Author's response to reviews

Title: Using cardiorespiratory parameters to assess functional impairment after knee anterior cruciate ligament reconstruction: a cross-sectional study

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Author's response to reviews: see over
Ms. 1170127068102985 BMC Musculoskeletal Disorders

Title: Cardiorespiratory responses to exercise are useful for muscular functional impairment characterization after knee anterior cruciate ligament reconstruction: a cross-sectional study

19-Feb-2014

Dear Dr. Catia Cornacchia

Executive Editor

BMC Musculoskeletal Disorders

We thank you for the opportunity to resubmit a revised version of the original manuscript. In addition, we thank the three reviewers for their constructive comments and insightful observations. We have made a number of extensive revisions and considerably improved major sections of the paper (highlighted in red in manuscript). Furthermore, we feel we have addressed all the reviewers' concerns in our revised manuscript and we have provided a detailed point-by-point reply to their comments. We believe that the revisions suggested by the reviewers have significantly improved the manuscript and hope it is now suitable for publication in BMC Musculoskeletal Disorders

Reviewer's report

Title: Cardiorespiratory responses to exercise are useful for muscular functional impairment characterization after knee anterior cruciate ligament reconstruction: a cross-sectional study

Version: Date: 30 January 2014

Reviewer: Shahril Shaarani

General

1. Is the question posed by the authors well defined?
   Yes.

2. Are the methods appropriate and well described?

   How was the sample size calculated?

   Answer: Sample size calculation has been included as requested by the reviewer (Page 6, lines 121-124).
How was patient selected?

**Answer:** This information has been included as suggested by the reviewer (Page 4 lines 86-87).

The study states the patients are physically active. The use of an activity level score would be useful.

**Answer:** This information has been included as suggested by the reviewer (Page 4 lines 85-86).

The addition of a control group with healthy subjects would increase the value of this research.

**Answer:** We partly agree with the reviewer, since we compared characteristics of the same patient before and after the experimental procedure, we believe that a control group is not necessary. In addition, it is unlikely that a healthy and physically active person would be willing to participate in the study, because that would mean reducing their level of physical activity to the same level as the experimental group. We should also consider ethical issues: the inclusion of a control group would bring healthy subjects into the clinic during opening hours which could result in less time being made available to actual clinic patients.

Was there any reason to test patients at 2 months?

**Answer:** Yes, there was. It was the earliest point during the rehabilitation phase that the patients reported no pain that could influence the test results.

What is the standard physiotherapy protocol in this research institute post ACL reconstruction? Are all patients compliant with it?

**Answer:** The standard physiotherapy protocol used in this study is described below. We chose not to include the entire protocol in the paper because we believe that this long and specific information does not add to the purpose of the study. All patients were compliant with the protocol.

**Week 1:**
- Straight leg raise exercises (lying, seated, and standing), quadricep/adduction/gluteal sets, gait training.
Well-leg stationary cycling, abdominal exercises and upper body conditioning.
Soft tissue treatments to posterior musculature, retropatella and surgical incisions.

Weeks 2 - 4:
Continue with pain control, gait training, and soft tissue treatments.
Incorporate closed-chain exercises (i.e. mini-squats, modified lunges, short step-ups) between 20°-70° OR in full extension. Avoiding going into the last 15°-20° of extension avoids stress onto the repair.
Aerobic exercises consisting of well-leg stationary cycling, and upper body weight training.

Weeks 4 - 6:
Leg weight machines (i.e. light leg press, calf raises, abduction/adduction).
Add hamstring curls without resistance.
Stationary cycling initially for ROM, increasing as tolerated.
Patients should have full extension and 110 degrees of flexion by the end of this period.

Weeks 6 - 12:
Increase the intensity of functional exercises (i.e. add a stretch cord for resistance, add weight).
Introduce resistive hamstring curls.
Add lateral training exercises (i.e. lateral stepping, lateral step-ups, step-overs).

Weeks 12-16:
Progress to running as able to demonstrate good mechanics and appropriate strength.
Begin to incorporate light sport-specific training.

Weeks 16-24:
Incorporate bilateral jumping and bounding exercises, making sure to watch for compensatory patterns and any signs of increased load onto the knee with take-offs or landings.
Was the testing done with patient supine or upright? There are studies to suggest differences in heart rate and VO2 in differences in position.

**Answer:** The tests were done with patients in an upright position. This information has been included as suggested by the reviewer (Page 5 line 102).

Are there any statistical differences between the baseline characteristics of the patients?

**Answer:** Considering that we compared the physiological variables of the involved vs. non-involved limb, there are no baseline data.

Statistical methods is adequate. However the sample size calculation is needed.

**Answer:** Sample size calculation has been included as requested by the reviewer (Page 6, lines 121-124).

Results section should be expanded to include data from table.

**Answer:** We included the percentage of change of each measured variable. (Page 6 lines 135-137). The absolute values were not included in the Results section as they were already shown in Table 1.

Abbreviation of FC in Table 1 is not documented

**Answer:** We corrected this abbreviation in Table 1 as requested by the reviewer and included all abbreviation meanings in the Table legend.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

The discussion need to expand on different testing methods in the early phase of ACL reconstruction – functional, radiological and genetic markers.

**Answer:** The discussion has been expanded as suggested by the reviewer (Page 7 lines 150-160 and page 9 lines 203-214).
In the paragraph starting from line 165, the author suggests only heart rate to assess functional status of the involved limb. The heart rate response to exercise is influenced by several factors. This paragraph needs more clarity to argue for this point.

**Answer:** This paragraph has been rewritten as suggested by the reviewer (Page 8 lines 187-192).

In Line 170 the authors correlate their findings with quadriceps weakness. As with the previous comment, this point needs to be supported with references.

**Answer:** This paragraph has been rewritten as suggested by the reviewer (Page 8 lines 187-192).

6. Are limitations of the work clearly stated?

No. This has to be included into the manuscript

**Answer:** Limitations were included as requested by the reviewer (Page 10 lines 216-222).

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

Yes

8. Do the title and abstract accurately convey what has been found?

Yes.

9. Is the writing acceptable?

The manuscript requires considerable revision for grammar and scientific context. Examples include:

-Line 61-62 – The sentenced should be changed to “A safe method to assess exercise efficiency without increasing ACL graft load is required in the immediate postoperative phase”.

**Answer:** The sentence has been changed as suggested by the reviewer (Page 3 Lines 60-62).

-Line 70-73 – This sentenced should be simplified and incorporated into the next
paragraph.

**Answer:** The sentence has been changed as suggested by the reviewer (Page 3 lines 69-72).

In addition, the manuscript was revised by a native English speaker.

Line 76 – “constant absolute power output” could be changed to “a constant submaximal intensity”. This will need to be throughout the manuscript.

**Answer:** The change has been made as the reviewer indicates (Page 4 Line 76 and Page 7 line 163).
Reviewer: Taís Malysz

Discretionary Revisions:
Line 9-10: I think that the authors could exclude the citation “(Cascio, Culp, & Cosgarea, 2004)” from the abstract.

Answer: The citation has been excluded from the abstract as suggested by the reviewer.
Reviewer: Fábio Minozzo

- Minor Essential Revisions
The article is interesting, although sometimes not so clear. I think some points should be clarified before recommending it for publication:

1- I understand the MS is about assessing the cardiorespiratory parameters of patients who underwent ACL reconstruction. However, I think the main goal stated by the authors, “verify whether the cardiorespiratory responses to lower limb exercise display counter-lateral differences, and if they could be used to assist athletes and health professionals in the rehabilitation programs” is a bit confused and, at the same time, too broad. The first part of the sentence is ok, but how could this assessment help these professionals in practice? Furthermore, why is assessing strength deficit not enough? The authors must agree that not everybody has a metabolic cart, while muscle strength is easier and more affordable.

**Answer:** First of all, we would like to thank the reviewer for their comments. In fact, some strength tests may be easier to do than a cardiopulmonary test, however maximal strength test, especially maximal quadriceps contraction, should be avoided in the initial phases after ACL reconstruction, because it may compromise the integrity of the ACL graft. In this context, cardiorespiratory responses to exercise represent an alternative and objective method of functional capacity evaluation of the lower limb. The results of our study could help health professionals since differences between limbs indicate difference in functional status of the limb. Thus, it is desirable that at the end of the rehabilitation procedure such differences disappear.

2- I have the impression that similar studies have been performed: several classic studies such as Astrand’s, Ekblon’s, Sargeant’s, and many others have posed similar, but not identical, research questions. In other words, as far I am concerned the results presented were expected somehow. However, I am not an expert on the matter, and since I few more comfortable with biophysics I would ask (recommend) the authors to better explain the novelty of their study. They have all the material needed, several studies were already cited... So, perhaps, they
only need to emphasize what is new in a clearer way for the researchers that are not exactly from their field.

**Answer:** Previous studies have shown that there are exacerbated metabolic and cardiorespiratory responses when dynamic sub-maximum exercise with the same absolute intensity were performed with a smaller muscular mass. However, these findings were demonstrated comparing very different muscular mass, such as: arms with legs, or one with two lower limbs. In our study, we were looking for cardiopulmonary differences to exercise performed by involved and uninvolved lower limbs after a surgery, therefore the muscular differences were not very big, but if the hypothesis was confirmed, it could contribute to the development of an easy and inexpensive rehabilitation monitoring protocol, with physiological bases, which may show the patient’s evolution within the first months of rehabilitation after ACL reconstruction, taking the non-involved limb as reference.

A better explanation has been included in the Introduction, and clinical implication has also been included in the paper (Page 3 lines 69-72 and Page 10 lines 232-238).

3-In the first paragraph of the discussion the authors try to link the investigation of the cardiorespiratory parameters and their importance for rehabilitation programs. Although I think this point is extremely important, the authors fail to justify why and how such parameters could be used during rehabilitation. I suggest that either the authors drop this point, turning their paper merely into a individual-limb-cardio-respiratory characterization of ACL reconstruction patients, or specifically explain how to use these parameters during a rehab program.

**Answer:** We rewrote the first and second paragraphs of the Discussion as suggested by the reviewer.

4- At the end, the authors explore the fact that HR was exacerbated when the affected limb was tested... So, is the relationship between VO2, power output, and HR really broken? How large is this effect? Furthermore, these are only punctual values taken after 5 minutes. I was curious to know the entire behaviour of such parameters throughout the exercise. In other to asses “running economy”, the authors should have taken into account the 5-min-parameters’ behaviour instead.
Answer: Indeed, there is a relationship between VO2, power output, and HR, however, this relationship is valid as we analyzed the same condition (e.g. same subject, same limb as is the remit of this study). It is widely recognised that an exercise performed by a small muscle mass may present with a ventilatory response which is excessive to the actual metabolic demand (i.e., increased $\Delta VE/\Delta VCO2$ (Clark et al. 1992), although the exact mechanisms underlying this phenomenon are still debated (Clark 2006). Piepoli et al. (1996) argued that afferent stimuli from the appendicular skeletal muscles play a major role in modulating the hyperventilatory response to exercise. More specifically, they postulated that overactivation of unmyelinated group IV muscle afferents (metaboreceptors) stimulates systemic sympathetic drive and ventilation to provide more well-oxygenated blood to the working skeletal muscles (the “ergoreflex”; McCloskey and Mitchell 1972; Rotto and Kaufman 1988). Therefore, it is possible that the same absolute exercise performed by the lower limb with lower functional capacity (postsurgical) overactivates metaboloceptors, producing higher cardiopulmonary responses.

5- The statistical analysis seems to be adequate, but I would like to know why two genders were used. Also, why did authors use only 2 women and 7 men? Wouldn’t that be better if only men or women were used? Since the number of women is only two, any interaction between the variables and gender is already compromised.
Answer: As requested by reviewer #1, we included the information about sample size calculation. Regards to gender, there is no significant effect of gender on physiological responses to exercise.

6- Finally, the language is not completely appropriate, although the MS is mostly clear, it is only fair to middling written. I made some grammar corrections, but since I am not a native English speaker myself I would suggest the authors to proof-read it with someone who is not only English-native speaker, but also is used to research papers.
Answer: The manuscript was revised by a native English speaker.
Ln 2-4 – I think the title is a bit confuse I would suggest “Using cardiorespiratory parameters to assess functional impairment after knee anterior cruciate ligament reconstruction” or something similar. At least I would avoid the use of “are useful for”, that sounds awkward.
Answer: Title was modified in accordance with the reviewer (page 1, lines 2-3).

Ln 8 – replace surgery with surgical; drop “in order to” ; replace previous with original
Answer: We replaced surgery by surgical and previous by original.

Ln 10 – “…there is no agreement in relation to a…”(sounds better)
Answer: We changed this in accordance with the reviewer.

Ln-11-13 – Consider reviewing the whole fragment (How does ACL affect metabolic? In which context?)
Answer: The sentence was rewritten in accordance with the reviewer.

Ln-14 - …study was TO verify
Answer: We changed this in accordance with the reviewer.

Ln- 16 – drop “the”
Answer: The word has been dropped as suggested by the reviewer.

Ln 17 – this instead of “these” (it is singular)... Fragment is also awkward
Answer: The word has been dropped as suggested by the reviewer.

Ln-18 – drop “it”
Answer: The word has been dropped as suggested by the reviewer.

Ln-51- quickly and as safely – drop this “as” – quickly and safely
Answer: The word has been dropped as suggested by the reviewer.

Ln-52 – replace consensus with agreement
Answer: We changed this in accordance with the reviewer.

Ln-53- ...in relation to a... instead “regarding”
Answer: We changed this in accordance with the reviewer.

Ln-55- replace “since” with “because” and drop the coma
Answer: We changed this in accordance with the reviewer.

Ln-58 – link this paragraph with the previous – they must be a single paragraph
Answer: The paragraph has been linked as the reviewer indicates.

Ln-61 – Another way to test strength (or whatever you think) applying lower tension on... (sounds better)
Answer: We changed this in accordance with the reviewer.

Ln-62- replace “would be” with “could be”
Answer: We changed this in accordance with the reviewer.

Ln – 99 – replace “In day” one with “On the first day”
Answer: We changed this in accordance with the reviewer.

Ln -103 – same – Same as above: “On the second day”
Answer: We changed this in accordance with the reviewer.