Author’s response to reviews

Title: Development of a Risk Score to Identify Patients with Type 2 Diabetes Mellitus and Multivessel Coronary Artery Disease Who Can Defer Bypass Surgery

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27 December 2018

George Siontis, M.D., Ph.D.
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Dear Dr. Siontis,

Thank you for the follow-up comments of your reviewers regarding our manuscript "Development of a Risk Score to Identify Patients with Type 2 Diabetes Mellitus and Multivessel Coronary Artery Disease Who Can Defer Bypass Surgery" (DAPR-D-18-00021) for publication in Diagnostic and Prognostic Research. We have addressed the comments made by the reviewers and have revised our manuscript accordingly. Please see our responses in italics to the reviewers’ comments below.
Comments to Reviewer #1:

1. As mentioned in my previous review, the paper could benefit from a discussion translating the risk score to NNT or other decision analytic measures. While I appreciate the author's resistance, these are commonly used measures. Objections can always be discussed in the discussion and other decision analytic measures can be used such as the net benefit, which need not depend on a single arbitrary cut point.

   We appreciate the reviewer’s comments and have calculated the NNT for 5-year survival (12.5) and reported such in the results. We have added the following to the discussion:

   Specifically, among high risk patients the ARR of CABG versus IMT at five years is 8% giving an NNT of 12.5 which is well within the range of other accepted treatments of cardiovascular disease. However, the NNT is based on the five-year rate of freedom from death, MI or stroke and is calculated for an ‘average’ patient with a 0.35 risk for these outcomes. It would be the same value if the five-year event-free survival rates were 2% and 10% yet, from the patient perspective, the difference in frame of reference may be very significant. Thus, while the NNT is reasonable, it is simply a point estimate and the patient specific benefit will have much greater variability depending on the baseline risk and frame of reference.

   2. Also as mentioned previously, the use of the median as the only cut point seems a bit arbitrary. This decision needs to be supported and continuous methods and alternate cut points need to be examined, if only to show that the results don't change. Also, it is diminishing the richness of the dataset, in opposition to Frank Harrell's general principles.

   We appreciate the reviewer’s comments and have modified our reporting of the results to include Kaplan-Meier curves based on quartiles. As the reader can derive from visual inspection, the median appears to be the point at which the survival curves change.

Comments to Reviewer #2:

1. The authors adequately addressed most of my comments in their revision. One important issue that was not addressed is about reporting the model's calibration. In the methods section they mention that

   "The calibration slope was determined to assess agreement.". But I could not find any mention of this in the results. I think that calibration needs to be reported.

   We appreciate the reviewer’s comment and have reported the calibration slope in the results.
On behalf of the authors of this manuscript, we are extremely grateful for the thorough and professional review. We feel that by responding to the constructive comments, the manuscript has been significantly strengthened and we hope it will now meet your standards for publication. If I can provide any additional information or clarification, please do not hesitate to contact me.

Sincerely,

David L. Brown, MD