

## **Inspiratory muscle training and functional capacity following coronary artery bypass grafting in high-risk patients: A pilot randomized controlled trial**

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Handling editor:

Michal Heger

*Department of Pharmaceutics, Utrecht University, the Netherlands*

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Review timeline:

Received: 24 October, 2021  
Editorial decision: 7 January, 2022  
Revision received: 4 February, 2022  
Editorial decision: 10 February, 2022  
Revision received: 16 February, 2022  
Editorial decision: 18 February, 2022  
Revision received: 19 February, 2022  
Editorial decision: 26 March, 2022  
Revision received: 11 April, 2022  
Editorial decision: 11 April, 2022  
Revision received: 26 April, 2022  
Editorial decision: 1 May, 2022  
Published online: 17 June, 2022

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1<sup>st</sup> Editorial decision

07-Jan-2022

Ref.: Ms. No. JCTRes-D-21-00178

**INSPIRATORY MUSCLE TRAINING ON FUNCTIONAL CAPACITY SUBMITTED TO CORONARY ARTERY BYPASS GRAFTING WITH HIGH RISK FOR PULMONARY COMPLICATION: RANDOMIZED CONTROLLED CLINICAL TRIAL**

Journal of Clinical and Translational Research

Dear Dr Cordeiro,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Feb 06, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: I thank the authors for their time spent drafting the manuscript, my main comments are regarding the trial methodology as currently reported in the manuscript. I provide the following comments which I feel need to be addressed:

My main comment is that this manuscript needs to be revised so it is clear that this is a pilot study. The absence of a power calculation and a sample of 29 means it is likely the trial is underpowered to detect a significant difference between groups for the primary outcome (6MWT). The manuscript should be revised to report on the feasibility of delivering the intervention in this high risk group of patients, with effectiveness outcomes as secondary outcomes.

Title:

Please include the word 'pilot' in the study design. The title could be improved by some revisions 'Inspiratory muscle training and functional capacity following coronary artery bypass grafting in high risk patients: a pilot randomized controlled trial'

Introduction:

- heading of this section is not in English
- the knowledge gap is well identified

Methods:

- Eligibility - could participants have COPD of any disease stage/severity?
- Eligibility - sex/gender mentioned twice - please retain 'both sexes' only
- Eligibility - how was 'difficulty in understanding the imposed techniques' assessed? Was a validated measure of cognitive function used?
- Was group allocation concealed?
- Was the trial registered (prospectively/retrospectively)?
- Were CONSORT guidelines followed in the conduct and reporting of the trial?
- Further detail regarding the randomisation process is required - it is not clear how the balls

were used to randomize participants.

-P6 line 5-6 - not in English

-Who delivered the intervention? What was their background, experience and were they provided with any training in the intervention protocols?

-I would encourage the authors to adhere to the TIDier guideline of intervention reporting to improve the ability to replicate the intervention delivered.

-Was the training load progressed beyond the 40% of MIP prescribed at baseline? If so, how was this achieved?

-Was the examiner who completed the outcome assessments blinded to group allocation?

-Were two 6MWT performed as per the ATS guidelines (i.e., were participants allowed a practice test to allow for familiarization effects)?

-Was a validated measure used to assess post-operative complications (POMS, Melbourne Group Score)?

-Both groups received usual care - it is important to describe in the manuscript what pre and post-operative usual care was at the recruitment hospital during the study.

-How was the sample size of 29 determined? Was a power calculation performed? It is very possible that the lack of between group differences you observed for many outcomes was due to a lack of power rather than a lack of effect of the intervention.

-Please explain why the 6MWT was chosen as the primary outcome.

## Results

Did all 14 intervention participants adhere to the IMT intervention protocol as prescribed?

## Conclusions

Are the studies by Cordeiro and Zanini that you refer to also of IMT interventions? Further details are required. What differences were there (if any) between your intervention protocol and previously published?

Is there enough time in the pre-operative period to commence training as you suggest?

Further work is needed in the discussion to compare and contrast your findings to what is already known in the area - what this study is contributing is not clear currently.

## Tables

Table 1 - MV time - change 'horas' to 'hours'

## Figures

Figure 1 - the reasons for exclusion listed in the text and in the figure differ (i.e., text - 2 due to combined surgery, figure - 5 due to combined surgery). Please use the CONSORT flow diagram template and report how many participants completed measures at each timepoint and how many were included in the analysis. <http://www.consort-statement.org/consort-statement/flow-diagram>

## References

-please review - references 9-11 are incomplete

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## Authors' response

Reviewer #1: I thank the authors for their time spent drafting the manuscript, my main comments are regarding the trial methodology as currently reported in the manuscript. I provide the following comments which I feel need to be addressed:

My main comment is that this manuscript needs to be revised so it is clear that this is a pilot

study. The absence of a power calculation and a sample of 29 means it is likely the trial is underpowered to detect a significant difference between groups for the primary outcome (6MWT). The manuscript should be revised to report on the feasibility of delivering the intervention in this high risk group of patients, with effectiveness outcomes as secondary outcomes.

**Answer:** The entire manuscript was reviewed, responding to comments and making it clear in the title that this is a pilot study.

**Title:**

Please include the word 'pilot' in the study design. The title could be improved by some revisions 'Inspiratory muscle training and functional capacity following coronary artery bypass grafting in high risk patients: a pilot randomized controlled trial'

**Answer:** Title change made.

**Introduction:**

-heading of this section is not in English

**Answer:** We translate the introduction topic.

-the knowledge gap is well identified

**Answer:** Thanks.

**Methods:**

-Eligibility - could participants have COPD of any disease stage/severity?

**Answer:** Patients with moderate and severe COPD were included.

-Eligibility - sex/gender mentioned twice - please retain 'both sexes' only

**Answer:** Removed.

-Eligibility - how was 'difficulty in understanding the imposed techniques' assessed? Was a validated measure of cognitive function used?

**Answer:** The comprehension difficulty was assessed during the test attempt. If the patient could not perform, he was excluded.

-Was group allocation concealed?

**Answer:** Randomization and allocation were done blindly.

-Was the trial registered (prospectively/retrospectively)?

**Answer:** It was registered in the Brazilian Registry of Clinical Trials (ReBEC) under the number RBR-8dqrq.

-Were CONSORT guidelines followed in the conduct and reporting of the trial?

**Answer:** Our group always uses CONSORT as a basis for this type of study.

-Further detail regarding the randomisation process is required - it is not clear how the balls were used to randomize participants.

**Answer:** In this draw, there were two balls with a paper in each referring to the groups; then, a member of the team on duty choose one of the balls, being that the patient's group of allocation.

-P6 line 5-6 - not in English

**Answer:** We translate this part.

-Who delivered the intervention? What was their background, experience and were they provided with any training in the intervention protocols?

**Answer:** The intervention was performed by a physical therapist with three years of experience and practice of inspiratory muscle training.

-I would encourage the authors to adhere to the TIDier guideline of intervention reporting to improve the ability to replicate the intervention delivered.

**Answer:** The article was described based on CONSORT.

-Was the training load progressed beyond the 40% of MIP prescribed at baseline? If so, how was this achieved?

**Answer:** Every five days muscle strength was reassessed and 40% load was applied based on the new value.

-Was the examiner who completed the outcome assessments blinded to group allocation?

**Answer:** Yes. The evaluator was blind too.

-Were two 6MWT performed as per the ATS guidelines (i.e., were participants allowed a practice test to allow for familiarization effects)?

**Answer:** They took a first test a few hours after admission and on the next shift they took a second test.

-Was a validated measure used to assess post-operative complications (POMS, Melbourne Group Score)?

**Answer:** We used the clinical approach to evaluate complications. As in some studies, we trained two professionals, who were blind, to evaluate complications, through the analysis of medical records or complementary exams.

-Both groups received usual care - it is important to describe in the manuscript what pre and post-operative usual care was at the recruitment hospital during the study.

**Answer:** In the preoperative period, the patients were instructed on the surgical procedure, activities they could perform, all functional assessment, kinesiotherapy for upper and lower limbs and ambulation. In the postoperative period, they performed non-invasive ventilation, transfer from lying to sitting, kinesiotherapy and sitting in the chair on the first day. From the second day on, they were already walking around the unit. All these conducts were maintained until hospital discharge, increasing time and distance.

-How was the sample size of 29 determined? Was a power calculation performed? It is very possible that the lack of between group differences you observed for many outcomes was due to a lack of power rather than a lack of effect of the intervention.

**Answer:** 29 patients were evaluated. So, with standard deviation in the average distance walked in the control group (n=14) of 110 meters and in the training group (n=15) of 101 meters and, difference between the averages of the distances walked by the 9 meters groups, this sample of convenience allowed a statistical power of 74% (alpha of 5%).

-Please explain why the 6MWT was chosen as the primary outcome.

**Answer:** We chose functional capacity as the primary outcome, as other outcomes such as pulmonary complications have already been researched and the benefit of IMT has been

proven, as in the study by Hulzebos. However, few studies have observed the effects on the distance covered in the 6MWT.

#### Results

Did all 14 intervention participants adhere to the IMT intervention protocol as prescribed?

**Answer:** All patients adhered to and completed the IMT protocol.

#### Conclusions

Are the studies by Cordeiro and Zanini that you refer to also of IMT interventions? Further details are required. What differences were there (if any) between your intervention protocol and previously published?

**Answer:** Both studies applied IMT, however in the study by Zanini et al. three more groups were created also involving training of peripheral muscles. The main difference between these two studies and the present one is the performance of IMT in patients at high risk for pulmonary complications, which was used as an exclusion criterion in previous studies.

Is there enough time in the pre-operative period to commence training as you suggest?

**Answer:** Some studies suggest performing IMT 7 to 14 days before the surgical procedure. However, day-to-day contact time with the patient is shorter. We are currently conducting research evaluating the impact of IMT 24 hours before surgery.

Further work is needed in the discussion to compare and contrast your findings to what is already known in the area - what this study is contributing is not clear currently.

**Answer:** We have included four more studies in the discussion, comparing with our results.

#### Tables

Table 1 - MV time - change 'horas' to 'hours'

**Answer:** Modified

#### Figures

Figure 1 - the reasons for exclusion listed in the text and in the figure differ (i.e., text - 2 due to combined surgery, figure - 5 due to combined surgery). Please use the CONSORT flow diagram template and report how many participants completed measures at each timepoint and how many were included in the analysis. <http://www.consort-statement.org/consort-statement/flow-diagram>

**Answer:** Revised.

#### References

-please review - references 9-11 are incomplete

**Answer:** Revised.

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2<sup>nd</sup> Editorial decision  
10-Feb-2022

Ref.: Ms. No. JCTRes-D-21-00178R1  
INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT

RANDOMIZED CONTROLLED TRIAL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Mar 12, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear Dr. Cordeiro,

I have received your manuscript at the Journal of Clinical and Translational Research. Thank you for submitting your revised paper.

I have gone through the manuscript and noted excessive spelling/grammatical errors. These need to be resolved before we can proceed with the publication.

The editorial board therefore kindly requests that you to have a preferably native speaker go through the paper and polish the language in accordance with academic standards.

Please understand that this has always been the responsibility of the authors, as advertised clearly in our author guidelines (<https://www.jctres.com/en/author-guidelines/>).

Publishing properly written papers is a putative standard in science. We have worked hard to maintain a level of excellence with the journal in every respect so that we can serve past, present, and future contributors with a stamp of high quality and impeccable reputation.

If you do not manage to undertake the task yourself or get a colleague to help you, please contract a third-party language editor. Alternatively, contact the journal ([m.heger@jctres.com](mailto:m.heger@jctres.com)) so that we can try to engage a paid language editing service. JCTR has



dedicated language editors who undertake a deep dive in terms of content and language editing that is in accordance with the journal's standards.

Thank you for understanding and kindest regards,

Michal Heger  
Editor

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3<sup>rd</sup> Editorial decision  
18-Feb-2022

Ref.: Ms. No. JCTRes-D-21-00178R2  
INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT  
RANDOMIZED CONTROLLED TRIAL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was **FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION**.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Mar 20, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear Dr. Cordeiro and co-authors,

Please take my previous comments regarding language editing seriously.

Marking an entire text yellow so as to indicate you have gone through it, while leaving phrasing such as "-12 (-50,25 a 26,25)" in the text does not warrant me taking this revision seriously.



The text should be in English, not Portuguese. So actual English text and decimal point denominations (periods, not commas).

Table and figure designations (e.g., Table 1, Figure 3) should be capitalized.

These are just a few of the several issues I previously asked you to address, which should not be difficult.

Kindly use the track changes function in Word so that I can see what was specifically corrected in the next version.

We're almost there, and I hope that 1 more revision will get us to publication of your work.

Thank you,

Michal Heger  
Editor

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4th Editorial decision  
11-March-2022

Ref.: Ms. No. JCTRes-D-21-00178R3  
INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT  
RANDOMIZED CONTROLLED TRIAL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Apr 10, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief

Journal of Clinical and Translational Research

Reviewers' comments:

Dear Dr. Cordeiro and colleagues,

Thanks for submitting a revised draft. Unfortunately, the language is still off in many places and we strongly urge you that you engage a third-party service or a native speaker to help out. Let me know please if you need any further assistance (m.heger@jctres.com).

Thank you and kindest regards,

Michal Heger  
Editor

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5th Editorial decision  
26-Mar-2022

Ref.: Ms. No. JCTRes-D-21-00178R4  
INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT  
RANDOMIZED CONTROLLED TRIAL  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Apr 25, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Not sure whether you are testing my patience, but I urgently request that you correct the language to academic English.

It is quite evident that you neglected my comment 2 rounds ago, where I requested you to remove Portuguese text and notations.

You submitted the following:

-2 (-14.25 a 10.25)

5 (-6.08 a 16.08)

-7 (-16.52 a 2.52)

-1 (-11.40 a 9.40)

4 (-4.79 a 12.79)

-7 (-15.39 a 1.39)

-12 (-50.25 a 26.25)

-3 (-39.59 a 33.59)

-9 (-43.71 a 25.71)

I phoned up the Brazilian embassy and asked them to translate the "a" for me. Apparently, it means "to".

The sentence "As a secondary outcome, the influence of IMT on ventilatory muscle strength, pulmonary complications and length of hospital stay" is missing a verb. Did it migrate elsewhere out of protest?

And I could go on.

OK, one more:

We evaluated 29 patients..

Is the double period some kind of implicit statement?

Native speaker jumps to mind....

Last chance, or I will be forced to reject the manuscript.

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6<sup>th</sup> Editorial decision

11-Apr-2022

Ref.: Ms. No. JCTRes-D-21-00178R5

INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT  
RANDOMIZED CONTROLLED TRIAL

Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by May 11, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

I have one of 2 options; either I engage an academic editor to improve the language (cost of USD 90 to be paid upfront with guaranteed acceptance of the paper), or I reject the manuscript.

Please let me know what you choose to do (m.heger@jctres.com).

Kindest regards,

Michal Heger  
Editor

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7th Editorial decision  
01-May-2022

Ref.: Ms. No. JCTRes-D-21-00178R6  
INSPIRATORY MUSCLE TRAINING AND FUNCTIONAL CAPACITY FOLLOWING  
CORONARY ARTERY BYPASS GRAFTING IN HIGH RISK PATIENTS: A PILOT  
RANDOMIZED CONTROLLED TRIAL  
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers: