Reviewer's report

Title: Evaluation of the potential pleiotropic role of angiotensinogen gene polymorphism in atherosclerosis

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Reviewer: Wassim Y Almawi

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While the authors have responded to some of the comments raised in my first review, there are still some points that needs to be adequately responded to before I can say that the manuscript is ready for publication. I hope that the authors will take them in the right spirit.

Earlier point 1. "The is an association study, and does not address the functionality of the AGT variants with CAD and related traits. This must be reflected in both the title and body of the manuscript."

To which the authors responded: "We are not sure how we should reflect the fact that we do “not address the functionality of the AGT variants with CAD and related traits” in the title. It would be useful if the reviewer would make some concrete suggestion in this regard. However we have addressed in point in the Discussion.”

Critique: The title reads: Evaluation of the potential pleiotropic role of angiotensinogen gene polymorphism in atherosclerosis. My earlier point (which the authors misunderstood) points to the fact that the study does not address the role of the AGT variants, but rather their association with CAD and related traits. I suggest that the title be changed to: Association of the functional angiotensinogen gene polymorphism in coronary artery disease and related traits among Saudi subjects.

Earlier point 3. "Further to #1, and assuming that all participants were indeed Saudis, the authors must provide for the origin of the participants within Saudi Arabia. Were they all from the Riyadh area, or were from other country regions. If so, were the controls matched to cases with respect to their origin."

To which the authors responded: "If the study involved ethnic Saudis why would one have to match “with respect to their regional origin”, and how is this done anyway?"

Critique: I disagree with the authors on this point, and in fact insist that the authors adequately respond to this point. Saudi Arabia is a big country, and current inhabitants have unique ethnic backgrounds. Should the authors lack this piece of (crucial) information, they must address this in their discussion as a potential shortcoming.
Earlier point 5. "My main concern is the heterogeneous nature of the CAD cases. As such, Table 1 is of limited use as it is. I would like to see it altered to include the proportion of patients with specific CAD traits. For example, how many obese individuals had diabetes or hypertension? The same applies to the other traits."

To which the authors responded: "To our knowledge, it is very difficult and not necessary to have a homogeneous group of CAD. Indeed this would defeat the purpose of the study, which intends to discuss the possibility that CAD might constitute a product of such interactions with its disease traits. Furthermore, Table 1 portrays the populations (control and cases) of the various traits analyzed as the study is primarily about the interactions of individual traits with AGT as a cause for CAD. Besides, the constituent portion of CAD in each group is shown in Table 2c. Therefore, in our opinion, putting up a separate table simply to show these data values appears to be redundant."

Critique: It is the privilege of the authors not to respond to this comment, and it is my privilege not to accept their interpretation.

Earlier point 7. "The authors need to present biochemical profile of studied participants."

To which the authors responded: "We are not certain which variables should be presented and how, since we are discussing different disease traits. We have given the average values of some of the profiles (relative to CAD), such as BMI in Table 1, as we deemed necessary."

Critique: All what was required of the authors was to modify Table 1 to incorporate actual biochemical levels of key analytes, in particular serum glucose, lipid profile and kidney function tests. It is the editor’s decision to accept or not. I would have liked to see the raw data, which are more meaningful than the percentages cited in the table.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.