Author's response to reviews

Title: Impact of completeness of revascularization by coronary intervention on exercise capacity early after acute ST-elevation myocardial infarction

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Author's response to reviews: see over
Dear Drs Zamvar and Taggart,

We thank you and the Journal for considering our work for publication. We addressed all issues raised by the Reviewers, and provide a point-by-point answer below.

Best regards,

Dr. Wei Gao,
Email: dr_gaowei2012@163.com

Editorial office

1. Please remove the Running Title section in the Title page as this is not needed for publication.

Response: The running title was removed.

2. Please include the Grant section in the Acknowledgements.

Response: These two sections were combined.

3. Please complete the name of the Ethics committee who approved this study.

Response: We completed the name of the Ethics committee.

4. Please include a list of abbreviations used in the manuscript and their meanings.

Response: We added a list of abbreviations.

5. Please include an Authors Contributions section at the end of the manuscript, before the reference list. We suggest the following kind of format (please use initials to refer to each author's contribution): “AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study,
and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.”

**Response:** This section was added.

**Reviewer 1**

**Major Compulsory Revisions**

1) Basically, the authors are comparing patients who were revascularized completely or incompletely, but always according to optimal clinicians’ judgment. They essentially show that clinical judgment is better than looking simply at angiographic significance of any stenosis in any vessel to decide whether to stented or not these patients. There is no mention of checking the functional significance of these stenoses (e.g. FFR them) or, at least, of QCA. Stenosis significance is said to be >70% (in which projection? decided by who?). QCA data should be provided as a minimum.

**Response:** The Reviewer raises a good question. We did not assess the functional significance of these stenoses (e.g. FFR) or QCA at this time. However, we will include these assessments in a future study.

2) It would be much better to classify IR patients according to the amount of jeopardized myocardium (e.g using an anatomic score such as the BARI score) in order to check whether patients with more myocardium at risk (at least a "significant" amount) have reduced exercise capacity. Otherwise we are comparing patients with OM1 stenosis with others with proximal LAD stenosis.

**Response:** The Reviewer raises another good question. Since the evaluation of the area of ischemic myocardium requires a MRI examination, due to the retrospective nature of the study, and because the patients did not underwent MRI, variations in the amount of compromised myocardium could not be assessed. However, we used markers that are commonly used in routine clinical practice, such as troponines, which are generally thought to represent myocardium damage. This issue could be addressed in a future study.

**Minor Essential Revisions**

**Angio protocolo:** Aspirin AND clopidogrel indefinitely?

**Response:** Sorry for our mistake. It should be aspirin indefinitely, and clopidogrel for one year. This was corrected in the manuscript.

**Reviewer 2**
Major Compulsory Revisions

1) The conclusion that CR is of no benefit in my opinion should be toned down. There are several limitations suggesting to be more cautious when interpreting these data:
   a) The previously mentioned selection bias between the 2 groups of patients with MVD, potentially encouraging revascularization when more feasible or when perceived more clinically-relevant
   b) 97% of the patients had a Killip class I, meaning that this is a very low risk population. The benefit of complete revascularization is mainly expected in high-risk and hemodynamically unstable patients. Showing a benefit of CR in low risk population would require much larger studies and longer follow-up.
   c) The complete revascularization group received a staged PCI procedure within the same hospitalization with an apparently angio-guided strategy. In the absence of a clear evidence of ischemia, some procedures may carry only increased risk of events.
   d) Data from other similar studies provided opposite results, using clinical endpoints
   e) In parallel with the “ischemia-driven “ vs . the “angio-guided” strategy issue, it could be hypothesized that a strategy of “delayed” complete revascularization (i.e. performed a few weeks after the episode of STEMI) may hold different results as compared to a strategy of “early” complete revascularization.

   Response: We agree with the Reviewer. We toned down our conclusions, and added some limitations.

2) In the “catheterization protocol” paragraph the Authors should clarify how decision to perform complete revascularization with staged PCI was made. Was there any ischemia-driven decision or angio-guided decision. Alternatively, it should be simply stated that there was not a clear strategy for CR and every physician and center made the decision based on different protocols.

   Response: We agree with the Reviewer that this clarification is important. All PCI were performed based on angiography-based decisions. This was added to the manuscript in the Catheterization protocol section.

3) The authors state that a limitation of the study design was that there were no exercise performance data obtained prior to acute MI (Limitations paragraph). This would be rather unusual (we cannot predict a MI), so this in my mind is not at all a limitation and I suggest to remove these sentences.

   Response: We agree with the Reviewer. However, we believe that exercise performance prior to MI might be a confounding factor for exercise testing after MI, even if we cannot predict who will suffer from a MI and even if assessing pre-MI exercise performance would be difficult. Thus, we edited this limitation accordingly.

Discretionary revisions
5) Catheterization protocol: the Authors state that clopidogrel was prescribed indefinitely. This is rather unusual and deserve a comment.

**Response:** Sorry for our mistake. It should be aspirin indefinitely, and clopidogrel for one year. This was corrected in the manuscript.

6) Table 2 basically duplicates data described in the text and there are also some unclear data. For example, it is not clear if the number of stents implanted refers only to the first procedure or, for the CR group, it also includes the second PCI. Please specify. In general, I suggest either to remove the table or to fill the table with more data. For example: non-IRA lesion vessel, lesion type (ACC/AHA), CTO, bifurcation, ostial lesion, target-lesion average lesion length, average stent length.

**Response:** The number of implanted stents included the second PCI for the CR group. We decided to remove this Table, and to present these results in the text only.