The role of statin therapy in the prevention of atrial fibrillation: a meta-analysis of randomized controlled trials

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CRD summary
This review concluded that statins significantly decreased the risk of atrial fibrillation, with the benefit seemingly more pronounced in secondary rather than primary prevention. Lack of reporting of the review process, the potential for missed trials, substantial variation between the included trials and their methodological limitations, mean the reliability and applicability of the results and overall conclusions are uncertain.

Authors' objectives
To investigate whether statins could reduce the risk of atrial fibrillation.

Searching
PubChem Compound, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched for studies published in English up to December 2010; examples of the search keywords used were given.

Study selection
Randomised controlled trials (RCTs) that compared a statin with control treatment or placebo, regardless of the background therapy in either group, were eligible for inclusion. Trials had to report the incidence or recurrence of atrial fibrillation.

In included trials, the most frequently studied statin was atorvastatin; pravastatin was used in the most patients due to the size of the trials evaluating this statin. The statin was compared with placebo or usual care (where detailed). Most included RCTs diagnosed atrial fibrillation using serial electrocardiograph ECGs and/or 24-hour Holter ECG monitoring.

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

Assessment of study quality
The quality of the RCTs was assessed using the Jadad scale.

The authors did not state how many reviewers assessed study quality.

Data extraction
Data on the incidence of atrial fibrillation were extracted on an intention-to-treat basis, and odds ratios with 95% confidence intervals calculated.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Summary odds ratios and 95% confidence were calculated using a fixed-effect (Mantel-Haenszel) model if no statistically significant heterogeneity was observed; a random-effects model was used where significant heterogeneity was detected. Heterogeneity was assessed using χ² and I².

Sensitivity analyses were conducted to investigate the impact of trial quality, the statin used and the population; further post hoc analyses were conducted.

Publication bias was assessed using funnel plots and Egger's regression.

Results of the review
Twenty RCTs (23,577 patients; range 40 to 8,582) were included in the review. Of the 20 trials, two scored 1 point on
Jadad, four scored 2 points, five scored 3 points, three scored 4 points and six scored 5 points. Duration of follow-up ranged from seven to 37 days in post-operative patients, and one month to 3.7 years in patients with recurrent atrial fibrillation.

Overall (20 RCTs), statins significantly reduced the risk of atrial fibrillation compared with control (OR 0.49, 95% CI 0.37 to 0.65; I²=69%).

When analysed by statin, there was a significant reduction in the risk of atrial fibrillation with atorvastatin (OR 0.38, 95% CI 0.24 to 0.61; 11 RCTs; I²=71%) and simvastatin (OR 0.12, 95% CI 0.04 to 0.40; two RCTs; I²=0), but not pravastatin (four RCTs) or rosuvastatin (three RCTs).

When analysed by population, there was a significant reduction in the risk of atrial fibrillation in patients with prior atrial fibrillation (OR 0.34, 95% CI 0.18 to 0.64; eight RCTs; I²=74%) and no prior atrial fibrillation (OR 0.54, 95% CI 0.40 to 0.74; 12 RCTs; I²=47%), but not in the largest RCT with a mixed population.

Results of post hoc analyses were also reported.

The authors reported that publication bias may have been present for the population with no prior atrial fibrillation.

**Authors’ conclusions**

Statin therapy was significantly associated with a decreased risk of incidence or recurrence of atrial fibrillation. The benefit of statin therapy seemed more pronounced in secondary than in primary prevention. Variation across trials was explained by differences in statin types, patient populations and surgery types.

**CRD commentary**

This review addressed a clear research question supported by reproducible inclusion criteria. Relevant sources were searched, but unpublished studies were not sought and only studies published in English were included. The authors did not report whether the review process was conducted in duplicate, so the potential for reviewer error and bias could not be ruled out.

Appropriate criteria were used to assess trial quality, but the scale was not modified to include allocation concealment and the results were reported only as a summary score. Several trials were subject to methodological bias, although the authors did investigate the impact of this in their analyses.

There was substantial clinical and statistical heterogeneity across the trials, much of which (such as the variation in treatment regimens) was not considered in the review, making the reliability and generalisability of the summary estimates and overall conclusions uncertain.

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

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

**Research:** The authors stated that further studies were needed to explore the reasons why statin therapy appeared to be more effective in secondary prevention than in primary prevention of atrial fibrillation. They also stated that large-scale, prospective, RCTs were needed to establish whether statins bring a similar benefit and were an appropriate therapeutic option in all subgroups of patients for the management of atrial fibrillation.

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**Bibliographic details**


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Record Status
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.