

Peer Review File

Article Information: <https://dx.doi.org/10.21037/cdt-23-188>

Reviewer A:

In this paper, authors hypothesized that there might be a difference in collagen quantity between aneurysmal and non - aneurysmal aortic walls as a surrogate marker for aortic wall strength, and therefore they aimed to investigate collagen quantity in HIV infected patients on highly active antiretroviral therapy (HAART) presenting with TAAA. The manuscript is written in an appropriate scholarly style. As the authors themselves claim, this is the first such study. It is an interesting study, but several major changes need to be made to the paper to make it more accessible to publication in the journal.

Comments in detail:

1. Background is very short and unacceptable in this format. Some information about pathophysiology of collagen in HIV infected patients, risk factors and epidemiology of thoracic ascending aortic aneurysm in HIV infected patients and aortic wall strength in HIV patients are needed.

Response

- Page 3, Line 54-57

Expanded on the background.

HIV associated vasculopathy complicated by aneurysms usually tends to occur in advanced stages of the disease but the process of HIV vasculitis itself may present at any stage of the disease,

- Page 3, line 58-63

We have added the risk factors and epidemiology of TAAA in HIV patients.

-Page 3, line 66-69

We have explained the known mechanism to weak aortic wall strength in aortic aneurysm in HIV patients and that looking into collagen as a surrogate marker of aortic wall strength in HIV TAAA will be the first study of its kind.

2. Methods section: Probably more information is needed here.

- Should you precise

Response

Page 5 Line 86-90

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and or diastolic blood pressure ≥ 90 mmHg or currently using antihypertensive medication.

Body mass index is defined according to the World Health Organization as underweight $< 18,5$ kg/m², normal weight 18.5- 24.99 kg/m², overweight 25 -29.9 kg/m² and obesity > 30 kg/m².

- What do we know about hepatitis co-infections, syphilis infections, and smoking?

Response

Mentioned under introduction Page 3, Line 60-62

- Statistical analysis must be performed :

- precise why do you use means or median with interquartile range (normal distribution or not)

Response

Page 7 Line 131-132

Continuous data was reported with median with interquartile range as the data was not normally distributed.

- When you use a test, precise why you use it. eg : Why do you use Mann–Whitney U test and not t-test?

Response

Page 7 line 133-140

Comparison between the normal aortic tissue and abnormal TAAA wall tissue with regards to hydroxyproline concentration was analysed via Wilcoxon two sample test (non-parametric test for paired data) because the data was not normally distributed. For comparisons between aneurysmal vs normal aortic tissue of the twelve patient's vs six aortic valve leaflets data, a Kruskal-Wallis test was done (non-parametric ANOVA test that extends the two samples Wilcoxon test in the situation where there are more than two groups). Any missing imaging data or laboratory data were excluded from analysis.

3. Result section:

Table 1:

- why do you put body surface and BMI in race?

Response

It was a typographical error; however, we have decided to remove race from the table as 100% were Africans and it has been well explained in results section. (See Table 1). Page 7 line 142.

- What about duration on HAART, duration with HIV, WHO clinical stage?

Response

Page 3 line 54-57

All the patients were already on HAART upon admission and had suppressed viral loads implying a long duration on HAART, we do not know the exact number of years for each patient. HIV associated vasculopathy complicated by aneurysms usually tends occur in advanced stages of the disease as noted in the article by B Pillay, reference number 3 in the manuscript. So likely in stages 3 to 4. But the process of HIV vasculitis itself may present at any stage of the disease (Vega LE, Espinoza LR. Vasculitides in HIV Infection. Curr Rheumatol Rep. 2020 Aug 26;22(10):60.)

- As you precise for categorical data n (%), do the same for continuous variables (median [IQR] or mean \pm SD).

Response

Done, see Table 1

Remove % in second column (not necessary)

- Done, removed the % in second column (see table 1)

Many results are cited in the manuscript, but not table illustrated them. (p value?, table of comparison of Hydroxyproline concentration between aneurysmal vs normal aortic tissue vs aortic valve leaflets is needed.

Response

The comparison of the hydroxyproline concentration is illustrated in figure 6 and we have it in writing (Page 2 line, 38-41. Page 8 Line 167-171). We did not think that a table was relevant as it would be redundant.

- Try to categorize your participants in two groups of age (<55 or 60 years and > 55 or 60 years. Perhaps, you can find the difference in collagen concentration in the aneurysmal and non-aneurysmal aortic tissue. Old age is associated aortic aneurysms.

Response

This is a pilot study with a small sample size. We are unable to categorize the participants into the above-mentioned age groups as it will not give a meaningful comparative result. However, we will consider your suggestion in a future larger study.

4. Discussion section: Authors should compare and discuss their results with results obtained from other papers concerning this theme (Kariyanna doesn't treat the same theme, Ref 13).

Response

Change to the applied theme. See new reference 16.

5. Conclusion section: Conclusions are very general and are not supported by the result.

Response

Page 13, Line 276-280

We have modified the conclusion and it is supported by our results.

We removed this statement under conclusion- In this preliminary analysis, the contributors to weakening of the aortic vessel wall are likely multifactorial as evidenced by the mixed findings of inflammation, degeneration, elastic tissue fragmentation and atherosclerosis.

It might have been assumptive.

I encourage authors to perform this very first important study. HIV infection confers an increased cardiovascular disease risk, which is thought to be due to a complex interplay of several factors.

Reviewer B:

1. Please recheck and ensure all abbreviated terms are defined the first time they appear in the title, the abstract, and the main text.

Done

2. The abbreviated terms used in figure/tables should be defined in the legends of each figure/table. Please add their full terms.

Done, Page 21,22 lines 449-468

3. Since the abstract has been published, please obtain permission for the reuse and submit the permission file to the editorial office. Also, pls acknowledge it in the Acknowledgement section.

<https://www.journals.ac.za/index.php/SAHJ/article/view/4910>

Permission granted by the editor in chief of SA Heart Journal Prof N Ntusi. Please see attached correspondence. They are acknowledged as well Page 15, line 316-317

4. Please add a statement on whether informed consent was taken from all the patients. (if the consent is not required, please also add a statement to explain the reason. For example, Because of the retrospective nature of the study, the requirement for informed consent was waived.)

Informed consent was obtained for all the patients in this study.
Page 8, line 131-132

5. You used studies while cited only one reference. Pls check.

202 However, we had predominantly women (75%), which contrasts with studies in some
203 first world countries, where the males predominate [7]. A possible explanation could

Corrected. However, we had predominantly women (75%), which contrasts with a study in the first world country, where the males predominate (7).
Page: 11,12 line 224-226

6. could you add citations for the following statement.

229 There have been reports that in the elderly (age 50 years or greater) HIV infected
230 patients there is an increase in collagen and elastic fibres in the abdominal aorta
231 compared to non-HIV infected patients. As we know HIV is a systemic disease, so the

Done it is cited as reference 19.
Page 13, Line 254.

7. The objects of the study were from Charlotte Maxeke Johannesburg Academic Hospital, while the ethics approval was obtained from the University of the Witwatersrand. Please check and explain. Normally they should be the same affiliation.

□

Materials and Methods

This was a prospective pilot study, which consecutively enrolled twelve HIV infected patients, on HAART above the age of 18 years who presented for elective TAAA surgery from the period 2019-2021 at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) Cardiothoracic department. We excluded patients with known underlying cardiovascular diseases (e.g., Myocardial infarction, pericarditis) or connective tissue diseases (e.g., Marfan syndrome) and patients presenting for

in 2013) available at: <https://www.wma.net/wp-content/uploads/2016/11/DoH-Oct2013-IAMA.pdf>. The study was approved by institutional ethics review board of University of the Witwatersrand (M200678). The authors are accountable for all aspects of the work in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Charlotte Maxeke Johannesburg academic hospital is the hospital that is affiliated to the university of Witwatersrand so it is the same affiliation.