Author's response to reviews

Title: Waist circumference and insulin resistance: a cross-sectional study of Japanese men

Authors:

Shinji Tabata (sthe8916@ba.mbn.or.jp)
Shinichiro Yoshimitsu (yoshimitsu4432shinichiro@yahoo.co.jp)
Tadamichi Hamachi (maxhardhot@hotmail.com)
Hiroshi Abe (ttabato@yahoo.co.jp)
Keizo Ohnaka (oonaka@geriat.med.kyushu-u.ac.jp)
Suminori Kono (skono@phealth.med.kyushu-u.ac.jp)

Version: 3 Date: 16 November 2008

Author's response to reviews: see over
Dear Dr. Cassady-Cain,

Thank you very much for your consideration to the above-referenced manuscript. We revised the manuscript in accordance with the reviewers’ comments. We would like to resubmit it for publication in BMC Endocrine Disorders. Changes were made regarding the following points.

**Reviewer 1: Altan Onat**
1. Categorization of smoking status and alcohol use: The relevant phrases were moved from the statistical analysis to the procedure section (lines 23-24 on page 5 & lines 4-5 on page 6).

2. Spearman correlation coefficient between the two variables studied: The correlation coefficient between waist circumference and HOMA-IR was calculated (lines 8-9 on page 7).

3. Confounding factors (lipids, blood pressure, and inflammation): The confounding was referred to as a weakness in the Discussion (lines 5-6 on page 10).

4. The significant elevation of IR already at levels of 80-84 cm: This important finding was emphasized in relation to obesity-related risk in Asians (lines 20-23 on page 8), with one reference added (ref 22). We are not sure whether Japanese men have less confounders in the relationship and did not refer to this point.

5. To use the term “to be associated with” rather than “predicting” in the Conclusions. The words were changed as suggested, but the term “in association with” was used in the context of the sentence (line 21 on page 10).

6. Limitations (study design and confounding factors): These points were discussed as weakness (lines 3-6 on page 10).

**Reviewer 2: Patrice Brassard**

Major Compulsory Revisions
1. [Comment: The introduction is quite short and the link between your background and the aim of the study is not straightforward.] We referred to some recent Japanese studies evaluating appropriateness of the cutoff of waist circumference (ref 9-11), and described problems in these studies (the end of the first paragraph of page 3).

2. [Comment: It would be important to add a hypothesis at the end of the second paragraph of the introduction.] Two hypotheses (purposes) were specified (the last line on page 3 to the first 2 lines on page 4).

3. [Comment: You should present the inclusion/exclusion criteria.] Disease conditions...
affecting glucose metabolism and insulin levels were exclusion criteria. This point was described in the Subjects section (lines 21-22 on page 4).

4. [Comment: were the subjects in whom fasting plasma insulin or glucose was not determined and WC not measured excluded from analysis?] We had described this point in the original manuscript, but we revised the text for clarity (the bottom line on page 4 to the first line on page 5).

5. Items from the questionnaire: Brief description was added (line 20 on page 5 to line 5 on page 6).

6. Characteristics of the study subjects in table 1: We included more information in terms of medical history, current medication and lifestyle, and also of lipid profile as suggested by comment 6 of Reviewer 3.

7. The utilization of geometrical means: This was specify (lines 14-15 on page 6).

8. Limitations regarding use of two estimates and a limited range of age: These limitations were specifically stated in the paragraph describing limitations. We also added problems of cross-sectional study and confounding in the paragraph as advised by Reviewer 1 (lines 1-6 on page 10).

9. [Comment: you highlighted that "obesity, particularly visceral adiposity, has been known to be positively related to insulin resistance". Could you provide a similar analysis between BMI and insulin resistance?] We examined the relation between BMI and HOMA-IR, and found that BMI was as strongly associated with HOMA-IR as waist circumference. This point was explained in a new paragraph of the Discussion (the second paragraph on page 9). Thus we deleted words "particularly visceral adiposity” and “Nonetheless” in the second paragraph of Discussion (page 8).

10. [Comment: why did you arbitrarily choose 2.00 and not used the cutoff utilized in the Japanese study you are citing?] The cutoff of 2.00 was "arbitrarily" defined because there was no standard for the definition. Earlier studies did not have specific reasons for their definition. Because of this arbitrariness, the ROC analysis had been repeated using different cutoffs of HOMA-IR as shown in Table 3. In the revision, we also calculated odds ratios of elevated HOMA-IR based on different cutoffs of HOMA-IR, and the results were almost the same (lines 11-12 on page 9).

11. [Comment: Are the subjects from the present study fitter than the general population? If yes, they won't be similar in terms of insulin resistance and WC. You should nuance this section.] We changed wording to imply that the study population may not be representative (lines 7-13 on page 10).

Minor Essential Revisions

All of the suggested corrections were incorporated as follows:

1) In the introduction, "a measure of visceral obesity" was changed to "an estimate of visceral obesity" (line 6 on page 3).
2) In the methods section, transition of the nationwide programs were explained more specifically and the items were described briefly (lines 14-17 on page 4).
3) In the statistical analysis section, "arbitrarily" was added following HOMA-IR of "odds
ratios of elevated HOMA-IR defined" (line 10 on page 6).
4) In the conclusion, "in men" was added in the last sentence (line 22 on page 10).

Reviewer 3: Eunjung Rhee
Major point:
1. [Comment: Why were only men analyzed?] Women, particularly those at 40s or 50s, are very few in the SDF. We added a sentence to this effect (lines 9-10 on page 4).

2. [Comment: Why the cutoff have to be re-analyzed? Stronger explanation is needed.] We referred to several studies on waist circumference, and pointed the problems of these studies, in response to comment 1 of Reviewer 2 as well (lines 16-21 on page 3).

3. [Comment: were the subjects with diabetes included in the study?] Diabetic subjects with or without oral medication were included in the study to maximize the number of subjects with insulin resistance. HOMA-IR is probably not affected by oral medication for diabetes (ref 14). HOMA-IR was higher in such men. These points were described in the Methods and Discussion (lines 2-5 on page 5 & lines 13-16 on page 10).

4. [Comment: Medication hx should be included in the result.] As replied to comment 6 of Reviewer 2, we added such information in Table 1.

5. [Comment: How were the waist circumference measured?] The method was described (lines 14-16 on page 5), but we did not perform the quality control procedure.

6. [Comment: Lipid levels of the participants should be included in the analyses.] We added lipid profiles in Table 1.

7. Definition of insulin resistant: See reply to comment 10 of reviewer 2.

8. Representativeness of the study subjects: See reply to comment 11 of Reviewer 2.

9. [Comment: You'd better show all the ROC results with various sensitivity and specificity with various HOMA-IR levels.] Table 3 was expanded to include more information.

We hope that we responded to each comment satisfactorily to improve the manuscript. We should appreciate your consideration in advance once again.

Best wishes,

Shinji Tabata, MD, PhD
Corresponding author
Self-Defense Force Fukuoka Hospital
1-61 Kokurahigashi, Kasuga-shi 816-0826, Japan
e-mail: sthe8916@ba.mbn.or.jp