Statin therapy for the prevention of atrial fibrillation: a meta-analysis of randomized controlled trials

CRD summary
This review concluded that statins were useful for preventing atrial fibrillation but the effect in secondary prevention was not superior to primary prevention. Atorvastatin was more effective than pravastatin, with lower doses being the most effective. These conclusions should be treated with caution given the unclear quality and heterogeneity of the included studies.

Authors’ objectives
To investigate the primary and secondary preventive effects of statins for atrial fibrillation and the efficacy of individual statins and their doses.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to 2010 for trials published in English or Chinese; search terms were reported. Scientific abstracts from the American College of Cardiology, American Heart Association, European Society of Cardiology and North American Society of Pacing and Electrophysiology were searched between 2001 and 2010. Reference lists of included trials were searched.

Study selection
Published randomised controlled trials that compared one or more statin with placebo or an active control in patients who received primary or secondary prevention for atrial fibrillation were eligible for inclusion. Trials that assessing additional treatments were included provided that they assessed a statin. Trials had to report atrial fibrillation as an outcome.

Atorvastatin was studied in 11 trials, pravastatin in five, rosuvastatin in three and simvastatin in one. Most studies diagnosed atrial fibrillation with an electrocardiogram and/or 24-hour Holter monitor or pacemaker. Mean follow-up ranged from two days to six years. Mean patient age ranged from 52 to 71 years. Diagnoses and definitions of atrial fibrillation varied between studies (details tabulated in the paper).

Studies were selected by two reviewers independently.

Assessment of study quality
Study quality was assessed for random sequence generation, allocation concealment, blinding of participants and study personnel, outcomes, selective outcome reporting and other sources of bias.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Numbers of patients with atrial fibrillation were extracted and used to calculate odds ratios (OR) with 95% confidence intervals (CI). These were calculated on an intention-to-treat basis. Patients who did not complete the study were assumed to be free of an event.

Data were extracted by two reviewers independently. Disagreements were resolved by discussion or referral to a third reviewer. Authors were contacted for clarification where necessary.

Methods of synthesis
Results were pooled using random-effects meta-analysis. Heterogeneity was assessed using the Q test (p<0.10) and I² statistic (>50% indicated high heterogeneity). Subgroup analyses were used to assess the effects on primary and secondary prevention, assess different statins and compare different doses of atorvastatin. Sensitivity analyses were used to assess the impact of study quality by excluding studies from the analysis based on their quality score.
Publication bias was assessed using funnel plots and Egger's test.

**Results of the review**

Twenty trials were included (32,311 participants). All studies were randomised, 11 were double-blind placebo controlled, one was single-blind placebo controlled and eight were open-label.

Statins were effective in preventing atrial fibrillation (OR 0.59, 95% CI 0.45 to 0.76; 20 trials, $I^2=71\%$). Very similar results were seen after seven trials that did not have atrial fibrillation as a prespecified endpoint were excluded from the analysis.

Subgroup analyses found that statins were effective in primary prevention (OR 0.67, 95% CI 0.51 to 0.88; 14 trials, $I^2=66\%$) and secondary prevention (OR 0.40, 95% CI 0.20 to 0.83; six trials, $I^2=77\%$). Atorvastatin was the more effective treatment overall (OR 0.43, 95% CI 0.27 to 0.66; 11 trials, $I^2=65\%$) and for the subgroup of atorvastatin doses of 10 to 40mg/day (OR 0.29, 95% CI 0.19 to 0.45; eight trials, $I^2=23\%$).

There was some evidence of publication bias overall and for the atorvastatin studies.

**Authors' conclusions**

Statin therapy was useful for prevention of atrial fibrillation but the effect in secondary prevention was not superior to primary prevention. Atorvastatin was more effective than pravastatin with lower doses being the most effective.

**CRD commentary**

This review specified inclusion criteria for study design, interventions, participants and the main outcome. The search was limited by language. The authors searched for unpublished studies and assessed publication bias. Study selection and data extraction were performed by two people to reduce errors and bias. The authors did not report whether they used similar methods for the quality assessment and the full results of the assessment were not reported, so it was difficult to verify the quality of the evidence. Studies were pooled even where heterogeneity was high but various subgroup and sensitivity analyses were used to explore differences between the studies.

The conclusions of this review should be treated with some caution given the unclear quality and heterogeneity of the included studies.

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

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

**Research:** The authors stated that more randomised controlled trials of individual statins were needed to determine their efficacy and optimal dosage for the treatment of atrial fibrillation.

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