Reviewer’s report

Title: A Cardiorespiratory Fitness, Body Mass Index, and Cancer Mortality: A Cohort Study of Japanese Men

Version: 2
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Reviewer: Shuzo Kumagai

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Generally speaking, this manuscript had long showed significant association between CRF and cancer mortality independently of BMI, which has been published in 2003 by Dr. Sawada, but they found "no clear relationship between BMI and cancer mortality and notably they did not find statistically significant interaction between BMI and CRF either". In other words, they did not report positive novel findings from their previous publication. For these reasons, the originality of this study is not high at all. It was thought that it was necessary to raise the quality of the study by increasing the case numbers of the cancer death that was an endpoint in increasing target people and more longer follow-up periods for an observation period in future.

1. Is the question posed by the authors well defined?

There was contradiction in the hypothesis that "higher CRF and moderate BMI would be associated with lower cancer mortality risk independently and jointly with the lowest risk among individuals in the highest CRF group and moderate BMI group". When CRF and BMI are independently associated with cancer mortality, there would be no interaction between CRF and BMI.

2. Are the methods appropriate and well described?

1) The statistical analysis on the interaction of smoke with BMI and CRF is rigorous and well considered.

2) Although VO2max makes the low fitness group as the reference, what is the reason for having set 2nd tertile of BMI as reference?

3) With respect to the BMI, Firstly "participants with BMI less than 18.5 were excluded to minimize potential bias from undiagnosed cancer that may have led to weight loss". However, patients with cancer usually undergo weight loss at the late stage of cancer. What’s more the percentage of BMI less than 18.5 is not few in fit Japanese population. Therefore at the primary analyses, that exclusion may not be done while it could be done in the sensitivity analysis.

Secondly, participants were divided into tertiles and "the second tertile was used as the reference group which had a reference that published in 2011 with data were from a large study of East Asians. However, the tertile and using the
second tertile as the reference group is not convincing. In that report BMI 22.5-27 group showed lowest mortality while this BMI range is overlapped with the second tertile (21.6-23.6) and the third tertile (23.7-37.4) in this present manuscript.

Thirdly, in Figure I, "BMI were divided according to classification from WHO". It is confusing that why they did not keep consistent to use BMI tertile. Additionally, there was no number of two groups of BMI<25 and BMI >=25 showed in the result section or in the figure 1.

3. Are the data sound?
Yes.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

In terms of the combined effects of CRF and BMI, this manuscript found no interaction between BMI and CRF. It is still needed to further discuss.

In the Table 2, author did not have any explanation about association between cancer mortality and CRF regardless of BMI in smoker's group only.

Table 3 shows the cancer death rate is related to CRF in the 2nd tertile of MBI, and not in 1st and 3rd tertile of BMI. However, author did not explain for this result.

Table 4 shows that significant association between CRF and cancer mortality is observed in the group of follow-up period less than 10 years, but not in longer follow-up period. The reason is not explained.

I guess that order of the cause-specific cancer mortality in Japanese is different from North American. However, total cancer mortality is associated with CRF in both Japanese and north American. Is it thought that the mechanism is common?

6. Are limitations of the work clearly stated?

Limitation were clearly stated while there could be other considerations. The sample were recruited just from a company so the results may not be generalized to other Japanese population.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes.
8. Do the title and abstract accurately convey what has been found?

9. Is the writing acceptable

   The writing in the results of the abstract is confusing, especially the last sentence.