Author’s response to reviews

Title: Brain Natriuretic Peptide Levels are Associated with Peripheral Arterial Disease in Type 2 Diabetic Patients

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Version: 4 Date: 17 February 2014

Author’s response to reviews: see over
Dear editors

We feel sorry about the flaws in our manuscript and having given you so much trouble. Now we have revised it as suggested. We would be grateful for your further review and advice. We will continue to do better. Thank you for your help.

Qusetion 1. Please include a brief comment in the discussion regarding reviewers 1, first concern.

Answer: We have added a brief comment in the discussion according to the reviewers 1, as shown below:

All of our subjects had a clear diagnosis of T2DM and those with diabetic complications that could affect the metabolism of BNP were excluded or limited. In our study cohort, the high morbidity of PAD was positively correlated with the BNP level even after adjustment for other risk factors.

Qusetion 2. A clear and specific aim is still missing in the abstract.

Answer: We have revised the background, as shown below: “The effects of brain natriuretic peptide (BNP) on the risk of cardiovascular disease and atherosclerosis have been studied. However, little information is available regarding peripheral arterial disease (PAD), particularly among subjects with type-2 diabetes
mellitus (T2DM). The aim of our study was to assess the potential relationship between BNP levels and PAD among T2DM patients.”

Question 3. Since patients with EF<50% were excluded how come that mean EF was 56±5%?

Answer: We have been doing a series of studies on cardiovascular disease. With the numerous effective information gained from these studies, we have set up many databases. Thanks for your warning, we carefully checked the data source and regrettably found out that we mistakenly copied statistic data from the wrong set of data. We rechecked all the data in the article and fortunately, other data were not mistaken. We have taken our lesson and will do our research more carefully.

Question 4. Figure 1 does not provide further information and should be omitted.

Answer: We have omitted Figure 1 as suggested. Relevant content in the manuscript has been omitted accordingly.

Question 5. The cross-sectional design should be stated as an important limitation of the study.

Answer: The reviewer’s critique is very reasonable. For different
methods, the proof strength is different. The strength of cross-sectional design is relatively weak. When cross-sectional design is used to explore disease causes and prognosis, diseases and affecting factors are investigated at the same time, so there is no time causality. Thus, the results gained may only provide clues to devise further effective measures for preventing diseases. This characteristics of cross-sectional design was a limitation of our study, and we highlighted it in the methods according to your suggestion. The study cohort was 507 T2DM outpatients in which BNP levels were measured. Cross-sectional associations between BNP levels (in tertiles) and PAD were examined. And in discussion we give its limitation of this article and further research suggestion.

Question 6. Although the authors describe in their methods that? Totally five hundred and seven outpatients with T2DM at the Second Affiliated Hospital of Zhejiang University from January 2012 to January 2013 were recruited?, in their discussion of potential limitations, they report that they have focused on a selected patient cohort hospitalized in an endocrinology department..? Which of the two is correct?

Answer: sorry, we have failed to express clearly. The patients were outpatients recruited from the endocrinology department of the Second Affiliated Hospital of Zhejiang University.
**Question 7.** There was no difference between groups regarding current smoking. What about ex-smokers? What about pack-years?

**Answer:** In the baseline questionnaire, participants answered the question “Have you smoked in your lifetime?” with “no” or “yes”. We classified participants into never smokers (No), current smokers (yes). Participants were asked about the total years they had smoked and the average number of cigarettes smoked per day. Pack years of cigarette smoking were not calculated. We did not do deep research in this respect. We should give more attention in the future.

8. English needs extensive editing.

**Answer:** We have invited a well-known expert to edit English.