Author’s response to reviews

Title: Effect of Pre-discharge cardiopulmonary fitness on Outcomes in Patients with ST-Elevation Myocardial Infarction after percutaneous coronary intervention

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Author’s response to reviews:

Dear Editor,

Thank you very much for having given us the opportunity to revise our manuscript (BCAR-D-19-00237) entitled: "Individualized exercise prescription in Phase I cardiac rehabilitation reduces incidence of cardiovascular events in patients with STEMI after PCI ". We carefully addressed the comments of the Reviewers and Editor. Please, find attached our itemised replies.

We hope that with these clarifications and alterations, our manuscript will be acceptable for publication.

All authors believe that this manuscript represents valid work and approved the final version. Neither this manuscript, nor one with substantially similar content, has been published or is being considered for publication elsewhere.
We are looking forward to hearing from you soon.

Best wishes,

He Cai, MD, PhD

Pengyu Cao, MD, PhD

We thank The Academic Editor for her/his positive assessment of our manuscript. We carefully addressed all issues raised by reviewers and better highlighted the study limitation.

Reviewer reports:

L Compostella (Reviewer 1):

The paper deals with a very interesting topic: long-term prognosis of patients after an STEMI treated by primary PCI and submitted to structured and comprehensive cardiac rehabilitation. It is particularly relevant that the number of study cases is high, and the follow-up period is rather prolonged.

The text is overall well written, and the methods are correct.

We thank Reviewer 1 for her/his careful review and positive assessment of our manuscript and all the revised words or sentence have been marked by red colour in our revision.

Major comments:

1. The title of the paper focuses on individualized exercise prescription during phase 1 cardiac rehabilitation. This is indeed a very interesting issue, and the high number of patients involved in the study could give an important highlight on the topic and a specific recommendation. Unfortunately in the paper (especially in Discussion), it seems to me that little space is given to this topic, while greatest relevance is given to long term prognosis of STEMI patients based on their exercise tolerance. This is another very interesting topic, not well developed till now in literature (at least not well studied with CPX), but it is different from what is written in the title.

Furthermore, in Introduction (page 3, lines 43-48) the Authors write "we reviewed the efficacy and safety of individualized exercise prescriptions in Phase I cardiac rehabilitation". It seems to me that no evaluation of efficacy and safety of this kind of individualized CR was performed (no new CPX was performed after discharge from phase 1 CR to evaluate CRF improvement (or not)
after exercises individualized on CPX parameters), while (as written above) focus was on long
term prognosis.

I invite the Authors to evaluate what could be the most relevant topic that they will analyze with
this study, and modify accordingly at least the title and the purpose of the study. In my humble
opinion, it could be easier to modify title and aims (and conclusions), focusing on long term
prognosis of STEMI pts according to their initial (post-STEMI) VO2 at AT, or W-max, or
VE/VCO2 slope.

Answer:

To address these concerns, we simplified the wording in the Introduction to improve the flow of
ideas. The results showed that the relevance was given to long term prognosis of STEMI patients
based on their individualized exercise prescription.

Therefore, we modified the title: “Effect of Pre-discharge cardiopulmonary fitness on Outcomes
in Patients with ST-Elevation Myocardial Infarction after PCI”.

We modified the aims in the introduction and abstract: ”The purpose of this study was to
analyze cardiopulmonary fitness in Phase I cardiac rehabilitation on the prognosis of patients
with STEMI after PCI”

We modified the conclusions in the discussion: “In conclusion, this study found that
individualized exercise prescription of Phase I cardiac rehabilitation reduced the incidence of
cardiovascular events in patients with STEMI after PCI, and improved long term prognosis in
patients with STEMI based on their pre-discharge cardiopulmonary fitness”.

2. It is somehow disappointing that the Authors did not find significant differences between IEP
and NIEP groups, regarding incidence of cardio-genetic death, re-hospitalization, heart
failure, stroke, or atrial fibrillation (page 5, lines 50-52). Thus, it seems that individualized
exercise could not give any major advantage, except for total MACE. I ask the Authors to
give some comments on this in Discussion.

Answer:

We addressed this concern on Discussion: Other study (Powell R et al, BMJ Open. 2018 Mar
14;8(3):e019656) also show that individualized exercise could not give any major advantage.

It is somehow disappointing that we did not find significant differences between IEP and NIEP
groups, regarding incidence of cardio-genetic death, re-hospitalization, heart failure, stroke, or
atrial fibrillation. The reasons are as follows: first, cardiac rehabilitation include patient
education, nutrition guidance, medication guidance, smoking cessation and psychological
prescription, etc. except for exercise prescription. It shows that other Phase I cardiac rehabilitation parts also plays an important role in cardio-genetic death, re-hospitalization, heart failure, stroke, or atrial fibrillation (Pavy B et al. Arch Cardiovasc Dis, 2013. 106(12):680-9).

Second, our study showed that cardio-genetic death, re-hospitalization, and total MACE decrease significantly when the VO2 at VT was greater than 10.5 ml/kg/min. our results showed that pre-discharge cardiopulmonary fitness in Phase I cardiac rehabilitation could improve the long term prognosis of the STEMI patients.

3. In my humble opinion, instead of the Fig. 1 and Fig. 2, that report ROC for some CPX parameters, it could be more easily understandable for readers if the Authors could present Kaplan-Mayer curves of survival, or of MACE-free. Could the Authors consider to substitute the figures?

Answer:

We addressed this concern and increased the Fig. 1 and Fig.4 with Kaplan–Mayer curves of MACE-free survival at follow-up according to the group. We add a new table 8 to describe the MACE. So the previous Fig 1 and 2 became Fig 2 and 3 respectively in our revision. We also described them in the results of revision. MACE: Major adverse cardiac events.

Minor observations:

1. Methods (page 3 line 54): "This retrospective study …": the Authors describe this study as a retrospective one; but I do not understand if this statement is really correct, as the Authors describe elsewhere that they made a telephone follow-up (page 5, line 13), and the patients have been offered the opportunity to choose between individualized exercise prescriptions (page 4, line 13). Please give explication of these apparent incongruity.

Answer:

We addressed this concern: in our hospital, there are two ways to develop a discharge prescription for exercise. For patients who are willing to undergo CPX examination before discharge, we conduct individualized guidance for exercise based on the results of CPX. For patients who are unwilling to undergo CPX examination before discharge, we give a uniform exercise guideline based on Borg index “11-13”. Our study is a retrospective analysis of all the information and CPX results of STEMI patients after PCI after the discharge from January to December 2015.
In our cardiac follow-up center, staff will conduct a telephone follow-up of STEMI patients after PCI every three months to know the major adverse cardiac events (MACE). We reviewed all these results from the telephone follow-up recordings.

Because we study the past medical history including follow-up results, basic data, and CPX data to learn what factors may be associated with long term prognosis in patients with STEMI, we define this study as a retrospective study.

2. Page 3, line 17-21: "PCI operation leads to coronary spasm, endothelial cell injury, and even restenosis or thrombus; moreover, a poor prognosis may still exist in patient with STEMI after PCI [4]." I suggest to modify the sentence in a more "soft” way, for instance writing that PCI "may lead to …". Furthermore, prognosis after PCI is indeed much better than in cases of now revascularization or in conservative treatment. Another thing to remember is that cardiac rehabilitation improves prognosis after PCI, but may not be considered as an alternative to PCI, as it could be argued by the present formulation of this and following sentences.

Answer:

We modified the sentence in introduction :

In page 4 line 9-11: “However, PCI operation may leads to coronary spasm, endothelial cell injury, and even restenosis or thrombus; moreover, a poor prognosis may still exist in patient with STEMI after PCI.

In page 4 line 17-19: “Therefore, PCI associated with CR have been recognised internationally as the preferred treatment of STEMI, now PCI combined with CR has become the internationally recognized effective treatment for patients with STEMI.”

Joanna Kapusta (Reviewer 2):

The paper aims to explore the efficacy and safety of individualized exercise prescriptions in Phase I cardiac rehabilitation that are tailored to cardiopulmonary fitness, in a sample of 499 patients, with ST-segment elevation myocardial infarction (STEMI) after percutaneous coronary intervention (PCI).

We thank Reviewer 2 for her/his positive assessment of our manuscript, and all the revised words or sentence have been marked by red colour in our revision.
Comments:

1. Was the patient's assignment to the group of individualized exercise prescriptions (IEP) or the non-individualized exercise prescriptions (NIEP) group based only on the patient's decision (acceptance)? Were there also other eligibility criteria for the IEP and NIEP groups?

Answer:

Yes. Patients were assigned to individualized exercise prescriptions (IEP) group and non-individualized exercise prescriptions (NIEP) group only based on their decision (acceptance). We have added these in our revision (Page 5 line11-15). And all the patients in the IEP and NIEP groups had no contraindication for cardio-pulmonary exercise testing (CPX). (Page 5, line10-11)

2. I suggest that in addition to the data presented in the form of a table, in the subsection Material, put information on how many patients counted the IEP group and NIEP (this will allow the reader better orientation)

Answer:

We addressed the suggestions of Reviewer 2 and add this information in our methods (red colour).

3. In Table 4, the PP group (n = 30) does not seem to correspond to the PP group in Table 5 (n = 34). How many patients does the PP group count? Do the results refer to the same group in both Tables?

Answer:

We made a mistake in Table 5, and corrected it. The number of patients in the PP group was 30. The MACE events in IEP group were 34 cases (30 persons). The major cardiovascular events (MACE) were recorded twice for 4 patients because of re-hospitalization for heart failure (n=3), stroke (n=1).

4. I suggest that in addition to the data presented in the form of a table, in the subsection Material, also put information on how many patients counted the PP group, and how many GP group.

Answer:

We addressed the suggestions of Reviewer 2 and add this information in the methods part.
5. How many patients were "good prognosis" and how many "poor prognosis" in the NIEP group?? - I think that this is important information, because in the NIEP group there could be more patients with poor prognosis, compared to the IEP group, which could influence the results when comparing the groups (NIEP and IEP) in relation to the incidence of major cardiovascular events (MACE).

Answer:

We addressed the concerns of Reviewer 2, the number of "good prognosis" patients was 252, and "poor prognosis" patients was 128 (152 cases) in the NIEP group. The major cardiovascular events were recorded twice for 24 patients because of re-hospitalization for heart failure (n=13), stroke (n=10) or atrial fibrillation (n=1).

6. As the Authors describe, the study included patients in whom the CPX method was used as a cardiovascular exercise test - how many patients were excluded from the study due to the inability to carry out CPX ??? (who used a different exercise test, eg 6MWT- six minute walk test)

Answer:

We addressed the concerns of Reviewer 2, 41 patients were excluded from the study due to the inability to carry out CPX (Table 1). Therefore, patients in the IEP group were all examined by CPX.

7. What kind of exercises were carried out in the IEP group, and what kind in the NIEP group ?? I understand that these were individualized and non-individualized exercises, but what exercises exactly do you mean ??Breathing ?? Relaxation… ??

Answer:

We addressed the concerns of Reviewer 2, both IEP and NIEP groups perform exercise, which include aerobic exercise, resistance exercise and stretching exercise (relaxation). The intensity and time of exercise in IEP group are determined by CPX (heart rate under anaerobic threshold), while in NIEP group, the intensity and time of exercise is determined by patient's subjective sensation (Borg index "11-13").
8. Discussion. Page 7, line 15-16. "6-minute walking experiment" - please substitute "it" with "6 minute walk test (6MWT)".

Answer:

We addressed the concerns of Reviewer 2 and substitute "6-minute walking experiment" with "6 minute walk test (6MWT)" in page 8 line24.