Reviewer's report

Title: Determinants of Arterial Stiffness in COPD

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Reviewer: Christian Clarenbach

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The paper written by Bhatt et al. evaluates determinants of arterial stiffness in COPD in a multicenter cross sectional study. The authors demonstrate data regarding “classical” cardiovascular risk factors, vascular calcification, emphysema severity and inflammatory blood markers in an effort to identify determinants of arterial stiffness. Cardiovascular disease in COPD and arterial stiffness as a possible underlying mechanism, represent an important topic. However, there are some major comments on methodological issues that need to be addressed.

Major compulsory revisions

1. As the authors summarize in the conclusion (p. 12), “this study provides evidence that aortic pulse wave velocity is a predictor of cardiovascular disease”. In our opinion this conclusion is not supported by the presented analysis. Moreover, the conclusion of the abstract is substantially different.

2. In the paragraph “statistical analysis” the authors state that “variables significant on univariate analyses were entered into a multinominal regression model”. However, instead of presenting a table of univariate analyses, differences between quartiles of pulse wave velocities are demonstrated. The univariate analyses should be presented as well as the multinominal regression model which is missing. To properly address the study objective we recommend to perform univariate analysis with aortic pulse wave velocity as a continuous variable (dependent) and possible determinants as independent variables. Significant determinants from univariate analysis should be included in the final model. Otherwise information gets lost by categorizing into quartiles.

3. The authors present a second analysis demonstrating determinants of cardiovascular disease (including pulse wave velocity) in their COPD population. It is unclear why the association between variables and cardiovascular disease is evaluated in a second analysis while the focus of the paper is to identify factors associated with arterial stiffness.

Minor essential revisions

1. In the background section (p.5), the authors describe that arterial stiffness has been the target of pharmacologic and exercise interventions in COPD patients and that the referenced papers suggest a potential benefit which appears to be limited to those patients with more significant elevations in arterial stiffness. However, this limitation was only described in the pharmacologic intervention and
not in the referenced exercise intervention.

2. CAC and TAC are not introduced as abbreviations (statistical analysis, p.8).

3. No figure is presented. At least a figure illustrating the distribution of the aortic pulse wave velocity would be helpful.

4. The mean age mentioned in table 1 is 63.3 (SD 8.2) while the mean age in the results paragraph is 63.2 (SD 8.2).

5. C-reactive protein was measured for detecting possible inflammatory influences on the aortic pulse wave velocity. However, the authors did not discuss the negative findings concerning inflammatory factors as determinants of arterial stiffness in the context of the existing literature.

6. In the cited study by McAllister et al., emphysema severity was associated with arterial stiffness. This needs to be discussed since the present study did not find this association.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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