Author’s response to reviews

Title: Prevalence of cardiovascular risk factors in non-menopausal and postmenopausal inpatients with type 2 diabetes mellitus in China

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Author’s response to reviews:

Dear reviewers,

Thank you very much for your constructive feedback on this article. We have made revisions to the manuscript based on your comments. Below are details of how we have addressed the points raised.

Best wishes

Comments and responses

Maria Ida Maiorino (Reviewer 1)

In this cross-sectional study, authors evaluated the prevalence of CV risk factors and their correlation with CVD risk in a population of diabetic Chinese women. The topic is interesting, although the observational nature of the study does not allow to make significative inferences from results. The English requires some revision. Authors should address the following issues:
1. The major concern remains the lack of a non-diabetic age-matched control group. This should be added to the limitations.

Reply: Thank you very much! According to your suggestion, we added it to the limitations (Discussion section, line 37-40, page 12).

2. Mean HbA1c values is really high in each group (pre-menopausal, early and late menopausal women); it looks like strange, as the mean duration of diseases is 5.3 years. Have the authors some explanations about this point? Is this findings in line with the overall diabetic population in China or with the male diabetic population? Moreover, only 1.2 % of the studied population achieved the 3 target goals of HbA1c, blood pressure and blood lipids.

Reply: Thanks! First, Ji et al. [1] launched a cross-sectional, multicenter observational study in China, mean HbA1c values was 7.6%, and 3 target goals of HbA1c, blood pressure and blood lipids was 5.6%. However, a total of 25,817 adults with type 2 diabetes were outpatients. In our study, subjects were recruited from inpatients. As we all know, inpatients suffered from T2DM in more serious conditions than outpatients. Second, we collected the data as the patients were in the hospital, which they were in critical situation. Third, 73 out of 569 participants in our study accompanied with ketoacidosis, and 62.9% of patients had insulin-treated. All of these reasons leaded to high HbA1c values and extremely low 3 target goals of HbA1c, blood pressure and blood lipids. In several Chinese studies, the mean HbA1c values ranged from 8.2% to 11.2% [2-4], so the findings was in line with Chinese hospitalized diabetic population. We don’t know if this answers your questions.


3. Lipids values should be express also in mg/dL throughout the study.
Reply: We expressed the lipid values in mg/dL based on your suggestion.

4. The abstract appears quite long.

Reply: Thanks a lot! We simplified the abstract (Abstract section, line 21, page 1).

Silvia Pieralice (Reviewer 2)

1. For the present study, a mixed group of non-menopausal and postmenopausal women with type 2 diabetes was evaluated. It is well known that hypoglycemic agents are different in term of cardiovascular safety and protection, as well as in term of hypoglycaemia risk, which is an independent risk for cardiovascular events. The authors should specify the hypoglycemic therapy of patients enrolled and report the percentage of sulfanylureas (SU) treatment in the different groups.

Reply: Thank you very much. Your advice inspired us. We specified the hypoglycemic therapy of patients enrolled and report the percentage of sulfanylureas treatment in the different groups (see Table 1) and have also been added in the article (Results section, line 25-42, page 7).

2. Have insulin-treated patients been excluded from the analysis?

Reply: No, insulin-treated patients were included. In our study, hypoglycemic agents included insulin injections and oral medication, about 62.9% of subjects received insulin treatment. We added this to the article (Results section, line 29, page 7 and line 29, page 8). Thanks!

3. The authors state that "previous study demonstrated that the incidence of CVD among postmenopausal women were higher in women who did not experience menopause " (Pag 2, lines 36-37). This sentence can be quite ambiguous, please clarify the sentence.

Reply: Sorry for the problem. Compared to non-menopausal women, the incidence of CVD among postmenopausal women were higher. We modified it in the text (Background section, line 25-27, page 2).
4. In this survey, history of ketoacidosis was significantly higher in non-menopause group compared to others. A recent post-hoc analysis of UKPDS found a lower long-term risk of cardiovascular disease in individuals with T2D having ≥1 autoantibody test positive compared to autoantibodies test negative patients (Diabetes Obes Metab, 2019). Was there any difference of autoantibodies positivity and C-peptide levels in non-menopause group vs menopause groups?

Reply: Yes, in non-menopause group, most of the 35 patients were taken to the hospital for diabetic ketoacidosis, which was related to younger age [5-7]. We appreciate your point and read the literature you recommended carefully. There was no statistically significant differences in C-peptide levels among three groups (see Table 1)(Results section, line 36-46, page 6). Actually, we did not collect the data of autoantibodies test. According to your suggestion, we added this section as a shortcoming of the study. And we will explore the difference of autoantibodies positivity in non-menopause group vs menopause groups in our further study (Discussion section, line 46-48, page 12).


5. Pag. 11, line 7-29. Authors found a higher risk of CVD among diabetic patients who experienced menopause compared with non-menopausal women. However, due to the observational nature of the study, the mechanisms proposed to explain the association between higher risk of CVD, menopausal status and FPG is merely speculative. Indeed, no measures of sex hormones have been performed.

Reply: Thanks a lot. It was the limitation of our survey. Sex hormones will be performed in our further study (Discussion section, line 44-46, page 12).