HALF-TIME REVIEW

Oxygen Therapy in Myocardial Infarction – The SOCCER study

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Included articles

**Paper I:**


**Paper II:**


**Paper III:**

Background

For more than a century, Oxygen (O\textsubscript{2}) therapy have been one of the most common treatments in patients with chest pain/acute coronary syndrome (ACS). Early studies suggested that supplemental O\textsubscript{2} to patients with myocardial ischemia or infarction might have positive effects on the circulation and that it could also relieve pain [1-5]. The common assumption was that supplemental O\textsubscript{2} diminish the ischemia in the myocardium thus reducing the size of the ischemia and the risk for malignant arrhythmias [6]. Several studies, however, contradict this claim, indicating that supplemental O\textsubscript{2} to both patients with ACS, as well as healthy patients, have negative cardiovascular effects such as a decrease in coronary blood flow, diminished cardiac stroke volume (SV) and output (CO), increased systemic vascular resistance and diminished left ventricular perfusion [7-11].

Many studies [12-17] have tried to answer how supplemental O\textsubscript{2} affects patients with acute myocardial infarction (AMI), but the results have been inconclusive because of limitations in their designs and/or method. This present project aims to evaluate the role of supplemental O\textsubscript{2} in patients with ST elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention (PCI).

Method

This was a dual-center, single-blind, randomized controlled trial which was conducted between 23\textsuperscript{rd} January 2012 and 5\textsuperscript{th} August 2015. Patients with first time STEMI, symptom duration less than 6h and a normal O\textsubscript{2} blood saturation (≥ 94\%) were in the ambulance randomized to either 10 L/min O\textsubscript{2}-therapy (the O\textsubscript{2}-group) or no supplemental O\textsubscript{2} (the air group). The study protocol, including inclusion and exclusion criteria, is outlined in Paper I.

At day 2-6 after PCI, the patients underwent cardiac magnetic resonance imaging (CMR) in order to evaluate the ischemic area before the PCI (MaR; Myocardium at Risk), the infarct size (IS) and the myocardial salvage index (MSI). A subgroup of patients underwent an extended echocardiography both at the initial admission and again after 6-months, in order to evaluate left ventricular ejection fraction (LVEF) and wall motion score index (WMSI). At 6-months, all included patients were contacted by a physician in order to evaluate whether the patients were readmitted to in-hospital care for heart failure and to estimate their level of health by using the EQ-5D questionnaire [18].
Cardiac Magnetic Resonance Imaging

Analysis of the CMR images were performed using the post-processing software Segment, v.1.9 R3084 [19] by a researcher blinded to all clinical data, including the patient’s study group allocation. A similarly blinded senior physician reviewed all image assessments before the final analysis. MaR is expressed as a percentage of the LV myocardium. IS is measured by taking partial volume effects in the periphery of the infarction into account. MSI is quantified as \((1 – IS/MaR) \times 100\%\).

We planned to include 100 patients, with 50 undergoing CMR in each study group. Assuming an MSI of \(60 \pm 20\%\) [20-23] in the O\(_2\) group (i.e. with current standard treatment), a total sample size of 100 would allow the detection of an MSI difference of 15 % points between groups with a power > 90 % (actual power 96 %) at a 5 % risk of an alpha error.

Echocardiography

WMSI has been shown to be a good predictor of mortality or readmission for heart failure [24] and reflects IS, regional and total contractility, and can assess myocardial remodeling [25,26]. Consequently, WMSI can also be used to assess the success of an acute PCI [26]. WMSI is assessed in 16 myocardial segments as 1-5, where 1 is normal and 2-5 represents decreased contractility. WMSI is derived as the sum of all segment scores divided by the number of segments visualized. The researchers performing and interpreting the echocardiographic examination were blinded to the patient’s group allocation.

A sub-group of 50 patients will have an extended echocardiography both at the index visit and 6 months after. Assuming a WMSI of 1.6 ± 0.2 [26] in the O\(_2\) group after the PCI, a total sample size of 50 will allow the detection WMSI difference of 0.2 between groups with a power > 90 % (actual power 0.93) at a 5 % risk of an alpha error. The same 50 patients will undergo a second echocardiography after 6 months to detect a difference in the WMSI change by 0.2 in the two groups with a power > 90 % (actual power 0.93) at a 5 % risk of an alpha error.

Results

Cardiac Magnetic Resonance Imaging

Paper II describe the results of the CMR. Of 229 patients eligible for inclusion, 69 was excluded. Of the 160 patients remaining, 95 underwent CMR; 46 patients from the O\(_2\)-group
and 49 from the air-group. In all aspects the two groups were quite similar without any important significant differences. There were no significant differences in CMR results either; MSI (53.9 ± 25.1% vs 49.3 ± 24.0%; 95% CI -5.4 – 14.6), MaR (31.9 ± 10.0% of the left ventricle in the O2 group vs 30.0 ± 11.8% in the air group; 95% CI -2.6 – 6.3) or IS (15.6 ± 10.4% of the left ventricle vs 16.0 ± 11.0%; 95% CI -4.7 – 4.1).

Echocardiography

Paper III describe the results of the echocardiography. A subgroup of 46 patients in the O2-group and 41 patients in the air-group underwent an echocardiography both at the index visit and once again 6 months after admission. There were no important significant differences between these two groups, however, those in the O2-group had more multivessel disease (50%) than in the air-group (26.8%). There were no significant differences in WMSI (1.32 ± 0.27 vs 1.28 ± 0.28) or LVEF (47.0 ± 8.5% vs 49.2 ± 8.1%) at the index visit between the groups. Neither were there any significant differences at the 6 months visit in WMSI (1.16 ± 0.25 vs 1.14 ± 0.24) or the LVEF (53.5 ± 5.8% vs 53.5 ± 6.9%).

Limitations

This trial only included patients from two university hospital sites and the results may not be applicable to all STEMI patients, although the characteristics and the management of our patients seemed to be similar to those in other studies [20,22,23,27]. Since this trial included only STEMI patients, the results might also not be generalizable to patients with others forms of acute coronary syndrome.

A number of included patients did not undergo CMR, which introduces a risk of bias. We believe this bias is limited, since the drop-out of patients were mostly due to technical and logistical problems.

Conclusion

We cannot show any harm or benefit with supplemental O2-therapy to STEMI-patients when measuring IS, MaR and MSI with CMR, as well as WMSI and LVEF as measured by echocardiography. Our results suggest that it is safe to withhold O2-therapy in normoxic STEMI-patients, but studies regarding patient outcomes are needed.
References


