Author's response to reviews

Title: Brachial Artery Flow-mediated Dilation Following Exercise with Augmented Oscillatory and Retrograde Shear Rate

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To Whom It May Concern:

Please accept the revised manuscript, “Brachial Artery Flow-mediated Dilation Following Exercise with Augmented Oscillatory and Retrograde Shear Rate.” We wish to thank each of the reviewers; Dr. Ferguson and Dr. Bruno, for their timely and insightful reviews which have improved this manuscript. We have addressed each of their concerns below.

Reviewer #1: Dr. Richard Ferguson

Major Compulsory Revisions
1. Methods, Paragraph 2 – Experimental design.
   This point has not influenced my decision on acceptance, but it certainly needs addressing. It is just a bit more than a minor revision! The experimental design is not well described and quite hard to follow, despite apparently being quite a straightforward design. There are obviously 4 experimental conditions: 20%, 40%, 60%, 60%+VitC. The way this section is written is rather confusing and is confounded by the different doses of placebo and VitC (500 or 1000mg). I am assuming consumption of the 1000mg placebo was because the VitC capsule happened to be 1000mg. This section needs re-organizing to make the design more clear.
   Thank for recognizing this confusing paragraph within this section. Each subject consumed a total of 1000 mg of sucrose or vitamin C prior to each exercise session. We have re-organized this section to improve the clarity.
2. Results.
   It might be a specific requirement of the journal but the textual commentary of the results are long and laborious, and it is often difficult to “see the wood for the trees”. The figures do help although I am confused as to why the 60% and 60%+VitC are presented on a separate figure. On the basis from the experimental design there are 4 conditions; 20%, 40%, 60%, 60%+VitC, it appears that the 60% data is being presented twice. Would it not be simpler and more appropriate to have all 4 conditions on the one figure? Or have I misinterpreted the experimental design?!
   We have substantially shortened the text in the results section with a focus on the pertinent information and we have expanded table 2. We agree with Dr. Ferguson that having the 60 mmHg condition represented twice is repetitive. We initially thought that having two distinct sets of graphs would highlight the comparisons that were made. We have now consolidated the graphs into two figures.
3. Discussion, paragraph 2 and 3.
It strikes me that much of the discussion is focused on the fact that greater doses of retrograde shear do not induce a greater impairment of FMD. This is logical and fair enough. However, one could look at it the other way round in that a rather minimal “dose” of retrograde (i.e in the 20% condition; approx. 100 to 110 s\(^{-1}\) in control and cuffed arm respectively), induces quite a substantial impairment of FMD, even with the overriding antegrade shear being present. I wonder if the authors could comment on this observation, if appropriate.

This is great observation and one we have overlooked. We have now added a short discussion on this topic.

Minor Essential Revisions
1. Methods, paragraph 2 – Experimental design
Please indicate, with an average or range, the number of days each exercise session was separated by.

This is now included in the methods section.

Discretionary Revisions
1. Methods, paragraph 1 – Subjects
It is perhaps more common to provide the subject characteristics here. They are currently provided in the Results, paragraph 1.

In line with our previous work in Cardiovascular Ultrasound, we have chosen to keep the subject characteristics in the results section.

Reviewer #2: Dr. Rosa Maria M Bruno

Minor discretional changes
Results section is quite redundant. We suggest to put p values #2 in tables.

We agree with Dr. Bruno and we have substantially shortened the results section and expanded table 2.

Discussion can be shortened and simplified, in particular the part about lack of proportionality between FMD impairment and increased retrograde shear rate, which should be more succinctly explained by unchanged oscillatory shear rate.

Based on previous results by Thijssen et al., we felt that lack of proportionality between the decrease in FMD and increased retrograde shear is an important topic to include.

Once again, we thank the reviewers for their time and effort in reviewing our manuscript. Thank you for considering our revised manuscript for publication in Cardiovascular Ultrasound.

Sincerely,

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