The effect of statin therapy on ventricular tachyarrhythmias: a meta-analysis

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CRD summary
The authors concluded that available evidence suggested statins may have been associated with reduced risk of ventricular tachyarrhythmias in patients with coronary artery disease. Further large-scale randomised trials were needed. Given the limited search, unclear quality of included studies and possible limitations in the analysis, the authors' caution is warranted.

Authors' objectives
To investigate the association between statin therapy and the risk of ventricular tachycardia/ventricular fibrillation in patients with coronary artery disease or non-ischaemic cardiomyopathy.

Searching
MEDLINE and unspecified Cochrane databases were searched for articles published in English between 1985 and February 2010. Search terms were reported. The references of review articles, prior meta-analyses and original studies were also handsearched for additional studies.

Study selection
Randomised or observational studies that investigated the association between statins and the risk of ventricular tachycardia/ventricular fibrillation in patients with coronary artery disease or non-ischaemic cardiomyopathy were eligible for inclusion. Ventricular tachycardia/ventricular fibrillation was defined as arrhythmic sudden death, documented ventricular tachycardia/ventricular fibrillation on monitor or appropriate shocks from an implantable cardioverter-defibrillator.

Included studies compared either any statin, any lipid-lowering medicine or pravastatin 40mg/day to no statin treatment in patients with acute myocardial infarction, coronary artery disease or non-ischaemic cardiomyopathy. The mean age of patients ranged from 56 to 68 years and 60.3% were men. In the statin group, the ejection fraction ranged from 20.1% to 48.0% and the prevalence of diabetes mellitus ranged from 11.0% to 34.7%. The percentage of patients who received angiotensin-converting enzyme inhibitor or angiotensin 2 receptors blockers ranged from 30.2% to 100%. The percentage of patients who received beta blockers ranged from 30.0% to 100.0%

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they assessed the quality of included studies.

Data extraction
The number of patients with ventricular tachycardia/ventricular fibrillation in each group was extracted and used to calculate risk ratios (RR) with 95% confidence intervals (CI). The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled risk ratios were calculated using a fixed-effect model if there was no evidence of significant statistical heterogeneity (p≥0.05). A random-effects model was used where there was evidence of significant statistical heterogeneity (p<0.05). Statistical heterogeneity was assessed using $\chi^2$ and $I^2$. Publication bias was assessed using Eggers test. Subgroup analyses were carried out according to disease type. Sensitivity analyses were performed excluding individual studies.

Results of the review
Nine studies were included for review (150,953 participants). Two randomised controlled trials (900 participants) and seven prospective observational studies (150,053 participants).
Across all patient groups, statin use reduced the risk of ventricular tachycardia/ventricular fibrillation by 31% (RR 0.69, 95% CI 0.58 to 0.83). There was evidence of moderate statistical heterogeneity (I²=57.3%). Sensitivity analyses that excluded the study with exclusively non-ischaemic patients did not significantly alter the results (RR 0.65, 95% CI 0.53 to 0.81; eight studies, 150,724 participants) Statins significantly reduced the risk of ventricular tachycardia/ventricular fibrillation in patients with acute myocardial infarction (RR 0.63, 95% CI 0.34 to 1.16; two studies, 148,175 participants). The results of sensitivity analyses excluding each study in turn were also reported. The authors reported no evidence of publication bias (p=0.957).

**Authors' conclusions**
Available evidence suggested that statins may have been associated with reduced risk of ventricular tachyarrhythmias in patients with coronary artery disease. Further large-scale randomised trials were needed.

**CRD commentary**
The review addressed a clear question with well-defined inclusion criteria. Only two databases were searched so relevant data may have been missed. The search was restricted to English language articles, so language bias may have been introduced. There did not appear to have been any attempts to identify unpublished data. Publication bias was assessed and ruled out, but the small number of included studies made it difficult to fully rule out publication bias. There was insufficient information on the review process to rule out the possibility of reviewer error and bias.

Study quality was not assessed so it was unclear how reliable the findings were. Most included studies were of weaker methodological design. For some studies, the numbers of patients who received angiotensin-converting enzyme inhibitor, angiotensin 2 receptors blockers or beta blockers appeared to differ between groups; it was unclear whether these results were significant and may have confounded the results. Both randomised and non-randomised studies were combined in the meta-analysis, which may have affected the reliability of the results. The authors reported that statins significantly reduced the risk of ventricular tachycardia/ventricular fibrillation when the result was not significant. Statistical heterogeneity was assessed but the authors set significant levels for heterogeneity at p≤0.05 rather than p≤0.10, as was more common for tests of statistical heterogeneity, so significant heterogeneity may not have been detected.

Given the limited search, unclear quality of included studies and possible limitations in the analysis, the authors' caution is warranted.

**Implications of the review for practice and research**
**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that further large scale randomised trials were needed investigating the effects of statins on ventricular tachyarrhythmias in patients with coronary artery disease or cardiomyopathy.

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