Author's response to reviews

Title: The long-term coronary heart disease risk of previously obese patients with type 2 diabetes mellitus

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Author's response to reviews:

12 April, 2013

Dr. Timothy Shipley,

The Editor-in-Chief, BMC Endocrine Disorders

Dear Dr. Shipley,

On behalf of all the authors, I would like to ask you to consider our revised manuscript entitled "The long-term coronary heart disease risk of previously obese patients with type 2 diabetes mellitus" for publication in your journal as an original investigation.

We have revised the manuscript on the basis of comments provided by two referees. We thank the referees for their careful reading of our manuscript and their constructive comments. All authors are in agreement with the content of the revised manuscript.

Thank you very much for consideration.

Sincerely,

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Reply to Referee 1

Thank you very much for your careful reading of our manuscript with many constructive comments to improve our manuscript. According to your suggestions, we rewrote our manuscript as follows:

1) We wrote in the limitation section in the Results and Discussion sections (page 9, line 10) that women constitute only one-quarter of the sample, and with only 48 cases of overall incident CHD, conclusions could only be applied to men.

2) Additional data regarding sex distribution across categories and 3 smoking categories (current smokers, ex-smokers, and never smokers) were added to Table 1. Not all patients in the present cohort had data on inflammation parameters (CRP, fibrinogen, or lipoprotein(a)) and we could not add these data to Table 1. We described this fact in the limitation section in the Results and Discussion sections (page 9, line 12).

3) Information on female analysis was added as Figure 1D.

4) Data on the approximate time interval between reported MAXBMI and measured enrollment-BMI were obtained in 315 of 319 patients. Accordingly, we reanalyzed the data of the cohort consisting of 315 patients and wrote this up in the revised manuscript. The results of the reanalysis with 315 patients were essentially the same as the results of 319 patients, except that the association of previous obesity and coronary heart disease became insignificant after full adjustment for risk factors of age, sex, smoking status, serum lipids, blood pressure and the presence of diabetic retinopathy. Data on the approximate time interval between reported MAXBMI and measured enrollment-BMI were presented in Table 1.

5) According to the reviewer’s suggestions, we described the presumable threshold effect rather than a graded increase of MAXBMI which suggested unrecognized factors acted in particular to previous obesity in the Results and Discussion sections (page 7, line 20).

6) We analyzed the Cox regression model with the difference between MAXBMI and BMI at enrollment (deltaBMI) as an independent variable and found that large deltaBMI also behaved as a risk factor for coronary heart disease. The results were presented in Table 2. As the hazard ratio between the two models (Model 2 of MAXBMI and that of deltaBMI) did not show a significant difference, we could not determine whether previous obesity or rather preceding weight loss was the predictor of coronary risk in the present study.

7) According to the reviewer’s suggestions, we referred to the reports of Guerci B et al. (Diabet Metabolism 1999; 25:412) concerning the relationship of diabetic retinopathy and CHD risk factors such as lipoprotein(a).

8) According to the reviewer’s suggestions, we referred to the reports of Onat A. et al. (Metabolism 2011; 60:499 and Acta Diabetol 2011 Jul 16 [Epub]) concerning the relationship of diabetic retinopathy and CHD risk factors such as dysfunction of HDL with low-grade inflammation. We also omitted the sentence “... metabolic memory of high glucose, dyslipidemia and hypertension before
Reply to Referee 2

Thank you very much for your careful reading of our manuscript with many constructive comments to improve our manuscript. According to your suggestions, we rewrote our manuscript as follows:

1) Our definition of Max BMI was: \[
\text{Max BMI} = \frac{\text{self-reported maximal weight before enrollment (kg)}}{\text{height at enrollment (m)}} \]
We have added our definition to the Materials and Methods section (page 5, line 7).

2) Data on the approximate time interval between reported MAXBMI and measured enrollment-BMI were obtained in 315 of 319 patients. Accordingly, we reanalyzed the data of the cohort consisting of 315 patients and wrote the revised manuscript. Data on the approximate time interval between reported MAXBMI and measured enrollment-BMI are presented in Table 1. The results of the reanalysis with 315 patients were essentially the same as the results of 319 patients, except that the association of previous obesity and coronary heart disease became insignificant after full adjustment for risk factors of age, sex, smoking status, serum lipids, blood pressure and the presence of diabetic retinopathy.

3) All participants included in this study were diabetes patients. To clarify this point, we added the following in the first line of the Methods section (p4): “This study was a part of the retrospective cohort follow-up study of T2DM.”