Reviewer's report

Title: High-intensity interval training and moderate-intensity continuous training in adults with Crohn’s disease: a pilot randomised controlled trial

Version: 0 Date: 19 Oct 2018

Reviewer: Jessica Elia

Reviewer's report:

General Comments:

Strengths:

1. This study investigates the impact of aerobic exercise in the Crohn's population. Well designed, objective IBD exercise studies including standardized physiologic and inflammatory outcome measures are lacking and needed.
2. This study includes a wide array of objective measures.
3. This study includes supervised exercise and a suitable follow-up period.

Weaknesses

1. The methodology of this study is unclear. Study subjects were "invited" to participate in supervised exercise sessions. What were the instructions exactly? Was there a mandatory minimum the subjects were expected to complete? Were the subjects allowed to exercise outside the supervised sessions? What were the instructions after the initial 12 week supervised sessions? Were subjects expected to continue independently or was continued exercise optional?
   a. Methodology should also include what the HIIT subjects performed between intervals.
   b. HIIT subjects defined RPE as "hard." HIIT is defined as "all out" or "extremely hard." Should this be redefined as "modified HIIT" as heart rate is unreliable in IBD subjects due to dysautonomia?
2. This study does not provide all objective data collected with analysis. Were the changes seen from baseline, 3, and 6 months statistically significant? Where is the FS data for pre, post, and 10 minutes post exercise (as stated in previously published pilot)? For example, based on Table 3, fatigue scores for both HIIT and MICT patients increased from baseline to three months. Were these changes statistically significant? Fatigue and over fatigue following exercise is a concern in IBD subject exercise prescription and should be addressed. Please address all results (including biomarkers, these are important
for disease inflammation, especially given adverse events) numerically as well as with interview results.

3. Safety is a concern.
   a. HITT: Consider that this study population consisted of stable, no or low-inflammation, few co-morbidity, Crohn's patients; a large percentage of whom were in employed. This is a high functioning group. This study does not include a threshold for patient safety acceptability. 3 adverse events occurred during HIIT training with 2 subjects. 2/13 subjects (15%) experienced adverse effects of headache, dizziness, and vomiting. IBD subject safety issues stem from physiologic concerns of dehydration, fatigue/over fatigue and autonomic dysfunction.

1. Once a subject had an adverse outcome, was removal from the study considered? Was subject removal from the study considered after the second adverse outcome? Were steps taken to prevent another episode?

2. This should be addressed in the discussion. Add to this number a disease flare in the follow-up period, 3/13 (23%). Either way this is not a safe intervention for IBD subjects. It may be cautiously considered for a high-functioning sub-population of IBD subjects under close supervision, but re-thinking a pre-training period to establish a baseline of athletic suitability should be considered.

b. MICT: 1 disease flare in the follow-up period. Moderate aerobic training has been shown to prevent flares in CD. 1/12 should be considered. Is this an anomaly? Was training too regimented/difficult? Would a range of RPE depending upon subject daily sx be a better strategy?

Additional Comments:

1. "...groups were offered..." Page 3, Line 35 Were the subjects offered supervised exercise? What were the instructions? Minimum number required? Supposed to attend all three? What were post 12 week instructions? Encouraged to continue? Instructed to continue? Please clarify.

2. EXACT follow journal style for abbreviations, write full length meaning first. Page 4, Line 79

3. "...cycle ergometer..." Page 6, Line 127 Clarify lower body cycle ergometer

4. Page 6, Line 127-130 Clarify performance of HIIT participants between intervals

5. "RPE-C, RPE-L" Page 7, Line 133 please define terms
6. Borg Scale Page 7 Initial Pilot stated Borg Scale 6-20, please state clarification

7. "encouraged to continue" exact language please. instructed to continue? What was the expectation? Page 7, Line 138

10. Please include all trial data, biomarker data speaks to disease inflammation. This is an important component of the study.

   a. Please include statistical analysis of all data results, cannot evaluate results without statistics.

   b. It appears the subjects became more fatigued with the exercise program and less fatigued after it was over...is this significant?

   c. Were the ventilation or peak oxygen changes statistically significant compared to controls or between groups?

   d. Please provide same for body mass, waist circumference, resting heart rate, etc. in addition to interview comments

10. HITT subjects RPE "hard" is this really "HIIT"? Page 12, Line 269-275

11. Figure 1 Please clarify 2 subjects with disease flares on follow-up, difficult to discern

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**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.

I recommend additional statistical review
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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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