Reviewer's report:

Title: Clinical and Postmortem Measures of Cardiac Pathology in Subjects with Alzheimer's Disease

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Reviewer: Angelo Di Iorio

This paper try to elucidate the link between atherosclerotic vascular disease and AD. The authors enrolled 57 subjects (35 with a pre-mortem clinical diagnosis of AD). Coronary artery stenosis and other gross anatomical measures were determined at autopsy, moreover medical records of those subjects were also collected.

The conclusions derived in the paper stated that: “while midlife risk factors for atherosclerotic vascular disease increase the risk for the later development of AD, once dementia begins, both risk factors and manifest disease diminish, most probably due to weight loss”.

Strength point of the paper:

1) a large and comprehensive post-mortem evaluation of AD and controls with measurement of many cardiac and neurological markers.
2) Figure 1 is very impressive.

Major Revision

1) Materials and methods (pg 4): subjects enrolled in the study were not evaluated with prefixed timing, "standardized clinical assessment were performed on most subjects every one-two years". This kind of approach in the clinical evaluation of the subjects (especially for controls) could bring into the study a bias, at least in the interpretation of the data. Among the many clinical evaluations which one was chosen as the reference and why. How they manage this problem.

2) In the paper were not considered the drugs assumed, and please, could the authors analyze also what kind of action, if any, they had in the AD, AVD relation?

3) Lack also a clinical classification of AD, a TC scan or MRI of the subjects (AD and controls) enrolled

4) Statistical Analysis: I have some concern about the statistical approach, Table 4 report the comparison of heart weight ventricular thickness, BMI etc. according to sex and groups. This is the core of the paper and mostly of the assumption discussed were based on this table. Authors, from my point of view need to revise this approach, Student-T was not the correct test to compare 4 groups
(Male-Female controls vs Male-Female AD), probably GLM or similar with an interaction term could be powerful and probably more appropriate.

5) Conclusions section (pg 11) the authors stated that “the greater statistical strength of the cardiac differences between control and AD groups for female may be due to the larger BMI”, this statement, to me, seem to be inconsistent with the reported data. If it was the case, adjusting the analysis for BMI the differences seen between groups will disappeared, but the authors did not show any adjusted analysis. Moreover they did not have any longitudinal data for BMI and for AVD-score that could elucidate what kind of relationship exist between AD-AVD, therefore their conclusion need to be modulate.

Minor Revision

1) Authors use AVD for atherosclerotic vascular disease, this is a little confusing since in many cases with VAD was define vascular dementia, could they use another abbreviation?

2) Results section: a strong trend (p=0.07) is improper.

3) Table 3 reported only two values that could be realistically reported only in the text.

4) Table 4 need to be re-elaborate a table with 4 column for data could be better.

5) I believe that p-value must be reported in the table instead as a foot-note.

6) The last paragraph of the conclusion section (pg 11) are not so pertinent.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'