Effect of statin therapy on contrast-induced nephropathy after coronary angiography: a meta-analysis

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CRD summary
The authors concluded that statin use may be associated with a significant reduction in contrast-induced nephropathy, but acknowledged a need for further research to confirm the conclusion. Concerns about the quality of included studies and the synthesis of non-randomised studies suggest that the cautious interpretation of findings recommended by the authors is justified.

Authors' objectives
To conduct a meta-analysis evaluating the impact of statin use on the incidence of contrast-induced nephropathy (CIN) in patients undergoing coronary angiography.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched from inception to December 2010. Search terms were reported. No language restrictions were applied. American Heart Association, American College of Cardiology, European Society of Cardiology, American Society of Nephrology and International Society of Nephrology conference abstracts were searched from 1998 and 2010.

Study selection
Randomised trials and non-randomised studies that compared statins with intravenous hydration and/or placebo for the prevention of CIN were eligible for inclusion in the systematic review. The primary outcome was incidence of CIN. Studies that included N-acetylcysteine were eligible only if it was administered in both study arms. Studies of direct comparisons of statin doses were excluded.

More than half of the included studies were retrospective designs. Where reported, the mean age of included patients ranged from 54.4 to 75.5 years. Most participants in most studies were men. The percentage of patients with diabetes varied substantially (16% to 72.9%). Statins were administered for acute or chronic therapy. Statin type and regimen varied for most studies.

Two researchers selected studies for the review. Disagreements were resolved by discussion.

Assessment of study quality
Study quality was assessed using the Jadad scale of randomisation, blinding and drop-outs. Possible scores ranged from 0 to 5.

The authors did not state how many reviewers were involved in the quality assessment of studies.

Data extraction
Two researchers independently extracted data according to intention-to-treat principles to enable calculation of odds ratios (OR) and 95% confidence intervals (CI). Differences were resolved with discussion.

Methods of synthesis
Odds ratios were pooled in a random-effects meta-analysis. The Q statistic was used to formally test for heterogeneity and I² was used to summarise the presence of heterogeneity. A sensitivity analysis was conducted which calculated the pooled odds ratio after leaving out each study in turn. Subgroup analyses explored the impact of acute and chronic statin use, patients with diabetes, people aged over 75 years, people with left ventricular ejection fraction less than 40% and people with creatinine clearance less than 30mL/min.

Results of the review
Ten studies (32,629 patients, range 130 to 28,871) were included in the systematic review. Three studies (670 patients)
were randomised controlled trials (RCTs): two were rated excellent and one was rated poor in the quality assessment. The seven non-randomised trials (31,953 patients) were rated poor in the quality assessment.

**RCTs:** The difference between statins and controls for incidence of CIN was not statistically significant (OR 0.76, 95% CI 0.41 to 1.41). There was no evidence of heterogeneity ($I^2=0\%$).

**Non-RCTs:** The pooled effect size was statistically significant (OR 0.60, 95% CI 0.36 to 1.00). There was strong evidence of heterogeneity ($I^2=88\%$). Sensitivity analyses that removed influential studies resulted in a loss of statistical significance.

**Subgroup analyses:** There was a trend towards statistical significance for acute statin use prior to a planned percutaneous coronary intervention (OR 0.73, 95% CI 0.53 to 1.01; four studies). CIN reduction was not statistically significant for chronic statin use. No statistically significant effects were found in any of the other subgroups examined.

**Authors' conclusions**
Statin therapy may be associated with a significant reduction in CIN for patients receiving coronary angiography. Receiving statins acutely prior to a planned percutaneous coronary intervention may prevent CIN. Definitive conclusions could not be drawn as most included studies were not randomised.

**CRD commentary**
The research question and inclusion criteria for this systematic review were relatively broad, but this appeared appropriate as limited research had been conducted on this subject. Criteria were sufficiently clear to enable replication. The search included good database coverage and attempts were made to locate unpublished evidence. Quality assessment was addressed. But the authors did not state how many reviewers were involved in the assessment (using two or more reviewers reduces bias) and did not report the results for each criterion, so there was limited information on study quality. The Jadad scale was designed to assess RCTs, which limits its applicability for non-randomised studies. Attempts were made to minimise error and bias in screening and data extraction. The authors attempted to reduce risks of bias by conducting separate meta-analyses for RCTs and non-randomised studies. There was very high heterogeneity in the meta-analysis of non-randomised studies. The conflicting results found in the included primary trials raised the question of whether a pooled effect should have been calculated for these studies. Sensitivity analyses indicated that when influential studies were excluded from the analysis there was no longer a statistically significant effect. A further potential limitation was that the authors did not report whether the subgroup analyses were planned beforehand or were based on a post hoc exploration of the data.

The authors' conclusion reflects the limited evidence presented. Concerns about the quality of included studies and chosen method of synthesis for non-randomised studies means that the cautious interpretation of this review recommended by the authors appears justified.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that the benefit of statin use to reduce CIN was uncertain until a large RCT was conducted. The authors suggested a need for research in high-risk patients and for economic analyses.

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