Title: The serum TGF-beta1 and Smad3 levels are closely associated with coronary artery disease

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Author's response to reviews: see over
Dear Editor,

We are submitting the revised manuscript entitled: "The serum TGF-beta1 and Smad3 levels are closely associated with coronary artery disease" (MS: 8302838081114067) again to BMC Cardiovascular Disorders.

We are very grateful to the reviewers for their thoughtful and constructive comments and suggestions. We followed their comments and suggestions carefully and have taken care of every comment and suggestion seriously. As such, what we have done are:

A, we have read carefully the manuscript and taken care of the English problems and this manuscript has been edited and proofread;
B, according to our experimental data, we have changed the Figures, Tables and main manuscript which are indicated in red.

Overall, when you read the current manuscript, you will find that it has been revised thoroughly. We certainly hope that the revision would make the manuscript acceptable.

If any concerns or questions, please contact Congxin Huang (huangcongxin@vip.163.com).

Thank you for your reconsideration.

Sincerely,

Congxin Huang
Reviewers’ Comments and Our Responses

Reviewer: Yvan Devaux

Comment 1: Study population. The control population significantly differs from the cases, in terms of age and cardiovascular risk factors. This should be indicated as a major limitation in the Discussion (not only in the Results).
Response: Although there is an age difference of about five years between the control population and CAD cases, the result should be acceptable to the epidemiologic study on CAD according to the previous reports (Schaan et al, 2007 and Tayebi et al., 2013), and furthermore CAD is mainly popular in the older people. As for the cardiovascular risk factors, they have been demonstrated to contribute to CAD occurrence, and hence they are different from the controls.

Comment 2: It is unclear why the authors compared the biomarker value of TGFB1 and Smad3 to that of Lpa, ApoA1 (...). Comparison with cardiac troponins and CK should be included, as well as statistical comparisons between the different AUCs (e.g. by the method of DeLong).
Response: Comparing with cardiac troponins and CK, the biochemical index, such as Lpa, ApoA1, SUA, BUN and TG, are used more extensively and have demonstrated to be related closely to CAD event.

Comment 2: The concluding statement that “serum TGFB1 and Smad3 levels may be more useful biomarkers than the currently used biochemical indicators” should be turned down.
Response: The sentence has been turned down.

Comment 2: Detection limits and accuracy of the ELISA used to measure TGFB1 and Smad3 should be mentioned in the Methods section.
Response: Detection limit of the ELISA used to measure TGFB1 was from 100 ng/l to 1200 ng/l, and the detection limit of Smad3 was from 2.5 pg/ml to 30 pg/ml. Their accuracy was both expressed in the correlation coefficient, which was required to be greater than 0.9999.

Comment 2: Legend of Fig 1 should contain information about statistical significance.
Response: The information has been added.

Comment 2: Fig 2 is not correctly referenced in the Result section. Also, showing different protein levels does not imply that the proteins “play important roles in the CAD pathogenesis”.
Response: The information has been added.
Response: We have changed the Figure 2 and the wording.

Comment 2: Group comparisons for P1 and P2 in Table 2 should be indicated as a footnote to the Table.
Response: Table 2 has been changed according to this comment.

Comment 2: Fig 4. AUCs of 0.68 and 0.71 indicate very modest biomarker value. The corresponding statement in the Results section should be tampered.
Response: We have changed the wording.

Comment 2: Finally, if data are available, investigation of the prognostic value of TGFβ1 and Smad3 would strongly increase the scope of the study.
Response: Thank you so much for the valuable suggestion from the editors and reviewers. In this present, we are carrying out the prognostic investigation.

Response: We have read carefully the manuscript and taken care of the English problems and this manuscript has been edited and proofread.

Reviewer: kai wang

Comment 2: It is highly recommended to observe the functional roles of TGF-β1/Smad3 in the development of CAD using SMC, endothelial cell or fibroblast cells.
Response: Thank you so much for the valuable suggestion from the editors and reviewers. We are studying the functional roles of TGF-β1/Smad3 in the development of CAD using human coronary arterial endothelial cells and smooth muscle cells.

Comment 2: There are a number of syntax errors and the English can be further improved. Such as P3 L18: “it is believed that its main signaling mechanism is linked to the Smad family”?
Response: We have read carefully the manuscript and taken care of the English problems and this manuscript has been edited and proofread.