Systematic review and meta-analysis of the effects of statin therapy on abdominal aortic aneurysms

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CRD summary
The review concluded that statin therapy appeared to improve all-cause survival after abdominal aortic aneurysm repair, but that no significant benefit of statins was found for aneurysm expansion rate. The authors' conclusion reflects the evidence presented, but some caution is warranted due to the possibility of publication bias and the small number of included studies which were observational in design.

Authors' objectives
To determine the efficacy of statin therapy on clinical outcomes in patients with abdominal aortic aneurysm disease.

Searching
PubMed (1966 to May 2010), EMBASE and the Cochrane Library were searched, with no language restrictions, up to July 2010; search terms were reported. The ClinicalTrials.gov website was also searched. PubMed related articles function was used, cross referenced with full results from other searches. References of relevant articles were also checked.

Study selection
Studies that compared statin therapy with no statin therapy in patients with abdominal aortic aneurysm were eligible for inclusion. Eligible studies had to include data in extractable form in two or more studies and report on abdominal aortic aneurysm clinical outcomes. Studies that reported on emergency abdominal aortic aneurysm outcomes were excluded.

In included studies, the most common type of statin used was simvastatin (where reported); atorvastatin, fluvastatin and pravastatin were also used. The type of abdominal aortic aneurysm repair included endovascular aneurysm repair alone and/or open repair alone (where reported). Individual inclusion and exclusion criteria, along with the criteria each study were adjusted for, varied across studies. Outcomes included aneurysm growth rate, 30-day mortality and long-term all-cause mortality. Study characteristics were provided in a supplementary online table (see URL for Additional Data).

The authors did not state how many reviewers were involved in selecting studies for the review.

Assessment of study quality
Two reviewers independently assessed the quality of the included studies using the Newcastle-Ottawa Scale, which considered patient selection methods, comparability of study groups, and assessment of outcome. A maximum of 9 points could be awarded (studies that scored 7 points were considered high quality).

Data extraction
Two reviewers independently extracted data to calculate odds ratios (ORs) for dichotomous outcomes and standardised mean differences (SMDs) for continuous outcomes, with 95% confidence intervals (CIs). Where studies presented median and range, the median was considered a mean and standard deviations were calculated from the interquartile range or confidence interval assuming normal distribution of data. Means and standard deviations were also calculated directly from graphs following Cochrane recommendations, or for Kaplan-Meier curves following methods described by Parker et al.

Methods of synthesis
Summary odds ratios and standardised mean differences, with their associated 95% confidence intervals, were estimated using a random-effects model weighted by inverse variance. Heterogeneity was assessed using $\chi^2$ and $I^2$.

Sensitivity analyses were performed considering study quality (high quality studies) and population size (over 200 patients).
Publication bias was assessed using funnel plots; sections of the Newcastle-Ottawa Scale were also examined to assess bias.

**Results of the review**

Twelve cohort studies were included in the review (n=11,933 patients; 2,469 in the statin groups and 9,464 in the control groups). There were 11 retrospective cohort studies and one prospective cohort study. Quality scores for the studies ranged from 3 to 8 (seven studies were considered to be of high quality). Maximum follow-up ranged from two years to over five years.

**Expansion rate** (seven studies, n=4,197 patients): A reduction in abdominal aortic aneurysm expansion rate was found in patients taking a statin compared with those who did not (SMD -0.37mm/year, 95% CI -0.65 to -0.08; I²= 89%). When the analysis was restricted to studies with over 200 patients, or to high quality studies, no significant treatment effects were found between the two groups and heterogeneity was substantially reduced.

**30-day mortality rate after aneurysm repair** (two studies, n=6,293 patients): No significant between-group difference was found in 30-day mortality following abdominal aortic aneurysm repair (OR 0.22, 95% CI 0.02 to 2.90; I²=71%). Sensitivity analysis was not possible.

**Short-term and long-term mortality rates after aneurysm repair** (four studies, n=7,335 patients): A significantly lower mortality rate was found at one year (OR 0.44, 95% CI 0.25 to 0.76; I² =59%), two years (OR 0.43, 95% CI 0.25 to 0.72; I²=72%) and five years (OR 0.57, 95% CI 0.42 to 0.79; I²=67%) after abdominal aortic aneurysm repair in patients taking statins compared with those who were not. When the analysis was restricted to studies with over 200 participants, or to high quality studies, the estimates remained significantly unchanged from the overall analysis.

Significant statistical heterogeneity was found for all sensitivity analyses, except at one year follow-up.

Funnel plots for abdominal aortic aneurysm expansion, as well as two-year and five-year mortality lacked symmetry, which suggested the possibility of publication bias. The funnel plot for one-year mortality demonstrated adequate symmetry.

**Authors' conclusions**

Statin therapy appeared to improve all-cause mortality after abdominal aortic aneurysm repair, but no significant benefit of statins was found for abdominal aortic aneurysm expansion rate.

**CRD commentary**

The review question was supported by defined inclusion criteria. The literature search was not restricted by language, although no attempts were made to locate unpublished studies, which raised the possibility of publication bias. Funnel plot asymmetry was found for most of the outcomes (indicating possible publication bias), but the small number of included studies made this more difficult to interpret. Appropriate steps were taken to minimise errors and bias at data extraction and validity assessment, but it was not clear whether similar methods were used at study selection.

Study quality was assessed, but only summary scores presented; study quality was deemed to be high for most of the included studies. Greater information on the included patients would have been useful. The methods used to synthesise studies were appropriate and included some relevant subgroup analyses.

The authors’ conclusion reflects the evidence base presented, but some caution is warranted due to the small number of included studies (which were observational in design) and the possibility of publication bias.

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

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

**Research:** The authors stated that it would be useful to separate aneurysm-related mortality from all-cause mortality, as well as analysing endovascular aneurysm repair and abdominal aortic aneurysm repair separately. Data collected from ongoing abdominal aortic aneurysm screening services may further inform results on statin therapy and abdominal...
aortic aneurysm expansion.

**Funding**
Not stated.

**Bibliographic details**

**PubMedID**
21254006

**DOI**
10.1002/bjs.7343

**Original Paper URL**

**Additional Data URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aortic Aneurysm, Abdominal /drug therapy /mortality /pathology; Cohort Studies; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /therapeutic use; Publication Bias; Treatment Outcome

**AccessionNumber**
12011001500

**Date bibliographic record published**
20/04/2011

**Date abstract record published**
21/09/2011

**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.