Antiarrhythmic effect of statin therapy and atrial fibrillation: a meta-analysis of randomized controlled trials

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CRD summary
This poorly reported review concluded that statin use can significantly reduce the risk of incidence or recurrence of atrial fibrillation in patients in sinus rhythm undergoing cardiac surgery or following acute coronary syndrome. This conclusion reflects the results of the review, but the limited searches and lack of methodological reporting may limit the reliability of the findings.

Authors' objectives
To assess the effectiveness of statins in preventing atrial fibrillation (AF).

Searching
MEDLINE was searched from January 1980 to June 2007; the search terms were reported. In addition, the conference proceedings (2001 to 2007) of the American College of Cardiology, American Heart Association and the European Society of Cardiology were handsearched and references from recent reviews and selected trials were checked. Only publications in a peer-reviewed journal listed on MEDLINE were considered.

Study selection
Eligible studies were parallel, randomised controlled trials (RCTs) comparing a statin versus control treatment or placebo. Trials had to report the incidence or recurrence of AF and a follow-up of at least 3 weeks. In the included trials, AF was measured using electrocardiography and the duration of follow-up ranged from 30 days to 6 months. The studies compared one of two statins (pravastatin, atorvastatin) versus standard therapy or placebo in populations (mean ages of 54 to 68 years) with either paroxysmal or persistent AF, scheduled cardiac or coronary bypass surgery, or acute coronary syndrome.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state how many reviewers performed the validity assessment or how disagreements were resolved.

Data extraction
The number of events in each trial was extracted, where possible, on an intention-to-treat basis and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

The authors did not state how the data were extracted for this review, or how many reviewers performed the data extraction.

Methods of synthesis
A mixture of fixed-effect and random-effects meta-analysis models were used to calculate the pooled ORs with associated 95% CIs for overall incidence or recurrence of AF. Heterogeneity was assessed using the $\chi^2$ statistic, and a fixed-effect Mantel-Haenszel model used where the data were sufficiently homogeneous. Publication bias was assessed using a funnel plot. Sensitivity analyses were used to examine the impact of including a study published only in abstract form, and excluding studies with a Jadad score of less than 3.

Results of the review
Six RCTs (n=3,557) were included in this review: three assessed statins in recurrent AF, two addressed post-operative AF and one studied new-onset AF in acute coronary syndrome.
The Jadad quality scores ranged from 2 to 5 out of a maximum of 5 points. Five trials studied atorvastatin and one studied pravastatin. The funnel plot was reported to be relatively symmetrical and unlikely to indicate major publication bias.

Statins were significantly associated with a decreased risk of AF recurrence compared with control treatments (OR 0.39, 95% CI: 0.18, 0.85, p=0.02). These benefits seemed stronger in the secondary prevention of AF, but were not statistically significant (OR 0.33, 95% CI: 0.10, 1.03, p=0.06), than for new-onset or post-operative AF where the benefit was not statistically significant. Atorvastatin produced a stronger effect when considered in isolation versus control (OR 0.30, 95% CI: 0.12, 0.78, p=0.01).

Random-effects models were used for all analyses. Sensitivity analyses did not significantly alter any of the results.

**Authors' conclusions**

There is evidence to suggest that statin use can significantly reduce the risk of incidence or recurrence of AF in patients in sinus rhythm who have a history of AF, are undergoing cardiac surgery, or after acute coronary syndrome.

**CRD commentary**

This review addressed clear clinical question with appropriate and detailed inclusion criteria. The decision to limit included studies to those published only in MEDLINE-listed journals was not justified in the paper and may have introduced language and/or publication bias. The review methodology was generally poorly reported, and it was difficult to establish if appropriate steps had been taken to minimise error and bias at the study selection, quality assessment and data extraction stages. The analysis appears to have been appropriate and incorporated the validity assessment, and the results were clearly interpreted in line with the available evidence. Overall, despite some limitations in the search process and poor reporting of review methodology, the authors' conclusions accurately reflect the evidence of the review and appear reliable, although the limited search suggests a need for some caution.

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

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

Research: The authors stated that larger RCTs are needed to examine the appropriate dosages in relation to low-density lipoprotein cholesterol levels, and to establish if statins are an appropriate intervention for all subgroups of patients when managing AF.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.