Author's response to reviews

Title: Effect of statin use on outcome of symptomatic cholelithiasis: a case-control study

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Version: 4 Date: 9 June 2014

Author’s response to reviews: see over
Responses to peer review comments “Effect of statin use on outcome of symptomatic cholelithiasis: a case-control study” article

Dear Editor and Reviewers, we kindly thank you for your valuable comments and we answer the following:

1) Reviewer comment: to draw conclusions from the study, an important aspect is to know the time during which the patients had been taking statins, something that has not been reflected in the study.

Response: We agree, it is an important aspect to know the time during which the patients been taking statins but unfortunately the time the individual patients had been taking statins is exactly not known, as this was a retrospective study. The patients had taken statins many months or years, however, and statin treatment is reimbursed in Finland. This is one weakness of our study and it is said in Discussion (page 11, line 271) "weakness of our study paragraph". We added it in clearer form in text (page 11, line 273): nor on the duration of the statin treatment in individual patients.

2) Reviewer comment: In table 1, Why is not calculated the P-value in the only two conditions in which no statistical differences between the two groups (hypertension and coronary artery disease/coronary heart failure/valvular?"

Response: We agree with the reviewer that these two p-values were marked incorrect since the differences between the two groups concerning these two baseline characteristics were statistically
significant; we corrected these two values in table 1 to be presented in form $p < 0.001$

3) **Reviewer comment:** The conclusions of the study says: "Stain treatment may also be associated with less bleeding during laparoscopic operations" but the study has not shown statistical significance in this aspect.

**Response:** We Agree and we chanced discussion sentence (line 248-253, page 10): “However, no statistically significant differences were observed in the bleeding parameters between the groups.“
To form:
On average, more bleeding was observed among non-users compared with users during laparoscopic operations, but the difference remained statistically insignificant with a $p$ value of 0.07. However, this finding is in line with the shorter operation time among statin users. Possible mechanisms behind these findings may include smaller size of cholesterol particles and gallstones. More research with larger sample sizes is warranted to confirm these findings.

4) We also changed (this was not suggested by the reviewers) line 126 in page 5: “Mikkelı central Hospital ethical committee approved the study protocol.” To form: “According to the Finnish legislation, no ethical assessment or approval is mandatory for a register-based study” since this is exactly the statement referred to in this research, (and do not apply to our more extensive material, as originally).
This study statement of research ethics committee of northern Savo is attached below.

With my best regards,

Sincerely yours,

Jukka Pulkkinen, A researcher, MD
STATEMENT OF RESEARCH ETHICS COMMITTEE OF NORTHERN SAVO

IMPACT OF STATIN USE OF SYMPTOMATIC CHOLELITIASIS: A CASE-CONTROL STUDY

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This letter is to confirm that according to the Finnish legislation, no ethical assessment or approval is mandatory for a register based study such as Impact of Statin use of symptomatic cholelithiasis: a case-control study.

The Finnish law (Medical Research Act 1999/488, 2004/295, 2010/794) states medical research requiring the approval of an appropriate ethics committee as following: research involving intervention in the integrity of a person, human embryo or human foetus for the purpose of increasing knowledge of health, the causes, symptoms, diagnosis, treatment and prevention of diseases or the nature of diseases in general. Register based scientific research is stated also in the Act on the Openness of Government Activities (621/1999) and Personal Data Act (523/1999). According to these Acts the administrative approval by the participating hospital is adequate which in this case has been received.

Kuopio 2.5.2014

Soini Lehto
Chairperson