Author’s response to reviews

Title: The ratio of AGE to sRAGE independently associated with albuminuria in hypertensive patients

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Manuscript ID BEND-D-17-00287, entitled "The ratio of AGE to sRAGE independently associated with albuminuria in hypertensive patients"Dear Editor-in-Chief:Thank you for your kind review of our manuscript and for the valuable reviewer comments. We have read the comments carefully and revised the manuscript based on their suggestions. Changes to the manuscript have been highlighted in yellow. Below we have listed the reviewer comments and our point-by-point responses.We are very grateful for the opportunity to submit a revised manuscript and are looking forward to your next correspondence. With best regards: Po-Hsun Huang

Technical Comments:1. Please change 'Introduction' to "Background".Response: We have revised it accordingly. (BACKGROUND, page 5, line 1)

Editor Comments:BMC Endocrine Disorders operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer reports:Antonino Dipino, MD, PhD (Reviewer 1): Thank you for the possibility to review this manuscript. In this work the Authors explored the relationship between microalbuminuria and AGE/RAGE ratio in a population of hypertensive patients. The main findings the higher AGE levels and lower sRAGE levels in patients with microalbuminuria (without statistical significance), furthermore they found an independent association between microalbuminuria and AGE/RAGE ratio. Like the authors correctly explained the lack of a system that may discriminate between the different fractions of sRAGE is one of the major limitation of this study. Moreover, I believe that several points are needed to be clarified. 1 - the authors measure AGE levels with a commercial ELISA kit. However, it is not clear what is the AGE that is identified with this method or the method identify all the serum glycated proteins. It is needed to clarify this point in the appropriate section.

Response: The AGE evaluated by this ELISA kit
includes N-epsilon-(Carboxymethyl) lysine, pentosidine and other AGE structures, but not N-epsilon-(Carboxyethyl) lysine or methylglyoxal. We have added information into the Methods section. (METHODS, Laboratory investigations, page 9, line 16)

Response: We are sorry for the clerical mistake. It means “-70℃”.

(METHODS, Laboratory investigations, page 9, line 13)

- a more detailed description of the study population is needed. In particular it is not clear if patients with diabetes are included in the study. Table 1 shows that in both groups there are subjects with prediabetes at least, according to fasting glucose levels. Diabetes is a key determinant of microalbuminuria and AGE/RAGE levels, so it is needed to clearly explain whether the population include or not subjects with any alteration of glucose homeostasis or taking hypoglycemic drugs. So, you should declare if you performed screening for diabetes (OGTT or HbA1c) in the population. If available, the prevalence of IFG, IGT and HbA1c levels should be provided. If the prevalence of patients with alteration of glucose homeostasis is high it is needed to adjust the multiple regression analysis according to presence/absence of prediabetes/diabetes. Response: This study did not include patients with diabetes and patients taking hypoglycemic drugs. (METHODS, Study subjects, page 7, line 18) Because we only evaluated the fasting plasma glucose, we added a variable to distinguish the patients with (≥ 100 mg/dl) and without impaired fasting glucose (}