Reviewer's report

Title: Correlation of Renin Angiotensin and Aldosterone System Activity with Subcutaneous and Visceral Adiposity: the Framingham Heart Study

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Reviewer: GUIDO LASTRA

Reviewer's report:

Dear Editor

I have reviewed the manuscript entitled "Correlation of Renin Angiotensin and aldosterone activity with subcutaneous and visceral adiposity: The Framingham Heart Study". In this paper, O'Seaghdha and coworkers evaluated the correlation between markers of systemic activity of the Renin Angiotensin Aldosterone System (RAAS) and specific measurements of both subcutaneous and visceral obesity in a large cohort of 992 women and 897 men from the third generation Framingham Heart Study.

In this paper, the authors evaluated adiposity by computed tomography and measured systemically aldosterone, plasma renin activity and calculated the aldosterone to renin activity ratio. They did not find any significant correlation between SAT, VAT and their measurements of systemic RAAS activity.

This paper is based on a large and well established population from the Framingham Heart Study and certainly is interesting and provocative. The topic studied and discussed is indeed important and has potentially a high impact on public health. However, in my opinion the paper in its present form is not suitable for publication and I would suggest a major revision. I would be willing to review a corrected manuscript.

1. The authors have to clearly elaborate and differentiate the systemic versus tissue (local) RAAS activities. Not finding correlations between SAT, VAT or systemic activity of the RAAS does not necessarily means that there is not inappropriate activation of the system at a local level, which could affect several tissues. This has been demonstrated in multiple experimental conditions.

2. The study should include analysis of subpopulation. The average reported BMI is 26, so the population studied is in a category of overweight. Specific analysis in obese, overweight and lean individuals should be presented in this paper, and would contribute to improving the accuracy of the study. Even further, differential analysis specific for BMI, waist circumference, and percentiles of VAT/SAT should be entertained and reported. Equally it would be interesting to evaluate correlations with blood pressure.

3. The authors should present markers of local activation of the RAAS. I understand this would imply more invasive procedures and taking samples of adipose tissue, so it might be technically challenging, but would add value to the paper and allow to better support the conclusions.
**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests