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
Response to Reviewers' comments

Dear Drs Zamvar and Taggart,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive feedback, and have made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and their discussion, therefore providing a more complete context for the research that may be of interest to your readers.

We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,

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Reviewer #1

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 stent or not these patients. There is no mention of checking the functional significance of these stenoses.
(eg 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:** In clinical practice, stenosis severity is typically determined during or shortly after the procedure, and most physicians commonly rely on visual estimation. The completeness of revascularization was based on the clinicians’ judgment, consistently with previous studies (Kalarus et al., Am J Heart 2007; and Meliga et al., J Interven Cardiol 2011).

To validate our visual assessment, we also performed QCA on 254 coronary lesions with 30-80% visual stenosis in 208 MVD patients. These lesions were further classified into <50%, 50-69% and ≥70% stenosis groups. The results presented below indicate that there are no statistical differences in stenosis between the assessment using QCA and visual judgment (Chi-square test, p=0.411). Therefore, as a convenient and easy to perform method, it is reliable to define and classify stenosis by visual judgment. Of course, in future studies, we will try to combine different methods, including QCA, to strictly define stenosis. We added these data in the text (page 9).

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<th>&lt;50%</th>
<th>50%~&lt;70%</th>
<th>≥70%</th>
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<tr>
<td>QCA</td>
<td>39</td>
<td>179</td>
<td>36</td>
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<tr>
<td>Visual assessment</td>
<td>29</td>
<td>185</td>
<td>40</td>
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2) It would be much better to classify IR patients according to the amount of jeopardized myocardium (eg 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 CAD severity in MVD patients was assessed according to a modified Gensini’s stenosis scoring system (Gensini, J Am Cardio 1983). This score is computed by assigning a severity score to each coronary stenosis based on the degree of luminal narrowing and its topographic importance. Reduction in lumen diameter was evaluated and assigned a score of 1, 2, 4, 8, 16 and 32 for 25%, 50%, 75%, 90%, 99% and complete occlusion, respectively. A multiplier was also assigned to the value of each affected segment based on the functional significance of the myocardial area supplied by that segment: 5 for the left main coronary artery; 2.5 for the proximal segment of the LAD; 2.5 for the proximal segment of the circumflex
artery; 1.0 for the right coronary artery, the distal segment of the LAD, the posterolateral artery and the obtuse marginal artery; and 0.5 for all other segments (page 9).

There was no difference in Gensini’s scores between the CR and IR groups (CR= 63.2±37.0 vs. IR= 65.2±36.5, P=0.814) (page 11 and Table 1).

Reviewer #2

During the process of revision, the results of the PRAMI trial were presented at the annual ESC meeting and published on the N Engl J Med. 2013 Sep 19;369(12):1115-23. I strongly suggest the Authors to update their discussion based on the results of this trial.

Response: In the PRAMI trial, after PCI completion in the infarcted artery, eligible patients were randomly assigned to undergo no further PCI procedures or to undergo immediate preventive PCI in non-infarcted arteries with more than 50% stenosis (preventive PCI). In the present study, staged PCI (i.e., treatment of stenosed arteries that were not treated during the initial procedure) in patients without angina was discouraged. Therefore, the intervention method used in our study was different from that of the PRAMI trial.

The PRAMI trial showed that in patients with STEMI and MVD undergoing infarcted-artery PCI, preventive PCI in non-infarcted coronary arteries with major stenosis significantly reduced the risk of further adverse cardiovascular events, compared with PCI limited to the infarcted artery. In contrast, in our study, we conclude that CR may not always offer benefit over IR with regard to the improvement of post-STEMI ischemia. This is of relevance to clinicians making management decisions, and implies that CR should not be an automatic choice for all patients with STEMI and MVD. We believe that it is reasonable to recommend that multivessel revascularization should be only used in patients with instability criteria or with a very high clinical risk, and that intervention should be deferred in most other patients until the results of ischemia-proving tests are available. In the PRAMI study, patients were randomized into two groups, and those with preventive PCI might not undergo CR (like in our study), and those without preventive PCI might otherwise undergo CR. Therefore, the results from the PRAMI trial could not be compared with ours.

This was added to the discussion (page 14).