Author's response to reviews

Title: Flow Mediated Dilation of the Brachial Artery: An Investigation of Methods Requiring Further Standardization

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Author's response to reviews: see over
Dear Dr. Saltman:

We are pleased to re-submit this manuscript entitled “Flow Mediated Dilation of the Brachial Artery: An Investigation of Methods Requiring Further Standardization.” We have revised the manuscript in response to the excellent comments from the reviewer.

The specific response follows the reviewer’s comments, in a point-by-point fashion below.

Please contact me with any questions.

Respectfully,

Alon Peretz, MD, MHS

Reviewer 3

In the results section the second paragraph indicates the diameter for 37 sessions with proximal cuff and 25 with distal is 3.8 and 4.2 respectively. I am assuming that this is because more subjects were tested in the proximal, so that is a subject pool with additional subjects that likely are on the small side in terms of artery. This needs to be clarified.

We thank the reviewer for the observation made and agree about the importance of clarification of this point.

If the distal cuff population was a subset of the proximal, then it seems imperative that the data be analyzed in terms of only those subjects that received both. Excess variability in the proximal cuff condition may be because of the obviously different additional subjects.

We would like to clarify that the distal cuff population is not a subset of the proximal. As addressed in the methods of the manuscript, part of our study population was evaluated with both distal and proximal occlusion, while another part was assigned to either proximal or distal occlusion. In our analysis of test repeatability, we accounted for the correlation between distal and proximal comparisons done on same subjects, using a generalized estimating equations (GEE) approach. The difference in artery diameters is identical when the analysis is limited to the subjects who received both distal and proximal occlusion. This information has been added to the paper.

Of course, if I am wrong and the number of subjects receiving both was the same, then I assume some subjects received additional scans with the proximal cuff.

We greatly appreciate the reviewer’s important observation. The explanation for the difference in artery size is likely due to the different protocol for artery identification and
localization used in the proximal versus distal approaches. Due to the cuff location on the upper arm, the artery is imaged in a more distal location when the cuff is located proximally than when it is imaged more distally. To reduce confusion, we have added a relevant paragraph to the methods section of the manuscript, and addressed the potential transducer site effect in the results section.