selective invasive strategy, the routine invasive strategy reduced MI, severe angina and rehospitalisation over a mean follow-up of 17 months. However, routine intervention increased early mortality.

CRD commentary
The authors addressed a clear question. Attempts were made to identify relevant literature, but publication bias was not assessed and it was unclear whether foreign language papers were included. The methods used to select studies were not described, so it is not known whether any efforts were made to reduce errors and bias. The included studies were not
assessed for validity; although they were all RCTs, there may be differences in individual study methodology which could affect the findings of the review.

The studies were appropriately combined according to the outcome measure. However, owing to the presence of heterogeneity in some of the analyses, this synthesis should have been reconsidered. The authors did not state a priori which sensitivity analyses they planned to conduct, and this might have influenced the validity of these findings. The authors' conclusions were appropriately based on their findings. However, due to a number of methodological limitations, it is unclear whether these findings are reliable.

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

**Practice:** The authors stated that future strategies should explore means of minimising the early hazard and enhancing the later benefits of a routine invasive strategy by focusing on higher-risk patients, optimising the timing of the intervention, and maximising the use of adjunctive evidence-based therapies.

**Research:** The authors stated that longer-term follow-up of the patients included in these trials was necessary, particularly with respect to mortality.

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**Other publications of related interest**

This additional published commentary may also be of interest. Bates E. Review: routine invasive management after unstable angina or non-ST-segment elevation MI reduces risk for death or MI. ACP J Club 2005;143:68-9.

**Indexing Status**

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