Reviewer’s report

Title: Biomarkers of cardiovascular risk across phenotypes of osteoarthritis

Version: 0 Date: 07 May 2019

Reviewer: Staja Booker

Reviewer's report:

Overall, this study is well-done and due diligence was given to the measurement of study variables and in validating findings. This topic is important given that OA and CVD are two common and potentially debilitating issues. With that said, there are several matters that the authors should attend to.

1. The introduction could be strengthened by providing statistics on prevalence rate of OA and CV concurrently.

2. Pg 2, line 79- "ankel" is misspelled.

3. Pg. 7, line 143-144: Please clarify if the statement "258 (70.5%), 257 (70.2%) and 174 (47.5 %) persons respectively" refers to those with OA, Oslo controls, and UK controls respectively.

4. Please state the design of this study in the methods section- case-control?

5. Authors should provide metrics (range of scores- what is considered normal vs. high) for interpretation of measures (PWV, A1x, ABI) in the methods so that readers can interpret figures 1a-2b. For example, what does an ABI of 1.25 mean?

6. Since missing data were not imputed, were they excluded from analysis? How did this affect power- any power calculations?

7. List age and sex as co-variates in the methods section "Covariates"

8. I appreciate the authors diligence in using objective measures to model arterial stiffening; however, did the authors assess for cardiovascular conditions, such as hypertension, hypercholesterolemia, history of myocardial infarction or other CV issues? It could be that diagnoses of CV conditions are more related to OA than actual arterial stiffening.

9. The authors should provide more discussion on the possible mechanistic pathways by which CVD risk is related to hand OA specifically. Currently the authors cite studies to support greater CVD risk in persons with hand OA but stop short of explaining why this is observed in only hand OA vs. knee/hip OA. The purpose of discussion sections are not only to provide supporting evidence but to "explain, expound, and explicate" the findings.
10. What are the clinical implications of this study?

11. Please provide labels for vertical axis for Figures 1a-2b. Also add "unadjusted models" to the figures 1a and 2a title.

12. The following covariates, Use of NSAIDs and heart rate, are not reported in Table 1 or Supplementary Table 1.

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

Yes

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

Yes

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

Yes

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:

Acceptable

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