Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes

CRD summary
This review concluded that compared to delayed angiography, early coronary angiography and subsequent potential intervention reduced the risk of recurrent ischaemia and shortened hospital stay in people with acute coronary syndromes without ST-segment elevation. Data came from good quality studies and overall the review appeared well conducted. The authors conclusions are likely to be reliable.

Authors' objectives
To determine the optimal timing (early versus delayed) of coronary angiography in people with acute coronary syndromes without ST-segment elevation.

Searching
MEDLINE was searched to January 2010. Search terms were reported. Searches of online sources, which included Google Scholar and two trials registries, and citation searches of identified studies using Web of Science were undertaken.

Study selection
Randomised controlled trials (RCTs) that compared routine early versus delayed diagnostic angiography in people with acute coronary syndromes without ST-segment elevation were eligible for inclusion. Early was defined as soon after admission and delayed was defined as including pretreatment with optimal medical therapy and subsequent angiography. Subsequent treatment decisions were based on angiographic results and clinical decisions. Studies that compared invasive versus conservative strategies were excluded. Outcomes of interest were all-cause mortality, myocardial infarction, major bleeding, recurrent ischaemia, reintervention, stroke and a composite of death, myocardial infarction or stroke. Length of hospital stay was reported.

In the included studies 34% of participants were women. Mean ages ranged from 63 to 68 years in the early groups and 65 to 69 years in the delayed groups. Some participants had diabetes, hypertension, hyperlipidaemia, were smokers or had prior myocardial infarction, percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Median time to angiography ranged from 1.16 to 14 hours in the early group and 20.8 to 86 hours in the delayed group. Length of follow-up ranged from one to 12 months.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
Risk of bias was assessed on items such as method of randomisation, allocation concealment, description of losses to follow-up, whether outcomes were centrally adjudicated or site-reported, blinding of outcome adjudicators and use of intention-to-treat analysis.

It appeared that two reviewers independently assessed quality. Disagreements were resolved by consensus or arbitration with two other reviewers.

Data extraction
Data were extracted on an intention-to-treat principle in order to calculate risk ratio (RR) and 95% confidence interval (CI). For length of hospital stay, relative difference was calculated using logarithmic transformation and evaluation of the standard deviation based on interquartile ranges and point estimate based on the logarithm of the mean.

Two reviewers independently extracted data. Disagreements were resolved by consensus or arbitration with two other
reviewers. Where published data were for less than six months follow-up, authors were asked to provide outcome data for up to one year follow-up.

**Methods of synthesis**
A fixed-effect and a random-effects method were used to calculate pooled risk ratios and 95% CI for dichotomous data and relative difference for continuous data. Results for random effects were reported. Heterogeneity was assessed with Q and \( I^2 \). Subgroup analyses were undertaken based on presence of ST-deviation and elevated cardiac biomarkers (above the upper limit of normal range).

**Results of the review**
Four RCTs (4,013 participants) were included. One trial had 3,031 participants, others ranged from 220 to 410 participants. Proper modes of randomisation, allocation concealment, reporting of losses to follow-up and use of intention-to-treat analyses were reported in all trials. Outcome assessors were blinded in all trials and assessment was done by central committees in those trials that were multicentre.

There was no statistically significant difference between the early and delayed groups for mortality (\( I^2=0\% \)), myocardial infarction (\( I^2=49\% \)), reintervention (\( I^2=33\% \)) and stroke (\( I^2=0\% \)). For the combined outcome of death, myocardial infarction or stroke the early strategy was associated with fewer events, although this did not reach statistical significance (RR 0.91, 95% CI 0.82 to 1.01, \( I^2=0\% \); three trials).

The early strategy was associated with a reduction in recurrent ischaemia (RR 0.59, 95% CI 0.38 to 0.92, \( I^2=61\% \)) and a shorter duration of hospital stay (28%, 95% CI 22% to 35%, \( I^2=0\% \)). Results suggested a possible increased risk of major bleeding with the delayed strategy, but this did not reach statistical significance (RR 0.78, 95% CI 0.57 to 1.07, \( I^2=0\% \)).

Subgroup analyses did not indicate any significant difference in the combined outcome when analysed according to cardiac biomarker levels and ST-deviation.

**Authors' conclusions**
Early coronary angiography and subsequent potential intervention reduced the risk of recurrent ischaemia and shortened hospital stay in people with acute coronary syndromes without ST-segment elevation.

**CRD commentary**
The aims of the review were clearly stated in terms of the inclusion criteria for participants, intervention and study design. The search was limited to one database, but was complemented by checking other sources that included looking for unpublished studies. This would have reduced the likelihood of publication bias. There was no mention of any language restrictions applied so it was unclear whether language bias may have affected the review. Methods of data extraction aimed at reducing reviewer error or bias; methods for study selection and quality assessment were unclear. Study validity was assessed appropriately. Methods of synthesis appeared appropriate. Heterogeneity was investigated.

The included data came from good-quality studies and the review appeared generally well conducted. The authors conclusions are likely to be reliable.

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

**Research:** The authors stated that further evidence was needed to clarify the relative effects of early or delayed angiography for people with acute coronary syndromes without ST-segment elevation. Ongoing trials may contribute to this.

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