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# SUPPLEMENTAL OXYGEN NOT BENEFICIAL IN MI PATIENTS WITH NORMAL O<sub>2</sub> LEVELS: META-ANALYSIS

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Av: Michael O'Riordan

11 april 2018

”TCTMD”

<https://www.tctmd.com/news/supplemental-oxygen-not-beneficial-mi-patients-normal-o2-levels-meta-analysis>

Nedladdat från: <http://www.ardavan.se>

# Supplemental Oxygen Not Beneficial in MI Patients With Normal O<sub>2</sub> Levels: Meta-analysis

After DETO<sub>2</sub>X-AMI, the ESC tightened up their recommendations against routine use, but US guidelines still consider it a reasonable option.

Supplemental oxygen therapy in patients with suspected or confirmed myocardial infarction and normal blood oxygen saturation levels is not associated with any clinical benefit, a new meta-analysis shows.

In eight randomized controlled trials with 7,998 patients, including the most recent DETO<sub>2</sub>X-AMI study, oxygen therapy did not reduce the risk of in-hospital mortality, nor did it reduce the risk of death at 30 days, infarct size, or cardiac troponin levels.

“In patients who are not hypoxic, additional oxygen is not recommended,” Justin Ezekowitz, MD (University of Alberta, Edmonton), one of the study co-authors, told TCTMD. “I think the guidelines should pay a lot of attention to oxygen as a drug. It has a therapeutic range, and it’s used like a drug so it should be treated as a drug. Therefore, it should be graded with a recommendation based on the evidence and the evidence does not support additional oxygen in patients who are not hypoxic. It’s pretty straightforward.”

At present, the European Society of Cardiology (ESC) 2017 guidelines for the treatment of STEMI do not recommend routine oxygen in MI patients when oxygen saturation (SaO<sub>2</sub>) is 90% or greater, but the 2013 guidelines from the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) still consider oxygen reasonable within the first 6 hours of presentation with unstable angina/NSTEMI (class IIa, level of evidence C). The ACCF/AHA guidelines even state that supplemental oxygen may have “salutatory placebo effects” in normoxaemic patients. The 2014 US guidelines for the treatment of NSTEMI ACS patients suggests oxygen in normoxaemic patients may be associated with “untoward effects,” however.

Jeffrey Anderson, MD (Intermountain Healthcare/University of Utah School of Medicine, Salt Lake City), who chaired the 2013 ACCF/AHA focused update for the management of patients with unstable angina/NSTEMI, said the most recent clinical guidelines are more conservative than they were 20 years ago, when supplemental oxygen was given to nearly every MI patient who walked through the door. Giving patients with chest pain/suspected MI supplemental oxygen when they presented to emergency department had become “almost a reflex.”

The new meta-analysis, however, lines up nicely with data from the most recent clinical trials, he said, and clearly show there’s no benefit of oxygen therapy in patients with normal blood oxygen saturation.

“Obviously, we can’t recommend oxygen as a beneficial treatment,” said Anderson. “In general, we shouldn’t encourage the use of things that aren’t working. We should be practicing evidence-based medicine, doing those things that are going to impact clinical

outcomes. So I agree, we should indicate in our next guidelines, likely in the next draft, and be even more explicit, that oxygen is not indicated because of a lack of benefit.”

### **Definitive Results From DETO2X-AMI**

In August 2017, Robin Hofmann, MD (Karolinska Institute, Stockholm, Sweden), and colleagues presented data from the DETO2X-AMI trial at the European Society of Cardiology Congress 2017, a study that soundly rebuked the routine use of supplemental oxygen therapy in patients with suspected MI. As reported by TCTMD, the trial showed no effect of oxygen on mortality at 1 year, as well as no difference in the rate of rehospitalization for MI or effect on cardiac troponin levels, when compared with patients treated with ambient air.

The new meta-analysis, which was led by Nariman Sepeshvand, MD (University of Alberta), and published March 29, 2018, in *Heart*, includes trials of varying size, length of follow-up, and clinical endpoints. With 6,629 randomized patients, DETO2X-AMI trial is the largest trial included in the analysis, and at 1 year, has the longest follow-up. To TCTMD, Ezekowitz said their goal with the new study was to not only assess the effect of supplemental oxygen on mortality, but to determine if providing oxygen in the setting of acute MI reduced other clinical endpoints, such as infarct size.

Overall, supplemental oxygen therapy did not reduce the risk of in-hospital mortality (OR 1.11; 95% CI 0.69-1.77) or death at 30 days (OR 1.09; 95% CI 0.80-1.50) in patients with suspected acute MI. Additionally, there was no benefit to oxygen when the analysis was restricted to individuals with confirmed acute MI. Infarct size was not affected by supplemental oxygen use in a small subgroup analysis restricted to 370 patients in 3 studies, nor were various cardiac biomarkers, including cardiac troponin levels that were used as a marker of myocardial necrosis.

Ezekowitz said they also analyzed whether supplemental oxygen reduced pain, which is one of the reasons it has been historically given to patients. “There really was no difference in the pain scores across the trials,” he said.

Ardavan Khoshnood, MD, PhD (Skåne University Hospital, Lund, Sweden), the lead investigator of the SOCCER trial, which showed supplemental oxygen therapy had no effect on the amount of myocardium salvaged in STEMI patients undergoing PCI, said the latest meta-analysis “clearly shows there is no positive nor negative effects of oxygen in patients with myocardial infarction and a normal blood oxygen saturation.”

Based on the meta-analysis, in which he was a co-author, Khoshnood believes that all clinical guidelines need to be updated to reflect the evidence. No patient with STEMI, and “probably also NSTEMI,” should receive supplemental oxygen therapy as long as they are hemodynamically stable and foremost have a normal blood oxygen saturation.”

Ezekowitz said the clinical guidelines are beginning to reflect the new evidence. For example, the ESC guidelines were updated in 2017 and he expects the US guidelines to change soon. The Canadian guidelines only recommend supplemental oxygen in hypoxic MI patients, while the Australian experts recommend against routine use if SaO<sub>2</sub> > 93%.

## **'Hard to Undo Practice'**

To TCTMD, Ezekowitz said it's difficult to change physician behavior when it comes to using oxygen in patients who present to hospital with suspected MI. Even patients have come to expect it, with countless television programs showing hospitalized patients receiving supplemental oxygen. "It's hard to undo practice," he said. "Sure, there could be a placebo effect, a comforting effect, in terms of something is being done, and that shouldn't be undervalued. However, when we look at cost and risk we need to be careful about making that the thing we hang our hat on."

In their analysis, Ezekowitz pointed out, they did not observe any evidence of a placebo effect, although he acknowledged it's possible they did not measure the right variables.

Additionally, the cost of oxygen is not inconsequential, particularly when other factors, such as the cost of safely storing, maintaining, and delivering the compressed oxygen canisters, are incorporated into the equation, said Ezekowitz. There are other issues, such as the need for personnel required to monitor oxygen saturation levels and patient immobilization once started on therapy. "Once you start to add up the costs, it's more than the simple cost of oxygen, which seems like it would be free," he said.

Anderson agreed with the direct and indirect costs of oxygen, noting that medicine has become so expensive that only therapies with proven clinical benefit should be used. He suggested, however, there might be some room for treating patients in the "grey zone," such as unstable patients with normal oxygen levels. Given the absence of harm, and the possibility some of these patients might deteriorate and become hypoxic, some physicians may still use their discretion to use supplemental oxygen. For the most part, though, he agreed that it has no role in normoxaemic MI patients.

## **Sources**

Sepehrvand N, James SK, Stub D, et al. Effects of supplemental oxygen therapy in patients with suspected acute myocardial infarction: a meta-analysis of randomized clinical trials. *Heart*. 2018; Epub ahead of print.

## **Disclosures**

Ezekowitz and Khoshnood report no relevant conflicts of interest.