Reviewer’s report

Title: Progression of coronary atherosclerotic plaque burden and relationship with adverse cardiovascular event in asymptomatic diabetic patients

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Reviewer: Emmanuel Akintoye

Reviewer's report:

Yang et al performed a retrospective analysis of 197 patients who underwent CCTA to evaluate the impact of coronary plaque progression on cardiac events in asymptomatic diabetic patients. Overall, they concluded that the CACS and change in calcium volume was inversely related to adverse cardiac outcomes; while low attenuation "lipid-rich", soft plaque volume was positively associated with adverse outcomes during follow-up.

While the authors need to be congratulated for performing such rigorous review and analysis, there are major concerns in the data that raises concern about the validity of their conclusion. One major concern is that the conclusion from this paper is contradictory to widely acceptable results of CAC. Large body of evidence have shown increasing CAC score or CAC progression to be a major predictor of future cardiac events (see BMJ. 2013 Mar 25;346:f1654; J Am Coll Cardiol. 2013 Mar 26;61(12):1231-9, Hypertension 46(1):238-43). Hence, the conclusion from the paper by Yang et al that CAC score or progression is inversely associated with cardiac event is surprising and deviates from the body of literature. In review of the methods presented by Yang et al, there are notable limitations in the data that could explain the unexpected result. One of such limitations is the very small sample size in group with CAC>10 (n=41). This might have created a form of selection bias that cannot be accounted for with statistical analysis. Also, the number of events is low (especially for group with CAC>10) to perform valid multivariable analysis. As a rule of thumb, for logistic regression, you are expected to have 10 events per each covariate in the model.

Therefore, internal validity of the analysis is a concern and, hence, conclusion/inference may not be justifiable

Minor points
Title:
The title does not seem consistent with the content as the outcome of interest was not captured. As it stands now, it seems coronary calcification (rather than adverse cardiovascular event) is the outcome. Suggestion: "Progression of coronary atherosclerotic plaque burden and relationship with adverse cardiovascular event in asymptomatic diabetic patients" will be a better title

Methods:
A more detail information on number of patients that were excluded and reason for the exclusion needs to be presented as this will provide more information into whether there is a selection bias that may explain the "unexpected" result of the analysis

The authors stated that patents were enrolled based on having a CCTA performed between 2011 and 2015, while follow up data were prospectively collected between 2017 and 2018. However, it is unclear what the authors did to information/events that occurred between 2015 and 2017. The commencement of follow up data needs to be clearly stated for the subjects

Stats:
"Univariable analysis was used to evaluate differences in continuous variables between the two groups" What statistical test was used? Univariate analysis is not a statistical test

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**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 am able to assess the statistics
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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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