Reviewer’s report

Title: Autonomic nervous system response to remote ischemic conditioning: heart rate variability assessment

Version: 0 Date: 16 Jul 2019

Reviewer: Eduardo Migliaro

Reviewer's report:

Osorio and colleagues present a reasonably well written paper on the autonomic effects of RIC as measured by heart rate variability. Overall there appears to be an increase in SD2, marked in the older cohort, as a consequence of RIC. I have several comments to make:

Abstract
Methods and results are mixed
SD2 not defined
Poor grammar in the first line of the conclusion
The final sentence in the conclusion cannot be justified from this study

Background

No specific comments

Methods

Is there a power calculation? What was the intended primary outcome and how did you come to the numbers needed to study. If a pilot study and not calculable then please state.

How were the recruits selected should come earlier (inclusion & exclusion criteria)?

Results are presented early in the methods section

Any exclusion based on drugs that are known to interact with the autonomic nervous system, or affect RIC?

Please reference line 22 on page 7 "During aging...."; and does this paragraph belong in the methods?

What were the conditions for each participant. Were they fasted? Time of day? Were they rested in a quiet room, free from distraction? Did they take their usual medications?
ECGs were taken at 5 minute intervals from -10 minutes up to 45 minutes (10mins post the final cuff deflation. This protocol does not allow assessment of any delayed effects - which can be seen up to 2-3 hours post RIC, and in a 'second window of protection (SWOP)' 24 hours later. The authors make some comment to this in the discussion.

Results

Footnotes in the table would be useful for the definitions of the various parameters

Please quote the statistical tests used for the correlation studies

Can you provide the summary baseline characteristic of the participants/cohorst in a table, including co-morbidities and drugs

Discussion

The results are reasonably well discussed. The influence of other cardiovascular disease and risk factors is not discussed, in particular the confounding effects of DM.

Any confounding from the degree of discomfort influenced by the volunteers. Any pain scales recorded that could be used to correlate? Conditioning in other forms exists too (including surgical incision) - i.e. this may not be a phenomenon due to limb reperfusion and release of a chemical messenger, but simply due to infliction of discomfort.

There is a degree of uncertainty in the literature regarding which HRV parameters are important as a surrogate marker for CVD. This warrants discussion.

Please be clear on the limitations of your study

References

these are repeated twice in error

Figures

Is Figure 1A necessary?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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