Author's response to reviews

Title: Serial exercise testing in children, adolescents and young adults with Senning repair for transposition of the great arteries

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Author's response to reviews: see over
POINT BY POINT RESPONSE TO THE CONCERNS RAISED BY THE REVIEWER

Thank you for the article; overall I think the study is well done, with strength of following patients over time rather than performing a cross-sectional study. The primary finding of decreased exercise ability with increasing age in Senning patients is not surprising, but still an addition to the body of literature. Overall I think the Introduction, Methods and Results sections are well done and only require minor changes. I think the discussion could be improved more substantially prior to publication.

We would like to thank the reviewer for his interest in our work and his positive feedback. We are also grateful for the opportunity to submit a revised version of this manuscript to BMC cardiovascular disorders.

Major compulsory revisions:
Overall I found the discussion somewhat difficult to follow. I think it needs to be reorganized. After the brief summary of findings in Discussion paragraph 1, which is fine, the discussion turns to the decline in exercise capacity with age.

We took into account the suggestions of the reviewer and entirely rewrote and reorganized the discussion part of our manuscript. In order to do so, we changed the structure of the discussion according to the proposition of the reviewer.

This can be divided as follows:
1. I would like more focus on the question of why exercise capacity would decrease more rapidly in this patient population relative to controls. Do you believe it is all about RV contractility (noting that the R2 value of the correlation was only 0.25) or other factors about this population? My opinion is that this section should be the primary focus of the discussion. I would include here discussion about the changes seen by echo in the RV over time and more about how that may relate to exercise function. I would note, however, the limitations of echo in assessing RV function as well as size (see Lai WW et al. Int J Cardiovasc Imaging 2008;24(7):691-8.; although the population is not the same, I think still relevant).

We agree with these comments of the reviewer and focused more strongly on the RV acting as the systemic ventricle in the first part of the discussion. In the limitations section, we emphasized on the limitations of cardiac ultrasound for the assessment of RV function.

2. The issue of changes only found in children/adolescents in this manuscript, and how that agrees or contradicts with the literature already published. I think the quality of your data is good, and can be defended more strongly relative to the findings of Budts et al and Reybrouck et al. However, I would note that when you subdivide your population, the n becomes quite limited. I think it is quite likely that the reason you don’t see a statistically significant change in the exercise measures in adults is simply limited power with only 16 patients.

We added a sentence on the fact that we might lack statistical power to show a significant change in our older age group.

3. Next is discussion about the role of the right ventricle in the findings, with comparison to Fontan patients. I don't think this is a strong comparison, given all the complexities of the Fontan circulation and multiple reasons that those patients have poor exercise capacity. I grant you the reference to worse performance in RV Fontans, but I still think this comparison is limited. I would suggest instead focusing these comments on issues with a systemic RV and
incorporating that into the earlier section (see 1).

*We did take this into account and left this paragraph out of the discussion in order to avoid confusion and keep our focus on the shortcomings of the right heart for supporting the systemic circulation.*

4. The idea of reduced exercise related to lack of physical activity is a distinct thought, which can then stay where it is located in the discussion.

*We did not make any changes on this paragraph.*

5. The final paragraph of discussion is about further decline in exercise capacity in adults as they grow older, related to RV function again. I think it works to finish with a more speculative note about patients growing older; I just had a little trouble following the paragraph, would suggest rewording.

*In agreement with the reviewer, we slightly changed the content of this paragraph by rewording it and being more speculative towards the future of this group of patients.*

Minor Essential Revisions: These are very small language changes:

*We thank the reviewer for his effort to suggest minor changes for further improvement of our manuscript and we took into account all the following points for minor revision.*

6. I would change "impossibility" to "inability", regarding increasing stroke volume. This is in abstract conclusions, and discussion paragraph 5 and conclusions

7. Background paragraph 1- instead of allows normal LV function, suggest allows for a systemic LV.

8. Results paragraph 1- missing word "ranged" between 13 and 29 years.

9. Results under echocardiography - should be table 2, rather than table 3

10. Under limitations, would add that different exercise modality is used for the children and the older patients