To the Editor:

We read with great interest the randomized trial by Ji et al\(^1\) of preoperative atorvastatin therapy to prevent atrial fibrillation (AF) following off-pump coronary artery bypass grafting. Their results showed that patients undergoing preoperative administration of oral atorvastatin had a lower incidence of postoperative AF vs preoperative administration of oral placebo (14% vs 34%, \(P=0.009\)). A recent meta-analysis by Liakopoulos et al\(^2\) of 13 studies also provided evidence that preoperative statin therapy was associated with a reduction in the incidence of AF after cardiac surgery. The meta-analysis, however, included only 3 randomized trials,\(^3–5\) and a number of randomized trials have been published since then. We herein would like to perform the first meta-analysis of only randomized trials of preoperative statin therapy for prevention of AF in cardiac surgery.

To identify all prospective randomized controlled trials of preoperative statin therapy enrolling patients undergoing cardiac surgery, public domain databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched (current through June 2010) using Web-based search engines (PubMed and OVID), exploding keywords that included hydroxymethylglutaryl-CoA reductase inhibitor, statin, cardiac surgery, and randomized controlled trial. Studies considered for inclusion met the following criteria: the design was a prospective randomized controlled clinical trial; the study population was patients undergoing cardiac surgery; patients were randomly assigned to preoperative statin therapy vs control (no statin or placebo); and main outcomes included incidence of postoperative AF. For each study, data regarding incidence of AF in both the statin and control groups were used to generate risk ratios (RRs) and 95% confidence intervals (CIs). Study-specific estimates were combined using inverse variance-weighted averages of logarithmic RRs in both fixed- and random-effects models. Between-study heterogeneity was analyzed by means of standard \(\chi^2\) tests. If significant statistical heterogeneity was not identified, the fixed-effect estimate was used preferentially as the summary measure. Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual trials one at a time and recalculating the pooled RR estimates for the remaining studies. Publication bias was assessed graphically using a funnel plot and mathematically using Begg’s adjusted rank-correlation and Egger’s linear regression test. All analyses were conducted with Review Manager version 5.0 (Nordic Cochrane Centre, Copenhagen, Denmark) and Comprehensive Meta-Analysis version 2 (Biostat, Englewood, NJ, USA).

Our search identified 8 prospective randomized controlled clinical trials\(^1,3–9\) of preoperative statin therapy enrolling patients undergoing cardiac surgery. In total, our meta-analysis included data on 841 patients undergoing cardiac surgery randomized to therapy with statins or control. Three\(^1,4,7\) of the 8 individual trials demonstrated a statistically significant benefit of statin therapy for postoperative AF in cardiac surgery patients. Pooled analysis of all the 8 trials demonstrated a statistically significant 45% reduction in incidence of AF with statin therapy in fixed-effects models (Figure: RR, 0.55; 95% CI, 0.44–0.68; \(P<0.00001\)). There was minimal trial heterogeneity (\(P=0.98\)) and accordingly no difference in the pooled result from random-effects modeling. In general, exclusion of any single trial from the analysis did not substantively alter the overall result of our analysis. To assess publication bias we generated a funnel plot of the logarithm of effect size vs the standard error for each trial (data not shown). There was no evidence of significant publication bias (\(P=0.71\) by Begg’s test; \(P=0.13\) by Egger’s test).

The results of our analysis, which was robust in sensitivity analyses, suggest that statin therapy may reduce the incidence of postoperative AF by 45% in patients undergoing cardiac surgery, and strengthens the results of the randomized trial by Ji et al.\(^1\)

### Figure

Incidence of postoperative atrial fibrillation among patients undergoing cardiac surgery randomized to preoperative statin therapy vs control. CI, confidence interval; IV, inverse variance.
References


