Reviewer's report

Title: The association of high-sensitivity c-reactive protein and other biomarkers with Cardiovascular Disease in Patients Treated for HIV: a Nested Case-Control Study

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Reviewer: John Koethe

Reviewer's report:

The authors present an interesting case-control analysis of serum CRP levels and the risk of acute MI, PCI, or stable/unstable angina among HIV-infected Italian adults on ART, which contributes to our current understanding of the relationship between inflammation and cardiovascular events in this population. The selection of participants, the laboratory assays chosen, and the analysis design are all well done. I have only a few suggestions:

Minor revisions:

1. ‘hsCRP’ is not itself a biomarker, the circulating molecule is ‘CRP’, and the authors measure it using the high-sensitivity assay. This is a minor point but the authors should note what the term ‘hsCRP’ actually means in the paper.

2. Intro, paragraph 3: “Several potential CVD markers have been investigated in HIV-positive patients….. but their association with CVD outcomes remains to be established”. This recent paper by Duprez from the SMART study also shows an association between IL-6, CRP, and d-dimer with CVD events. The OR for IL-6 is actually larger than for CRP. Duprez DA, Neuhaus J, Kuller LH, et al. Inflammation, Coagulation and Cardiovascular Disease in HIV-Infected Individuals. PLoS One 2012; 7:e44454.

3. “Cases and controls were matched on previous history of diabetes and smoking status” – other key determinants of CRP would be age, sex, and BMI. Could authors add why participants were not matched according to other characteristics?

4. Information on BMI is not included in the manuscript or table 1, but adipose tissue mass is an important determinant of serum CRP levels (as adipocytes and stromal cells demonstrate high expression of IL-6). If BMI is available, would add to multivariable models as a sensitivity analysis.

5. Were any of the samples below the limit of detection for any of the biomarkers?

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being
published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interests