Reviewer's report

Title: Oxygen Therapy in Patients with ST Elevation Myocardial Infarction based on the culprit vessel: Results from the Randomized Controlled SOCCER Trial

Version: 0 Date: 21 Aug 2019

Reviewer: Paul J. Young

Reviewer's report:

Thanks for the opportunity to review this manuscript. I offer the following comments for your consideration:

1. The introduction does not clearly explain why this study was needed or why its findings would be expected to be consequential. I strongly suggest that you redraft the manuscript so that it is clear that there is a biologically plausible reason why the effect of oxygen therapy would vary depending on the culprit lesion in patients with myocardial infarction. Without this information in the introduction the rationale for undertaking this study is not clear enough. Even with the benefit of hindsight provided by the information introduced in the Discussion, my overwhelming sense was that the prior probability of a difference in the effect of oxygen based on culprit lesion was very low.

2. I think that the introduction would be better if it ended with a hypothesis that makes sense in the context of the background information presented.

3. I may have misunderstood but it appears that patients were initially randomised to oxygen or no oxygen but then were excluded from the study if they did not require a coronary angiogram. If this is correct, then this is a major methodological flaw because excluding patients after they have already received treatment has the potential to introduce bias.

4. Related to number 3, I am also a little unclear about whether or not 'stratification' by culprit lesion occurred at randomisation. Stratification is a tool for ensuring there is balance in terms of treatments received within subgroups. If you are using the word stratification to mean something different to this, I think you may be using it incorrectly. Moreover, as valid subgroups should be defined based on pre-randomisation characteristics, a comparison of subgroups based on culprit lesion as defined at angiography many hours after randomisation is not a methodologically valid comparison.

5. The analysis presented is not an intention to treat analysis. As the number of patients with missing data is large and data might not be missing at random, this is potentially problematic.

6. Subgroup analyses should be undertaken by fitting an interaction term to evaluate the effect of treatment by subgroup.
7. There is no clear justification of why the effect size you were powered to detect is clinically important or why this represents the minimum important difference. Without such a justification, one is left wondering whether the study had sufficient power to exclude an important difference.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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