Statin therapy may influence the incidence of postoperative atrial fibrillation: what is the evidence?

CRD summary
This review concluded that statin administration reduced the incidence of atrial fibrillation in patients who had undergone cardiac surgery. The review had some methodological deficiencies which raised concerns, particularly the lack of reporting of validity assessment, the potential for reviewer error and bias, and the potential for publication bias; therefore, the reliability of the authors' conclusion is unclear.

Authors' objectives
To evaluate whether statin treatment reduced the incidence of postoperative atrial fibrillation in cardiac surgery patients.

Searching
Published trials were identified through a search of MEDLINE, EMBASE and the Cochrane Library up to 2008. Search terms were reported. Google Scholar was also searched.

Study selection
Comparative studies of statins in patients with new onset atrial fibrillation, who had undergone cardiac surgery, were eligible for inclusion. The incidence of atrial fibrillation was required as an outcome measure, or had to be calculable from published results. Studies in which the primary interventional approach could not be defined, studies administering lipid-lowering agents other than statins, and studies investigating ventricular or other arrhythmias were excluded.

Four included studies used atorvastatin alone (20 to 40mg/day with varying duration). Six of the included studies used a variety of statins including atorvastatin, cerivastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin; dosage and duration were not specified for over half of the studies. The average age of patients ranged from 60 to 69.4 years.

The authors did not state how the studies were selected for the review.

Assessment of study quality
It appeared that the authors assessed validity, but no details were reported.

Data extraction
Two independent reviewers used numbers of events to derive odds ratios (ORs) for each study. The reviewers also extracted known risk factors for atrial fibrillation including advanced age, male, hypertension, diabetes, low ejection fraction, chronic obstructive pulmonary disease, and advanced three-vessel and left-main-stem coronary artery disease, in order to compare the treated and untreated groups. The authors stated that they calculated risk differences and numbers needed to treat, but these were not reported in the results.

Methods of synthesis
The pooled odds ratios and corresponding 95% confidence intervals (CIs) were calculated using Mantel-Haenszel fixed-effect meta-analysis where there was no evidence of statistical heterogeneity. A random-effects model was used if statistically significant heterogeneity was observed. When event rates were zero, 0.5 was added; where there were no events for both statin treated and untreated groups, the study was excluded from meta-analysis. Statistical heterogeneity was assessed using a $x^2$ test and the $I^2$ test.

Subgroup analyses investigated: randomised controlled trials (RCTs); studies of patients who only underwent coronary artery bypass grafts; studies in which atorvastatin was the only lipid-lowering agent used; studies with less than 300 events.
patients in each group; and studies that were poor quality.

Publication bias was assessed using funnel plots

**Results of the review**

Ten studies (n=4,459 patients) were included in the review, including four RCTs (n=919 patients), four retrospective studies (n=3,053 patients) and two prospective studies (n=487 patients).

The incidence of post-operative atrial fibrillation was reduced in the statin-treated group compared with the untreated group (OR 0.68, 95% CI 0.59 to 0.79). Statistically significant heterogeneity was observed. A random-effects model did not influence results.

The statin-treated group reported less atrial fibrillation for the following subgroup analyses: RCTs (OR 0.55, 95% CI 0.41 to 0.73; four RCTs); studies of more than 300 participants (OR 0.69, 95% CI 0.52 to 0.91; five studies); studies administering atorvastatin alone (OR 0.55, 95% CI 0.41 to 0.73; four studies); studies performing coronary artery bypass grafts (OR 0.64, 95% CI 0.43 to 0.95; five studies); and higher quality studies (OR 0.58, 95% CI 0.47 to 0.71; five studies). Significant heterogeneity was detected for the coronary artery bypass grafts comparison, but not for any other comparison.

Publication bias was detected.

**Authors' conclusions**

Statin administration resulted in a reduction in the incidence of atrial fibrillation in patients who had undergone cardiac surgery.

**CRD commentary**

This review addressed a clear question, supported by appropriate inclusion criteria. Relevant databases were searched. It appeared that no attempts were made to identify unpublished studies and it was unclear whether language limitations were applied. Publication bias was considered in the review and may have been present. Suitable methods to minimise risk of reviewer error and bias were reported for data extraction, but not for study selection.

It was unclear whether validity was assessed; the authors report a pre-specified subgroup analysis of six out of seven "matching criteria", but it was not clear what kind of validity assessment (if any) was performed. The results were pooled using meta-analysis and heterogeneity was assessed. The authors acknowledged the hierarchy of evidence and reported that the four included RCTs were used to draw the main conclusions; it was unclear why other study types were included in the meta-analysis, as there did not appear to be any added value from these additional included studies.

The review had some methodological deficiencies which raised concerns, particularly the lack of reporting of validity assessment, the potential for reviewer error and bias, and the potential for publication bias. Therefore, the reliability of the authors' conclusion is unclear.

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

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

**Research:** The authors stated that a large-scale multi-centre RCT of statin treatment versus non treatment, with a primary endpoint of postoperative atrial fibrillation, is needed. Secondary outcomes should investigate the type and dosage of statin, and duration of use that will reduce postoperative atrial fibrillation most effectively.

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