Reviewer's report

Title: Impact of metabolically healthy obesity on the risk of incident gastric cancer: a population-based cohort study

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Reviewer: Zahra Bahadoran

Reviewer's report:

The study conducted by Yoshitaka Hashimoto et al. is historical cohort study included 19,685 Japanese individuals who participated in health-checkup programs (2003 to 2016); participants were categorized as metabolically healthy or metabolically abnormal obese according to four metabolic factors (hypertension, impaired fasting glucose, hypertriglyceridemia and low high density lipoprotein-cholesterol) and assessed for risk of gastric cancer. The study hypothesis is interesting and gives important clinical perspective into the filed. The authors have described their attempt to reproduce a study in which it was claimed that metabolically abnormal obese patients, but not those with metabolically healthy obesity, had an elevated risk for incident gastric cancer. The authors are appreciated for their well-organized methodology and good writing style. However there are some critical comments can improve the clarity of the manuscript if they will be addressed point by point.

1- In the abstract section, background needs to be revised to be more concise and focused on the main hypothesis of the study.

2- For follow-up period in the abstract, please provide median and inter-quartile range rather than mean.

3- Please provide incidence of gastric cancer as case per 1000 person-year.

4- Please provide a brief background about gastric cancer and obesity among Japanese population, where the study was conducted. Such information can highlight the importance of the study in this population.

5- The authors need to provide a focused background about difference between metabolically healthy or metabolically abnormal obese subjects; why the authors hypothesized that these two clinical status may be different for development of cancer? This question needs to be underlined and well clarified in the introduction section. This would help readers to judge the analytical logic and overall credibility of the study.

6- The authors need to refer to some studies indicating association between metabolic syndrome and incidence of gastric cancer, since individuals categorized as metabolically abnormal obese are actually subjects with metabolic syndrome. These studies well pointed out this possible relationship: (Front Oncol. 2018 Aug 23;8:326. doi: 10.3389/fonc.2018.00326. eCollection 2018), (Int J Environ Res Public Health. 2019 Mar...
In the method section, study sampling needs more details; sampling method and study population selection for the cohort should be described in brief. The authors also need to describe how their study population is representative for target population and how their study findings can be extrapolated to Japanese population? In specifying this information, readers are apprised precisely about what sampling method was used and its possible adequacy or inadequacy for supporting the conclusion.

In the statistical section the authors should perfume further analysis to indicate how each metabolic abnormality (hypertension, impaired fasting glucose, hypertriglyceridemia and low high density lipoprotein-cholesterol) had contributed in development of gastric cancer. By such analysis they can discuss which abnormality has greater potential impact in predicting gastric cancer.

Please indicate how confounding variables were selected for the statistical models and how the Cox Proportional Hazard Models were fit for covariates. The authors need to check P for Entry (PE) for each potential confounder by univariate model. Please also provide HR (95% CI) and P value for potential confounders, both in univariate and multivariate models.

In the result section, the authors should provide demographic background of the whole study population (e.g. mean ± SD of age, sex distribution, mean ± SD of BMI, waist circumference, etc.) rather than those provided in Table 1 for the groups.

In Table 1, please provide percent rather than numbers for sex distribution (just for male gender); please provide percent rather than numbers for smoking status, and each percent should be provided separately for Never-/Ex-/Current smoker.

In Table 1, information provided in the table for pack-years cigarette smoking is not clear at all.

In Table 1, please also indicate type of data provided for continuous and categorical variables.

Table 2, needs to be revised for changing row and column; please provide HRs (95% CI) and P value for each phenotype by three model (i.e. crude model, model 1 and model 2). Furthermore, HR (95% CI) and P value for potential confounders should be removed from the table and provided in another table (or preferably in the text).

Figure 1, which contains important about study population and their follow up during the study period, should be revised according to STROBE Statement for flowchart of cohort studies. Please provide more details about numbers of participants were excluded from
each cohort population (Metabolically healthy non-obesity, Metabolically healthy obesity, Metabolically abnormal non-obesity, Metabolically abnormal obesity).

16- Discussion section critically needs to be revised. It is too short and main important issues that the authors were be supposed to discuss, have been neglected. In the first paragraph the authors need to be focused on main findings rather than emphasizing on novelty of this work. They also need to address the mentioned studies earlier in my comments, which investigate the association of metabolic syndrome and its components with risk of gastric cancer. As suggested for further analysis to indicate contribution of each metabolic abnormality in development of the outcome, related findings need to be discussed as well.

17- Selection bias that the authors addressed in the discussion ("because we only included the participants who were re-examined in the health-checkup program") needs more clarification.

18- Conclusion section needs to be revised to highlight clinical importance of the findings; the authors should contextualize their findings and provide major possible implications of the study results. How their study findings may contribute to scree at risk obese subjects?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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