Reviewer’s report

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

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Reviewer: Alina Solomon

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This is an autopsy study of cardiac pathology in 35 patients with Alzheimer disease (AD) compared to 22 non-demented controls. The topic is particularly important, given the debates concerning the role of cardiovascular factors in AD. The detailed clinical data and thorough post-mortem evaluations (both neuropathological and cardiac) represent strengths of the study. Interestingly, the authors found that patients with AD had significantly less cardiovascular pathology, both clinically and at autopsy.

Major Compulsory Revisions

1. The conclusion of the abstract is ‘The results are in agreement with an emerging understanding that, while midlife risk factors for AVD 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’. There is indeed an emerging understanding that there may be differences between risk factors at midlife and at older ages, but the formulation ‘once dementia begins, both risk factors and manifest disease diminish’ is unclear. First, once the disease begins we can no longer talk about ‘risk’ factors. They should be called cardiovascular factors (or something similar). Second, I suppose ‘manifest disease’ refers to cardiac disease – it would be more clear to specify this. Third, what does ‘diminish’ mean in this context? Obviously cardiovascular factors or diseases don’t begin to disappear just because dementia has become manifest. I would recommend a more appropriate choice of words.

Fourth, have the authors checked the effect of weight loss on the relation between cardiac pathology and AD? Or at least the effect of BMI? I did not see any controlling for BMI (or changes in BMI) in the statistical analyses. The same comment for the conclusions at the end of the paper.

2. Introduction, page 3 – ‘once dementia begins, these same risk factors may diminish’ – see point 1 about the concept of ‘risk’ factors.

3. I am concerned about how the selection of subjects may have influenced the results. This is not discussed at all in the paper. Interestingly, in the article describing the Brain Donation Program at Sun Health Research Institute (reference 20) it is specified that ‘Queries of our database have shown, however, that our Alzheimer’s disease and non-demented control subjects have generally similar prevalences of major disease conditions’ and ‘The greater prevalence of a
medical history of coronary atherosclerotic disease and stroke in AD subjects supports many previous similar reports’ (page 232). How does this fit with the results of the present study?

4. Subjects with a neuropathological diagnosis of AD received first a clinical diagnosis of Alzheimer dementia when they were still alive. This is a very important point, given the neurodegenerative-vascular dichotomy that currently dominates the dementia field (which the authors themselves mention). Two of the consequences of this dichotomy are that: 1) cardiovascular factors and conditions may be overlooked in patients with AD, and 2) persons with a high load of cardiovascular risk factors and conditions may receive a diagnosis of vascular or mixed dementia ‘by default’ (excluding them from this study). This should be discussed.

5. In addition, it is known that persons with cognitive impairments often underreport other symptoms, and their medical comorbidity tends to be underdiagnosed and undertreated. This is a common problem in comorbidity studies in patients with dementia, and has to be mentioned.


7. Discussion, page 11 – ‘This may be of general health significance in that it appears that weight loss, even at advanced ages, may result in a reduction in cardiovascular pathology’. Is weight loss documented in the study participants? Has it been taken into account in the statistical analyses? If not, please rephrase.

Minor revisions

Table 4 – were comparisons made between female AD patients and controls, and male AD patients and controls? It would be much easier to read the results if they were grouped as AD versus controls instead of males versus females.

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.