Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data

Fox KA, Clayton TC, Damman P, Pocock SJ, de Winter RJ, Tijssen JG, Lagerqvist B, Wallentin L

CRD summary
This individual patient data review concluded that a routine invasive strategy reduced long-term frequency of death or nonfatal myocardial infarction compared to a selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome. There was no evidence that effectiveness was influenced by baseline risk. The results of this review are likely to be reliable.

Authors' objectives
To determine the effectiveness of routine invasive strategy compared to selective invasive strategy in reducing the long term frequency of death or non-fatal myocardial infarction in patients with non-ST-segment elevation acute coronary syndrome (ACS). A secondary objective was to ascertain whether effectiveness was influenced by baseline risk.

Searching
MEDLINE and Cochrane databases were searched from 1970 to 2009 using specified search terms. A collaboration to obtain individual patient data (IPD) was initiated.

Study selection
Trials that compared routine and selective invasive strategies in patients with ACS and reported long-term (five year) outcomes were eligible. The primary outcome was cardiovascular death or nonfatal myocardial infarction

The routine invasive strategy consisted of early coronary angiography within seven days of randomisation. The selective invasive strategy consisted of coronary angiography and revascularisation only for refractory or accelerating patterns of angina. Mean patient age was 63 years and 68% of the population were male. Forty seven per cent of the patients had ST-segment deviation at presentation.

The number of reviewers performing study selection was unstated

Assessment of study quality
Individual patient data (IPD) were checked for completeness and consistency by participating trialists. Baseline imbalances were described between trials but assessments of the integrity of randomisation were not reported.

Data extraction
A protocol was used to pre-specify the main analyses and identify a common set of baseline and outcome variables that included core variables on demographics, clinical history, risk factors for coronary artery disease, baseline electrocardiographic characteristics, biomarkers of myocardial necrosis and five year clinical outcomes.

Methods of synthesis
Five year cumulative event rates were estimated using the Kaplan-Meier method. The impact of the intervention was assessed using Cox regression models stratified by trial. Interaction tests were used to explore heterogeneity and to identify univariable associations between the primary outcome and baseline characteristics. A forward stepwise approach was used to develop a multivariable model with trial included only as a sensitivity analysis. The model was used to identify three risk groups and related to treatment effectiveness by tabulation (stratification by trial not reported).

Results of the review
IPD was available from 5,467 patients in three randomised trials. Two trials allowed crossover whereby patients randomised to the selective strategy would receive intervention (depending on pre-discharge tests).

The routine invasive strategy reduced cardiovascular death (hazard ratio 0.83, 95% CI 0.68 to 1.01) or nonfatal
myocardial infarction (hazard ratio 0.77, 95% CI 0.65 to 0.90) in comparison to a selective invasive strategy (combined hazard ratio 0.81, 95% confidence interval 0.71 to 0.93). There were 2.0% to 3.8% absolute reductions in cardiovascular death or myocardial infarction in low and intermediate risk patients and an 11.1% risk reduction in highest risk patients.

Other outcomes were reported.

**Authors’ conclusions**
The routine invasive strategy reduced long-term rates of cardiovascular death and myocardial infarction. The largest absolute effect was seen in higher risk patients.

**CRD commentary**
This IPD review employed appropriate methods for identifying eligible studies and assembling data. The searches were limited so the possibility of missing studies could not be ruled out. No checks on the integrity of randomisation were reported.

Standard fixed-effect methods were used to pool the studies to generate overall estimates of effectiveness. A prognostic model was developed to identify risk groups. The prognostic models were not stratified by trial and it was unclear whether or not the hazard ratios and risk differences associated with risk groups were stratified by trial. The estimate of absolute risk in the high risk category may have been overestimated if it was based on differential estimates of treatment effect in the three risk categories as there was no evidence of interaction, which indicated that treatment effectiveness did not vary substantially.

Despite limited reporting the main conclusion appears reliable, but the difference in baseline risk results should be interpreted with caution.

**Implications of the review for practice and research**
The authors did not state any implications for practice and research.

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