How should patients with unstable angina and non-ST-segment elevation myocardial infarction be managed: a meta-analysis of randomized trials

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CRD summary
This well-conducted review compared invasive and noninvasive strategies for patients with unstable angina and non-ST-segment elevation myocardial infarction. The authors concluded that the invasive strategy reduces the risk of fatal or nonfatal reinfarction and hospital readmission. The conclusions are likely to be reliable.

Authors' objectives
To determine whether patients with unstable angina and non-ST-segment elevation myocardial infarction (MI) should be managed with an invasive or noninvasive strategy.

Searching
MEDLINE and EMBASE were searched from 1966 to September 2003 for studies reported in English; the search terms were reported. The reference lists of all retrieved studies were also checked.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a minimum of 3 months’ follow-up were eligible for inclusion. The length of follow-up ranged from 6 to 23 months.

Specific interventions included in the review
Studies that compared noninvasive and invasive management strategies were eligible for inclusion. The proportion of patients who underwent angiography in the noninvasive arm ranged from 48 to 73%. The proportion of patients who underwent percutaneous transluminal coronary angioplasty ranged from 21 to 52% in the invasive group and from 12 to 32% in the noninvasive group. The proportion of patients who underwent coronary artery bypass grafting ranged from 16 to 38% in the invasive group and from 8 to 30% in the noninvasive group. The median time to angiography in the invasive group ranged from 6.2 to 96 hours.

Participants included in the review
Studies of patients in the early post-unstable angina/non-ST-segment elevation MI period were eligible for inclusion. Studies of patients with ST-segment elevation MI, stable angina or cardiac shock were excluded, as were studies in which all patients underwent angiography. The mean age of the participants was 62 years and the proportion of males ranged from 62 to 97%.

Outcomes assessed in the review
Studies that reported mortality, reinfarction or rehospitalisation were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion.

Assessment of study quality
Each study was assessed with regard to blinding, treatment allocation, withdrawals and standardisation of assessment. Two reviewers independently assessed the validity of each included study, with any disagreements resolved by consensus.
Data extraction
Two reviewers independently extracted the data from each included study, with any disagreements resolved by consensus. Data that enabled the calculation of an odds ratio (OR) with 95% confidence intervals (CIs) for each outcome, on an intention-to-treat basis, were extracted. For outcomes that were reported at multiple time points, data were extracted on the longest time-point with less than 15% loss to follow-up.

Methods of synthesis
How were the studies combined?
The studies were combined using fixed-effect and random-effects (DerSimonian and Laird) meta-analyses. Separate pooled ORs with 95% CIs were calculated for all-cause mortality, nonfatal MI, fatal and nonfatal MI, death or MI, and hospital readmission. The results based on the random-effects model were presented. Publication bias was assessed using the tests of Begg and Egger.

How were differences between studies investigated?
A sensitivity analysis was performed to determine the effect of study quality and atypical inclusion criteria on the pooled results. Heterogeneity was assessed by visual inspection of the forest plot and by calculation of the Q statistic. A meta-regression analysis was also performed to assess the effect of the following study characteristics: the proportion of patients in the noninvasive group who received angiography; the proportion of patients with multi-vessel coronary artery disease; baseline mortality in the noninvasive group; the proportion of patients who underwent revascularisation; the proportion of patients who had ST-segment depression or positive cardiac enzymes on admission; the mean time to angiography in the invasive group; and the length of follow-up.

Results of the review
Seven RCTs (n=9,212) were included in the review.

Six trials were considered to be of a high methodological quality, while one was considered to be of adequate quality. There was no evidence of publication bias.

There was no statistically significant difference between invasive and noninvasive strategies in all-cause mortality (OR 0.96, 95% CI: 0.72, 1.27; based on 7 RCTs), nonfatal MI (OR 0.79, 95% CI: 0.53, 1.16; based on 4 RCTs), or the composite outcome of death or MI (OR 0.84, 95% CI: 0.68, 1.02; based on 7 RCTs).

The invasive strategy was associated with a statistically significant reduction in the composite outcome of nonfatal and fatal MI (OR 0.73, 95% CI: 0.61, 0.88, P<0.001; based on 3 RCTs) and in hospital readmission (OR 0.67, 95% CI: 0.48, 0.94, P=0.02; based on 5 RCTs).

There was evidence of heterogeneity for the analyses of all-cause mortality, death or MI, and hospital readmission. The meta-regression found that the invasive strategy was associated with a greater benefit in studies with a higher proportion of patients with ST-segment depression on admission, and studies with a higher proportion of patients with revascularisation. Studies with a longer average time to cardiac catheterisation were found to have a greater benefit on hospital readmission only. No other study characteristics had an impact on the outcome.

Authors' conclusions
Compared with a noninvasive strategy, an invasive strategy can reduce the rate of fatal or nonfatal reinfarction and hospital readmission, but not all-cause mortality.

CRD commentary
The review addressed a clear research question using defined inclusion criteria. Relevant sources were searched for studies for inclusion, although the search was restricted to studies in English and there were no specific attempts to find unpublished studies. However, an assessment of publication bias did not indicate that studies had been missed. Methods were used to minimise reviewer error and bias in the study selection, data extraction and quality assessment processes.
The quality assessment used was appropriate and was considered in the results of the review. All but one of the included studies were considered to be of a high methodological quality, thus increasing the reliability of the review findings. Adequate details of each of the included studies were reported and, although differences were apparent, appropriate methods were used to explore potential causes of heterogeneity in the analysis. Overall, this was a thorough and well-conducted review and the authors’ conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that the results suggest that an invasive management strategy should be considered for all patients with unstable angina/non-ST-segment elevation MI, in particular those with ST-segment depression.

Research: The authors did not state any implications for further research.

Bibliographic details

PubMedID
15866246

DOI
10.1016/j.amjmed.2005.02.016

Other publications of related interest
This additional published commentary may also be of interest. Bates E. Review: Invasive management after unstable angina or non-ST-segment elevation MI does not reduce risk for death or MI. ACP J Club 2005;143:68-9.

Indexing Status
Subject indexing assigned by NLM

MeSH
Angina, Unstable /mortality /therapy; Decision Making; Electrocardiography; Female; Humans; Male; Middle Aged; Myocardial Infarction /mortality /physiopathology /therapy; Myocardial Revascularization; Odds Ratio; Regression Analysis; Thrombolytic Therapy; Treatment Outcome

AccessionNumber
12005003561

Date bibliographic record published
31/07/2006

Date abstract record published
31/07/2006

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.