Reviewer's report

Title: Statins and risk of gastric cancer in diabetes patients

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Reviewer: shoji shimoyama

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Major

1. In table 4 and figure 1, gastric cancers in statin users were earlier stage and exhibited better outcome than those in statin nonusers. The frequency of routine examination to detect gastric cancer (i.e., endoscopy) should be provided. Were the frequencies between statin users and nonusers the same? Assuming that statin users have more health interest, as the authors described in discussion, they undergo endoscopy more likely with the symptoms that would not be an enough reason for endoscopy in statin nonusers. Such factor may be a bias for detecting gastric cancer at an earlier stage, resulting in better survival. Thus, table 4 and figure 1 are merely results of a patient visit frequency.

2. Helicobacter pylori is a strong carcinogen for gastric cancer thus one of the strong confounding factors. The univariate and multivariate analyses (table 2) should involve all potential confounding background factors including Helicobacter pylori status.

3. In the same sense, total cholesterol (TC) and LDL-C levels should be provided and compared between statin users and nonusers, and between patients with and without gastric cancer. Furthermore, multivariate analysis should include TC and/or LDL-C levels, because, as the authors mentioned in 'Introduction', some investigators believe that low TC or low LDL-C levels are risks of malignancy. The authors should provide proof that risk reduction of gastric cancer is due to statin use per se, not by low LDL-C.

4. What was the mean (median) length between date of registry and date of gastric cancer diagnosis in statin users and nonusers? Since gastric cancer takes longer time to develop and to become manifest, gastric cancer developed in patients with too short registry period is due to a preexisting cancer, not by statin nonuse effect.

5. In table 2, the univariate and multivariate results should be presented by all variables included, along with risk ratios irrespective of p-value, for clarifying what variables are included in the multivariate analysis.

6. The authors should mention overall gastric cancer risk in general DM patient cohort. GC incidences among statin users and nonusers in the authors series should be compared with those in the general DM patient cohort.

Minor
1. Abbreviations should be explained by full spelling at first mention i.e., DM, LDL, etc. What is AGC in table 1?

2. ‘Statin exposure’ is defined as statin prescription for at least 6 months. So, ‘statin nonexposure’ may be a mixed cohort of statin never users and statin user for <6 months. In table 1, statin exposure period ‘0’ cohort may include patients who take statins for <6 months.

3. Histological type in table 4 did not follow the Lauren’s classification (intestinal and diffuse types). In addition, what was the histology of ‘others’? I imagine that this study comprised gastric adenocarcinoma patients, the ‘others’ histology should be omitted and reanalyzed.

4. IFG (in ‘Discussion’) should be IGF? In discussion, the proof or publications demonstrating that statin modulates IGF pathway.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.