Reviewer’s report

Title: Intrinsic and Extrinsic Epigenetic Age Acceleration are associated with Hypertensive Target Organ Damage in Older African Americans

Version: 0 Date: 05 Feb 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are minor issues

Statistics - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues
OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This is an interesting and generally well-designed study although there is a part of the methodology (assessment of kidney damage) in which I disagree with the authors and it is in the interpretation of these results that I disagree with the authors.

The rest of the design and methodology I consider appropriate.

REQUESTED REVISIONS:

Design: 1) the authors have used clinical blood pressure to correlate EAA with the hemodynamic parameter. It is possible that the evaluation of the hypertensive population and its degree of control would have been more appropriate by 24 hours ambulatory blood pressure monitoring (ABPM). It is well known the possible presence of an alert reaction to blood pressure measurement in the office and also to the existence of other hemodynamic factors that influence the target organ damage such as nocturnal hypertension or blood pressure variability; 2) In relation to the study of renal function, there is an important limitation, since only a single determination of albuminuria was performed and its variability is well known (as the authors comment). Therefore, it is recommended to make at least two determinations. So the results obtained at this point should be taken with caution.

Execution: there was a significant percentage of patients who were lost between phases 1 and 2. Specifically more than 460, representing approximately 25% of the study population. There is no information in the manuscript about this loss. If some of the losses were due to cardiovascular death, it could have been important for interpreting the results.

There is also a certain bias in the population studied, since there is a high percentage of women. Therefore, I believe that the authors should include these points within a section of limitations of the study.

Interpretation: in relation to albuminuria there is a point of discussion that I do not agree with. The authors comment that in diabetes, before the decrease in filtration, there is a progressive increase in albuminuria. However, they point out that this does not happen in hypertension which is inaccurate (European HTA ref). From here they make an inadequate interpretation and point
out that there may be a relationship between IEAA and albuminuria in diabetes and that IEAA may be a marker of diabetes. This point must be modified. In addition, although the authors take into account factors related to albuminuria, such as smoking, diabetes and obesity, dyslipidemia is not mentioned, which is also associated with the excretion of albumin in the urine. Finally, regarding antihypertensive treatment, there are drugs families that are more specific in controlling target organ damage such as the renin angiotensin system (RAS) inhibitors and albuminuria. The authors should comment on that.

ADDITIONAL REQUESTS/SUGGESTIONS:

Already mentioned

Note: This reviewer report can be downloaded - see attached pdf file.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

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