



Taking the Air Out of Oxygen Supplementation in Individuals With Diabetes and Acute Coronary Syndromes

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Oxygen supplementation has been a cornerstone in the initial treatment of individuals with acute coronary syndrome. While consensus for oxygen supplementation exists for patients with hypoxia, oxygen supplementation has also been routinely used in those presenting with acute myocardial infarction (MI) with normal oxygen saturations based on the rationale that oxygen therapy could improve oxygen supply to the ischemic myocardium, thereby reducing the infarct size and complications. Indeed, reports of oxygen supplementation to relieve angina pectoris were described as early as 1900 (1). These reports were followed by small studies that suggested benefit with oxygen supplementation in acute MI, but these studies were limited by lack of randomization and unblinded end point ascertainment (2–4). Nonetheless, supplemental oxygen was incorporated into routine clinical practice, as evidenced in 2007 cardiology practice guidelines that recommended routine supplemental oxygen to all patients with acute coronary syndrome during the first 6 h after presentation (5). This widespread belief in oxygen was highlighted in a survey of emergency department, cardiology, and ambulance staff in which 98% of respondents reported using oxygen supplementation

for suspected MI and 55% believed oxygen reduced the risk of death (6).

Despite the ubiquitous use of oxygen, there were early reports of potential harm with high-dose oxygen supplementation in individuals with acute MI (7). Over 40 years ago, the first randomized trial of high-dose oxygen in patients with an acute MI demonstrated that oxygen-treated patients had increased cardiac enzymes and a trend toward increased mortality compared with those not treated with oxygen (8). More recently, a study of 441 patients with ST-segment elevation MI, but without hypoxia, demonstrated that supplemental oxygen therapy (8 L/min) was associated with increased markers of myocardial injury, increased rate of early MI, and larger myocardial infarct size at 6 months compared with ambient air (9). In this setting, the DETO2X-AMI (Determination of the Role of Oxygen in Suspected Acute Myocardial Infarction) trial was performed (10). The DETO2X-AMI trial was an open-label, registry-based clinical trial that randomized 6,629 patients with suspected acute MI and oxygen saturation $\geq 90\%$ to receive supplemental oxygen at 6 L/min for 6–12 h or ambient air (10). While supplemental oxygen prevented hypoxemia compared with the control group, supplemental oxygen did not

improve the primary outcome of 1-year mortality (hazard ratio 0.97, 95% CI 0.79–1.21; $P = 0.80$). A subsequent meta-analysis of randomized clinical trials, including the DETO2X-AMI trial, demonstrated that supplemental oxygen therapy did not reduce the risk of in-hospital (odds ratio 1.11, 95% CI 0.69–1.77) or 30-day mortality (odds ratio 1.09, 95% CI 0.80–1.50) in those with suspected acute MI without hypoxia (11).

In this issue of *Diabetes Care*, Nyström et al. (12) present results of a prespecified analysis of the DETO2X-AMI trial among individuals with diabetes and a confirmed MI, a particularly high-risk cohort. Of the 5,010 individuals with confirmed MI enrolled in the DETO2X-AMI trial, 19% had diabetes. In the group with diabetes, the incidence of the primary composite outcome (total mortality, rehospitalization for MI, or rehospitalization for heart failure) at 1 year and the incidences of individual components of the composite outcome were similar in those treated with supplemental oxygen compared with ambient air. There was no statistical interaction between treatment and diabetes status for any of the outcomes. However, although not observed in individuals without diabetes and not statistically significant, the short-term adverse outcomes were

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See accompanying article, p. 2032.

17. Norouzirad R, Gholami H, Ghanbari M, et al. Dietary inorganic nitrate attenuates hyperoxia-induced oxidative stress in obese type 2 diabetic male rats. *Life Sci* 2019;230:188–196
18. Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus: atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus – mechanisms, management, and clinical considerations. *Circulation* 2016;133:2459–2502
19. Smit B, Smulders YM, van der Wouden JC, Oudemans-van Straaten HM, Spoelstra-de Man AME. Hemodynamic effects of acute hyperoxia: systematic review and meta-analysis. *Crit Care* 2018;22:45
20. Priestley J. *Experiments and Observations on Different Kinds of Air*. Vol 2. London, St. Paul's Church-Yard, 1775
21. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Rev Esp Cardiol (Engl Ed)* 2017;70:1082