Author’s response to reviews

Title: N-Terminal Pro-B-type Natriuretic Peptide and Microsize Myocardial Infarction Risk in the Reasons for Geographic and Racial Differences in Stroke Study

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Author’s response to reviews:

Date: March 5, 2017
Fabrizio D'Ascenzo
BMC Cardiovascular Disorders

Re: Manuscript # BCAR-D-17-00264R1
Dear Dr. D’Ascenzo,

We are pleased to hear that our manuscript entitled: “N-Terminal Pro-B-type Natriuretic Peptide and Microsize Myocardial Infarction Risk in the Reasons for Geographic and Racial Differences in Stroke Study,” will potentially be accepted for publication in BMC Cardiovascular Disorders after we have sufficiently addressed the reviewers’ final two comments.

Please find our responses to the reviewers’ comments in the enclosed letter. We have answered them point-by-point and have incorporated the changes into the manuscript. In doing so, we hope that our study is now suitable for publication as an original research article in BMC Cardiovascular Disorders.

Sincerely,

Madeline R. Sterling, M.D., M.P.H. (on behalf of my co-authors)
Response to Reviewer #1:

“The authors have addressed most of my concerns. One more limitation of this study is that LVEF was not measured or adjusted for. Dilated (or hypertrophic) cardiomyopathy with elevated filling pressures often presents with mildly elevated Troponin levels (i.e., micro-MI) and BNP levels. Please list this as a limitation. Otherwise, I am ok with the revisions as is.”

We are pleased to hear that our revised manuscript addresses the concerns of Reviewer #1. We agree with her that a limitation of our study is that we did not have left ventricular ejection fraction (LVEF) data on the participants in this case-cohort design, and we have acknowledged this limitation in the Discussion section of the manuscript (last paragraph of page 13).

Response to Reviewer #2:

I thank the authors (Sterling et al.) for the chance to re-review their manuscript of NT-proBNP and its ability to predict MI in the community study known as REGARDS. Notwithstanding the still open question of how do you define adequately a microsize infarct, I am sufficiently satisfied that the authors have made a good response to my comments and I have nothing further to add other than...congratulations.

We thank Reviewer #2 for his support of our revised manuscript. With respect to ‘how you define a microsize infarct,’ we recognize that microsize MIs are only very recently recognized and little is known about these very small events, their risk factors, and ultimately, their prognosis. We hope that, when published, this paper will not only contribute to our emerging understanding of this new entity, but also lead to additional researchers studying this phenomenon. At this early stage of the science, we have proposed an initial definition that will undoubtedly be made more precise as additional data emerge. Our starting definition of microsize MI has been previously used in the literature by Safford et al (2013)(1) and is based on clinical practice as well as an analysis of troponin assay 99th percentiles and 10% CV levels available on the International Federation of Clinical Chemists website.1 The level of 0.5 µg/L both corresponds to a commonly used clinical cutoff as well as a level higher than any commercially available troponin assay’s 10% CV level in use at the time of this study(2).

Nonetheless, we have made additional edits to the Methods section to more fully clarify the concept of microsize MI.

Final Note to the Editor:

We have taken the liberty of making a few grammatical changes to the manuscript, which are shown in the ‘Track Changes’ file.
Additionally, we have adjusted some of the EndNote citations to follow grammatical rules.

Finally, a few changes in author affiliation(s) on the title page (as shown by the superscripts) have been made; these changes occurred after the paper was submitted to BMC Cardiovascular Disorders in May of 2017.

Again, we thank you for allowing us to resubmit our paper and hope that we will see it in print in BMC Cardiovascular Disorders soon.

References
