Reviewer's report

Title: A Clinical Prediction Score for Diagnosing Unilateral Primary Aldosteronism May Not Be Generalizable

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Reviewer: Fabio Fernandes-Rosa

Reviewer's report:

The manuscript of Venon et al proposes the validation of a clinical prediction score for the diagnosis of unilateral primary aldosteronism. They have demonstrated that this prediction score, which presented 100% of specificity in the original cohort, presented lower specificity in the Canadian cohort of PA.

The study is technically well done, well written and the size of the cohort is adequate. Some points, however, must be clarified or discussed.

Major compulsory revision

1- Previous studies have already demonstrated that the prediction score of Kupers et al did not present 100% of specificity in different cohorts of primary aldosteronism. What are the contributions of the present study for the clinical management of patients with PA? This information should be added in the manuscript.

2- Recent studies have shown different population characteristics among PA cohorts despite recent guidelines for the management of primary aldosteronism. This could be reinforced in the discussion, with references of different cohorts as well as hypothesis for these cohort differences. Do the authors think that differences in ethnical background or differences in procedures of recruitment could influence in the differences observed among the different studies?

3- The scope of the present study is based in clinical and biochemical approaches for PA diagnosis. However, recent APA genetic advances must be included in the discussion section, maybe as a hypothesis for the difference of clinical score specificity across the different studies. In the present study PA is largely more frequent in females than males (table 2) and is known that somatic mutations in KCNJ5 are also more frequent in females. Could this represent a genetically bias between the derivation cohort and the cohort described in this manuscript?

4- In the discussion section, page 10, the authors suggested that the differences observed on AVS data among the present manuscript and the derivation cohort "may reflect differing definitions of a unilateral AVS or different definition of an adrenal nodule". This sentence is not clear. What are the “definitions of unilateral AVS or adrenal nodules” in the different cohorts? This point needs to be clarified.

5- Are there other clinical scores for the prediction of unilateral PA recently described? A description of these scores for comparison with the score used should be added in the discussion section.
Minor Essential revision

1- Table 1. This table reflects the score used in this manuscript but it was already proposed and described in a previous study. A reference of the original study must be added in this table.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests