Systematic review: comparing routine and selective invasive strategies for the acute coronary syndrome
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CRD summary
This reasonably well-conducted review assessed the efficacy of a routine invasive strategy compared with a selective invasive strategy on cardiovascular outcomes in patients with non-ST-segment elevated acute coronary syndrome. The authors' conclusion, that the current evidence does not clearly support the superiority of a routine invasive strategy over a selective invasive strategy in terms of the risk of mortality or nonfatal myocardial infarction, is likely to be reliable.

Authors' objectives
To compare routine invasive and selective invasive strategies on cardiovascular outcomes in patients with non-ST-segment elevation acute coronary syndrome (ACS).

Searching
PubMed, EMBASE and the Cochrane Controlled Trials Register were searched from inception to 18 September 2007; the search terms were reported. Reference lists and the investigators' personal files were also checked. Only peer-reviewed journal published in English were considered.

Study selection
Randomised controlled trials (RCTs) comparing a routine invasive strategy with a selective invasive strategy in individuals with non-ST segment elevation ACS were eligible for inclusion. Routine invasive strategy was defined as a strategy in which patients routinely had coronary angiography and revascularisation if appropriate. Selective invasive strategy was defined as a strategy in which patients had aggressive pharmacologic therapy and coronary angiography and, if appropriate, revascularisation. Revascularisation was only performed in the presence of cardiac ischaemia refractory to medical treatment or inducible by provocative testing. Studies that enrolled patients with stable angina, ST-segment elevation myocardial infarction (MI) or cardiogenic shock, or where all patients had had coronary angiography to limit the study bias, were excluded. Most of the participants had a history of coronary artery disease or had other risk factors for coronary artery disease (e.g. diabetes, smoking or hypertension). The mean age of the participants was 62 years and 71% were male. Studies that reported mortality, nonfatal MI, or a composite measure of death or nonfatal MI were eligible for inclusion.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
The validity of the included trials was evaluated on the basis of descriptions of randomisation methods, withdrawals, outcomes adjudication and blinding. Three reviewers independently assessed the validity of the included studies and any disagreements were resolved by consensus.

Data extraction
Relative risks (RRs) were calculated with 95% confidence intervals (CIs) for each outcome at final follow-up, up to hospital discharge and after 1-year follow-up. Three reviewers independently extracted the data from the included studies using a predefined data extraction form. Any disagreements were resolved by consensus.

Methods of synthesis
RRs with 95% CIs were combined in a meta-analysis using a random-effects model. Statistical heterogeneity was assessed using the Q statistic and the I^2 statistic. Sensitivity analyses were performed using Bayesian models. A stratified analysis to explore heterogeneity was planned (duration of follow-up, use of coronary stents and use of glycoprotein IIb/IIIa inhibitors), and the impact of each trial on the results was assessed. Evidence of publication bias was assessed using a funnel plot and the 'trim-and-fill' method of Duval and Tweedie.
Results of the review
Ten RCTs (n=10,648) were included in the review; 5,330 patients underwent the routine invasive strategy and 5,318 underwent the selective invasive strategy.

Nine studies reported standardised methods of randomisation, 8 studies reported a drop-out rate of less than 15%, 6 studies used intention-to-treat analysis, 4 studies reported adjudication of all outcomes, and at least 4 studies used blinding at some level of outcome evaluation.

No significant difference was found between the routine and selective invasive strategies for risk of mortality, nonfatal MI, or a composite measure of death or nonfatal MI at the maximum reported follow-up. The maximum reported follow-up ranged from 6 to 60 months. Evidence of statistical heterogeneity was found for nonfatal MI and the composite of death or nonfatal MI. With the removal of one large trial, estimates for composite death/MI (RR 0.84, 95% CI: 0.74, 0.97) and nonfatal MI alone (RR 0.77, 95% CI: 0.68, 0.88) significantly favoured the routine invasive strategy; the results for mortality did not significantly change.

No significant difference was found between the routine and selective invasive strategies for risk of in-hospital mortality, nonfatal MI, or composite death/nonfatal MI. Evidence of statistical heterogeneity was found for nonfatal MI and composite death/nonfatal MI.

No significant between-group differences were found at 1-year follow-up for risk of mortality, nonfatal MI, or composite death/nonfatal MI. Evidence of statistical heterogeneity was found in all analyses.

Pooled relative risks from the Bayesian statistical framework did not significantly alter the results. The funnel plot was asymmetrical, and the 'trim-and-fill' method indicated that one study needed to be imputed to make the plot symmetrical; the addition of an imputed study did not significantly alter the results.

Authors' conclusions
The current evidence does not clearly support the superiority of a routine invasive strategy over a selective invasive strategy to reduce mortality or nonfatal MI in patients with non-ST-segment elevation ACS.

CRD commentary
The review question was supported by clear inclusion criteria. Although several sources were searched, only peer-reviewed journals published in English were included. In addition, while publication bias was assessed, this may not be reliable because of the small number of studies included. The methods used to select studies for inclusion in the review, assess validity and extract the data were likely to have minimised the potential for error and bias. The validity of the included studies was assessed and the results reported. Standard meta-analytical methods were used to combine the studies and the statistical heterogeneity of the studies was assessed. In addition, the authors explored possible sources of heterogeneity. However, given the variation in population, management protocols with variable use of stents and glycoprotein IIb/IIIa inhibitors, and durations of follow-up that the authors highlighted, it might not have been reasonable to quantitatively combine these studies. Overall, this was a reasonably well-conducted review and the authors' cautious conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors suggested that clinicians should consider additional factors when choosing a treatment for a particular patient, such as applicability of available evidence to a particular patient, feasibility of the intervention in a particular setting, and patient values and preferences.

Research: The authors stated that future trials should try to identify the subset of patients with non-ST-segment elevation ACS who are most likely to benefit from a routine invasive strategy.

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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.