Reviewer's report

Title: Clinical characterization of patients with primary aldosteronism plus subclinical Cushing's syndrome

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Reviewer: Rosa Maria Paragliola

Reviewer's report:

I read with interest the paper "Clinical characterization of patients with primary aldosteronism plus subclinical Cushing's syndrome" by Yasuda and coll. The topic is interesting, but I believe that the manuscript should be extensively improved.

I reported my comments below:

Page 5, line 14: The definition of Cushing syndrome is not correct. Please distinguish between ACTH dependent and ACTH independent CS and provide a better definition of SCS.

Page 5, line 31: please check again the mentioned paper and provide a better description of its content.

Page 6, line 37: It could be useful if Authors added information about the utility of AVS on the basis of current guidelines.

Page 6, line 40: This section is a bit confusing. In particular, the Authors have considered the results of high dose dexamethasone suppression test, specifying that "Test results were assessed in accordance with the diagnostic criteria advocated by the Japan Endocrine Society". However, the Japan Endocrine Society (reference 6) state that "we did not adopt a high-dose DST in the new criteria for SCS". Furthermore, can Authors add the interpretation of CRH test results for the diagnosis? Has adrenal scintigraphy been performed only for the diagnosis of SCS or also for PA in selected case?

Page 9, line 14: the section should be rephrased. Please better specify the diagnostic criteria of PA after AVS.

Page 12, line 1: The term "Hematology" is not appropriate in this context.

Page 16, line 5-8: "Of special note was the fact that the PASCS group involving both hyperaldosteronism and hypercortisolism did not show any greater increase in serum potassium concentration as compared with the PA group". This finding is very interesting and it should be better argued, also proposing physiopathological hypothesis.

Page 16, line 44: Please rephrase the sentence.
Other general comments:

The discussion section is substantially well written. However, the references are limited and the Authors often cite the same papers. I suggest to consult other papers about the topics debated (see especially page 17).

Data about BMD are lacking in this study. The Authors should add more comments about this point in the discussion section. The studies performed by Chiodini and coll. can be useful in this context.

Preoperative diagnosis of SCS is very important, in particular to establish the correct management and follow-up. I suggest to add data about the use of adrenal scintigraphy in the diagnosis of SCS, aimed to predict post-surgical hypoadrenalism.

(see Ricciato MP, WJS 2014).

The English language should be carefully reviewed by a native English speaker.

**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.

Unable to assess

**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 recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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