**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:** 1  **Date:** 08 Jan 2020

**Reviewer:** J Grensemann

**Reviewer's report:**

In this manuscript, Khoshnood et al. report a sub-group analysis of the already published SOCCER trial evaluating the effect of supplemental oxygen on myocardial salvage index (MSI) in patients with ST elevation myocardial infarction. In this sub-group analysis, patients were grouped according to the culprit vessel, i.e. LAD vs. non-LAD. This is an interesting and novel idea and the rationale is now sufficiently outlined in the manuscript. The manuscript is well written, and the authors have adequately addressed the remarks of the previous reviewers. However, in my opinion, one remaining issue needs further clarification:

As Prof Young and Prof Szczeklik have commented, the group sizes were rather small and it is not clear if the study may be underpowered. Khoshnood et al. have calculated a sample size of 100 patients for the detection of an MSI difference of 15% between the O2 and air group with a SD=20 for a power of 0.96 and alpha of 0.05. This yields an effect size of 0.75 and the authors have apparently used a two-tailed approach to obtain a sample size of 100 patients. Unfortunately, CMRI results and thus MSI values were only available for 95 patients overall and for only 46 patients in the studied sub-group with a culprit lesion in the LAD. Therefore, the analysis does not fulfil the calculated sample size. Because the presented sample size calculation is identical to the calculation in the original SOCCER publication, I assume that the authors may have included the wrong sample size calculation for this sub-group analysis by mistake.

Lowering the power to 0.8 reduces the sample size to 58 for a two-tailed approach and to 46 for a one-tailed approach. Since Khoshnood et al. hypothesize that O2 in LAD lesions would not provide benefits, a two-tailed approach seems reasonable. The available 2x 23 = 46 patients would be sufficient to reject the null-hypothesis above a difference of 17%, at a SD 20 (effect size 0.85), power 0.8, alpha 0.05, two-tails. The last calculation could make sense for a secondary sub-group analysis, albeit the power is lower increasing the risk for type II error, which is already addressed in the limitations section.

Minor points: (page numbers referring to PDF-file)

- The primary outcome measure was the MSI. I suggest reporting the primary outcome measure before other values in the abstract and the tables.

- P14 L17: should read "previously"
- P15 L17 dropout instead of fallout

**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?**
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Yes

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