Early angiography in patients with chronic kidney disease: a collaborative systematic review

CRD summary
This well-conducted review found that compared to selective angiography, routine pre-discharge angiography following non-ST acute coronary syndrome significantly reduced risk of re-hospitalisation within one year in patients with chronic kidney disease. The review was a post-hoc analysis of chronic kidney disease patients enrolled in general trials. Given this and the possibility of bias, the results should be interpreted with caution.

Authors' objectives
To compare invasive with conservative strategies of angiography for non-ST acute coronary syndrome in patients with chronic kidney disease.

Searching
MEDLINE, EMBASE and The Cochrane Library (1966 to September 2007) were searched for English-language articles. Search terms were listed in the review. Reference lists of identified studies were screened manually for additional articles.

Study selection
Randomised controlled trials that compared patients with non-ST acute coronary syndrome (inducible ischaemia or recurrent spontaneous ischaemia) to routine, pre-discharge angiography (with revascularisation if indicated) or selective angiography were eligible for inclusion. Trials had to have a minimum of three months of follow-up. Outcome inclusion criteria were mortality, reinfarction or re-hospitalisation. Trials of patients with ST-elevation myocardial infarction or stable coronary disease were not eligible.

Patients with chronic kidney disease accounted for 19.4% of all patients in the included trials. Among the participants included, 81.6% had Stage 3 chronic kidney disease. Most of the patients with Stage 4/5 chronic kidney disease came from one trial. Mean age of patients with chronic kidney disease ranged from 65 to 72 years in patients with Stage 3 and 60 to 78 years in patients with Stage 4/5 chronic kidney disease. The proportion of men ranged from 43% to 58% in patients with Stage 3 and 0 to 100% in patients with Stage 4/5 chronic kidney disease. Between 0% and 75% of patients had diabetes and 34% to 100% had ST-segment depression. Angiography in the intervention arm of included studies was given within the first week; in most studies it was within the first 48 hours. The control intervention in all studies was symptom or stress-test driven angiography. In one trial, patients were also given thrombolysis. Follow-up in the included studies ranged from six weeks to one year; most studies had six-month follow-up. Details of drugs allowed in each of the included studies were given in the review.

Two reviewers independently selected the studies for inclusion. The authors did not state how discrepancies were resolved.

Assessment of study quality
Study quality was independently assessed by two reviewers on the basis of three criteria: intention-to-treat analysis, loss to follow-up and blinding. Discrepancies were resolved by consensus.

Data extraction
Two reviewers independently calculated risk ratios (RR) for each study. The principal investigator from each trial was contacted and asked to provide summary outcome data on patients with chronic kidney disease according to stage of disease.

Methods of synthesis
A DerSimonian and Laird random-effects model was used to calculate summary risk ratios and confidence intervals (CI). Heterogeneity was investigated using graphical inspection of forest plots, Q statistic, I² statistic, elimination of
outliers and meta-regression. The effect of each of the following outcomes was explored: proportion of patients with ST-segment depression on admission; proportion of patients with positive cardiac biomarkers; and percentage of patients with diabetes. Sensitivity analyses of the effect of using a fixed-effect rather than random-effects model and of using an odds ratio rather than a risk ratio were performed.

Publication bias was assessed using funnel plots and Begg and Egger tests.

Results of the review
Five trials (n=1,453) were included in the review. All studies used intention-to-treat analysis, had very low rates of loss to follow-up and assessed outcomes in a blinded manner. There was no evidence of publication bias.

The invasive strategy significantly reduced re-hospitalisation (RR 0.76, 95% CI 0.66 to 0.87); no significant heterogeneity was present. The invasive strategy was associated with lower risks of all-cause mortality, nonfatal myocardial infarction (MI) and the composite of these two outcomes; none of these effects was significant. Exclusion of two studies individually did not appreciably change the results. Results were similar for Stage 3 and Stage 4/5 chronic kidney disease. None of the factors included in the meta-regression explained any of the between-trial heterogeneity.

Authors' conclusions
An invasive strategy of routine post-acute coronary syndrome coronary angiography may be beneficial in patients with chronic kidney disease.

CRD commentary
The review had clear study design, intervention, participant and outcome inclusion criteria. The search strategy appeared comprehensive. The reviewers performed data abstraction, study selection and validity assessment in duplicate, which minimised chance of bias and errors during the review process. The restriction to English-language trials meant that language bias was a possibility. There was no evidence of publication bias. The meta-analysis and assessment of heterogeneity was appropriate.

The review was a post-hoc analysis of trials that were not specifically designed to study patients with chronic kidney disease. Only a small proportion of patients in the included trials had chronic kidney disease. Three trials that met all inclusion criteria, but did not have measures of serum creatinine were excluded, which could have resulted in selection bias.

Generally this was a well-conducted review, but given the possibilities of bias, the results should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that coronary angiography should be considered for patients who have chronic kidney disease and are admitted with non-ST elevation acute coronary syndrome.

Research: The authors stated that further studies of patients with advanced chronic kidney disease and with longer follow-up were required, as well as investigation of the role of comorbidities in modifying the effect therapy in chronic kidney disease patients.

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