Author’s response to reviews

Title: Association between renal function and bone mineral density in healthy postmenopausal Chinese women

Authors:

Shuang Li (ls330013@csu.edu.cn)
Junkun Zhan (zhanjunkun@csu.edu.cn)
Yanjiao Wang (917637923@qq.com)
Yi Wang (13874857512@139.com)
Jieyu He (9953726@qq.com)
Wu Huang (huangwu_2008@yeah.net)
Zhifeng Sheng (ls330013@163.com)
Youshuo Liu (liuyoushuo@csu.edu.cn)

Version: 2 Date: 03 Nov 2019

Author’s response to reviews:

Dear Dr. Nagai,

RE: BEND-D-19-00337R1

Thank you very much for your letter and advice. Following the suggestions of the reviewers, we have added the comments raised by the reviewers, and the amendments are highlighted in red in the revised manuscript. The responses to the reviewers’ comments are listed below this letter. We herewith submit the revised paper for re-examination.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

We look forward to hearing from you soon.
With best wishes,

Yours sincerely,
Dr Liu

Dear Sir or Madam:

RE: BEND-D-19-00337R1

Thank you for your valuable comments on our paper. We have revised the manuscript, and would like to re-submit it for your consideration.
Points for improvement:
Reviewer 1
1. The authors showed that eGFR was not associated with osteoporosis after controlling for age, menopausal duration. The eGFR itself is calculated by age, which means that age must be a strong confound factor for eGFR. Therefore, in this data, BMD could be heavily influenced by age (and menopausal duration). The point is that in this study the relation between GFR and BMD should be analysed in age, menopausal duration, matched subgroup, otherwise, this argument would be invalid.

RESPONSE: Thank you for pointing out the inadequacies in our study. We have analysed the relationship between eGFR and BMD after stratification by age and menopausal duration. eGFR did not correlate with BMD and osteoporosis risk after stratification by age or menopausal duration (Supplementary data: Table S1- S4). Ensrud et al. [1] showed that after adjustment for age, eGFR based on creatinine was not associated with hip fracture risk. Therefore, in the present study, it is possible to indicate that the decline in renal function is not independently associated with osteoporosis risk after controlling for confounders. Corrections have been made in Abstract (page 2, line 44-45, 47-48), Results (page 6, line 157-161, 169-171) and Discussion (page 8, line 208-209).

2. Although authors commented the limitation about the use of CKD-EPI (creatinine), at least, relatively good renal function should be assessed by cystatin-based GFR (MDRD and or CKD-EPI).

RESPONSE: Thank you for the comment. We agree that the great majority of studies concluded that formulas based on serum cystatin C are superior to SCr-based eGFR. However, Keddis et al [2] showed that SCr-based CKD-EPI equation was preferred over cystatin C-based eGFR in kidney transplant recipients because they are less biased, more accurate. To address this concern, we have added this limitation in Discussion (page 9, line 253-259).

3. In method part authors explained that subjects with renal dysfunction were excluded, how was the renal dysfunction defined? urine test, or imaging examination? Because this study included women with GFR 60-90, if patients have these abnormalities, the patients should be classified to CKD stage 2. The explanation should be clearly stated.

RESPONSE: Thank you for this valuable suggestion. We are sorry that we didn’t make it clear enough. eGFR declines with age. Impaired renal function is defined as eGFR < 60 ml/min/1.73m2 according to the previous study [3]. Some modifications were made in Methods (page 4, line 91, 94, 95-96) and Discussion (page 8, line 213; page 9, line 259-260).

While, in discussion part (page9, lane17), authors suggested that the overestimation of spine BMD might be caused by the calcification complicated with renal dysfunction. This conflicting explanation could confuse us.

RESPONSE: Thank you for this valuable suggestion. We agree that the expression of “Spine BMD may be overestimated due to acceleration of calcifications in the aorta and other tissues, especially in patients with renal dysfunction” is confused. Therefore, we have changed “The overlying aortic calcifications make it difficult to measure BMD at lumbar spine in the elderly” in Discussion (page 8, line 228-229).

4. In discussion part(page8, lane13~), the authors discussed about the skeletal site-specificity differences in this study, however, the trend of BMD reduction (cortical bone>cancellous bone) is also the feature of CKD-MBD. This study focused on renal function. If in subgroup analysis reduced renal function will have a correlation to low BMD, the contribution of CKD-MBD should be debated.

RESPONSE: This is a good question, thank you for bringing it up. CKD is associated with bone disorders, and we have added some comments in Discussion (page 8, line 233-243).

Reviewer 2
1. In this study the authors have tried to establish possible correlations between renal function and bone mineral density in healthy postmenopausal women. The study is cross-sectional and therefore any findings could only be the result of coincidence. As the authors have pointed out, the data in the literature regarding this possible correlation are very well represented. Studies with a much larger
sample size than the paper presented by the authors have shown correlations. The paper is therefore interesting but does not show anything different from what was established in the literature. The authors should highlight the differences with other studies in order to be published.

RESPONSE: Thank you for your valuable suggestions. The present study has notable strengths including its relatively large sample size, focus on the healthy postmenopausal Chinese women, where data on this population are rare. No participant had taken a drug known to affect bone metabolism and renal function. Besides, important confounding factors were adjusted in the regression analysis. We have highlighted these strengths in Discussion (page 9, line 244-248).

Still, there are some modifications in Methods (page 4, line 113; page 5, line 124), Discussion (page 7, line 181; page 8, line 208) and References (page 14, ref 23; page 16, ref 40-43).

Reference