Impact of preoperative statin therapy on adverse postoperative outcomes in patients undergoing cardiac surgery: a meta-analysis of over 30 000 patients


CRD summary
This review concluded that preoperative statins given to people before cardiac surgery led to an improvement in short-term clinical outcomes. The review appeared well conducted. However, most of the evidence came from retrospective observational studies. The authors also concluded that further results from RCTs were needed. These conclusions are suitably conservative.

Authors' objectives
To assess the clinical effects of preoperative statin treatment on people who underwent cardiac surgery.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched for studies published between 1966 and February 2008. Search terms were reported separately (see URL for Additional Data). No language restrictions were applied. Abstracts from seven relevant cardiology association meetings (2005 to 2007) and reference lists of identified studies and reviews were checked.

Study selection
Randomised controlled trials (RCTs) or observational studies that compared the effects of pre-operative commercially available statin therapy with no statins in adults who underwent cardiac surgery were eligible for inclusion. Studies had to report on clinical outcomes: incidence of all cause early mortality (within 30 days); myocardial infarction; atrial fibrillation; stroke; and renal failure.

Most participants (92%) in the included studies underwent coronary artery bypass graft (CABG); some had valve surgery (6.3%) or both (1.7%). Most were primary procedures (98.7%) and elective surgery (82%). Some participants had previous myocardial infarction, diabetes, renal failure and hyperlipidaemia. Mean ages ranged from 61 to 67 years and 72% were men. Where reported, statins used were simvastatin, atorvastatin, pravastatin, fluvastatin, cerivastatin or lovastatin. In one study some participants had non-statin lipid-lowering drugs. Some participants also received beta blockers or aspirin. Where reported, exposure to statins ranged from three days to 60 days; other studies reported only "taking statins preoperatively". Follow-up was either usual discharge or from six to 60 days.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection

Assessment of study quality
Quality was assessed using the Jadad Score (for RCTs) and Downs and Black Checklist (for RCTs and observational studies). Maximum Jadad score was 5. Maximum Downs and Black checklist score was 29.

Two authors independently assessed the quality of studies. Disagreements were resolved by discussion and consensus.

Data extraction
The incidence of outcomes were extracted and odds ratio (OR) and 95% confidence intervals (CI) calculated. Where necessary, authors of studies were contacted for missing information.

The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
When heterogeneity was absent, data were pooled using the Mantel-Haenszel fixed-effect method. Where heterogeneity was present, the Der-Simonian and Laird random-effects method was used. Pooled ORs with 95% CI, were calculated for dichotomous outcomes. Weighted mean differences (WMD) were calculated for continuous outcomes.

Heterogeneity was assessed using the Q statistic and $I^2$ statistic.

Differences in characteristics of included participants between treatment and control groups were investigated according to gender, previous disease and treatments.

A funnel plot and Egger's weighted regression statistic were used to assess publication bias. Duval and Tweedie's Trim-and-Fill method was used to estimate the number of unpublished studies needed to correct for publication bias.

Results of the review

Nineteen studies (31,725 participants) were included: three RCTs (317 participants); three prospective observational studies (1,185 participants); and 13 retrospective observational studies (30,223 participants). Study quality was judged moderate to good: Jadad score from 1 to 5 for RCTs; Downs and Black Checklist 22 to 28 for RCTs and 17 to 23 for observational studies.

Preoperative statins lowered the risk of short term mortality (OR 0.57, 95% CI 0.49 to 0.67; no significant heterogeneity $p=0.30$, $I^2=14.6%$; 10 studies), stroke (OR 0.74, 95% CI 0.60 to 0.91; no significant heterogeneity $p=0.10$, $I^2=45.1%$; seven studies) and atrial fibrillation (OR 0.67, 95% CI: 0.51 to 0.88; heterogeneity present, $p=0.003$, $I^2=69.9%$; seven studies).

There was no effect on myocardial infarction or renal failure.

When characteristics of included participants were investigated, pooled preoperative prevalence showed that people who received statins were more likely to be: younger; male; have had previous myocardial infarction, diabetes or hyperlipidaemia; and receive betablockers or aspirin before surgery. Those who did not receive statins were more likely to have had non-elective surgery and cardiopulmonary bypass.

Tests showed no evidence of publication bias.

Authors' conclusions

Preoperative statins lead to a substantial improvement in short-term clinical outcomes in people who underwent cardiac surgery. There was still a need for evidence from randomised trials.

CRD commentary

The aims of the review in terms of participants, treatment, study design and outcomes were clearly stated. The search covered a number of relevant sources and included looking for unpublished and non-English language studies. This was likely to have reduced the risk of publication bias, as confirmed by the authors' test for publication bias. The methods of study selection and data extraction were not described, so it was impossible to comment on these. Methods for quality assessment were aimed at reducing introduction of reviewer errors and bias. The quality of studies was investigated, although scoring systems are not considered to be the best methods. The authors combined results for RCTs and observational studies (most studies in the review were retrospective observational studies). Results from observational studies are not as reliable as those from RCTs as confounding factors can affect results. The authors' investigation into differences between participants showed that the statin and control groups did not necessarily have the same baseline characteristics. Overall the review was well conducted and the authors conclusions, which included a recommendation for more evidence from RCTs, appear to be suitable conservative.

Implications of the review for practice and research

Practice: The authors stated that it was reasonable to initiate intensified preoperative statin treatment in people with hyperlipidaemia, multiple cardiac risks or who were undergoing cardiac surgery.

Research: The authors stated that there was a need for further evidence from randomised controlled trials on
preoperative statin treatment in people undergoing cardiac surgery.

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