UNDERSTANDING THE ROLE OF OXYGEN IN ACUTE CORONARY SYNDROMES

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The routine administration of oxygen to patients presenting with features of acute coronary syndrome (ACS) is a practice that is deeply embedded in the routine of frontline health care professionals, and it has been a primary intervention for persons with ACS for more than 100 years. It is noteworthy that this tradition was supported by the American Heart Association (AHA) from 1975 through 2005 in the form of recommendations for treatment, and it was supported by the American College of Cardiology through 2007 as well. This practice of administering oxygen has been supported by research completed during the past century, which concluded that supplementary oxygen could diminish the size of myocardial ischemic injury resulting from ACS. However, the conclusions derived from the aforementioned research were generalized from animal models. More recently, members of the scientific community have questioned these generalizations and the validity of the studies, noting the vast differences in the 2 species (dogs and humans) in terms of coronary anatomy, collateral circulation, natural disease state, and hemodynamic responses. The routine administration of oxygen for all patients presenting with symptoms suggestive of ACS has become a treatment of tradition that may not be supported by scientific evidence. In fact, the 2010 Advanced Cardiac Life Support guidelines recommend oxygen supplementation for uncomplicated ACS only with an oxyhemoglobin saturation of \( \leq 94\% \) or with signs and symptoms suggestive of respiratory distress.

Less familiar to frontline practitioners are the critiques surrounding the 1970s recommendation to routinely administer oxygen to all patients presenting with suspected ACS. In addition to the generalization of the original animal studies to human cases, several studies documented the potentially harmful effects of administering supplementary oxygen in the absence of hypoxemia. In addition, no conclusive study has been performed to indicate that the administration of oxygen is beneficial in the reduction of myocardial ischemic pain. Strangely, this information has not captured much attention in the practice setting in terms of deterring the routine administration of oxygen. The query raised over the years relates to the administration of supplementary oxygen to persons who are normoxic and the potential to induce a state of hyperoxia that could result in potentially negative cardiovascular effects.

Hypoxia has been described by some researchers as an oxyhemoglobin saturation of less than 90% and by others as less than 94%. For the purposes of this article, we consider persons with an oxyhemoglobin saturation of 94% or greater to be normoxic. The aim of this article is to review the evidence available and clarify for frontline practitioners the indications for supplementary oxygen and the potential harmful effects of hyperoxia as it relates to ACS.

Background and Context

ACS is an umbrella term used to describe any group of clinical symptoms compatible with acute myocardial ischemia ranging from ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or unstable angina. ACS is almost always associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the related artery. Myocardial infarction results when heart muscle cells die as myocardial oxygen demand exceeds oxygen supply. Occasionally this phenomenon can happen when the oxygen-carrying capacity of the blood is reduced, as is the case with pulmonary edema, and it is typically evident by respiratory distress and/or oxyhemoglobin hypoxemia. More commonly, however, the delivery of otherwise well-oxygenated blood is prevented from perfusing the affected area of the myocardium. This phenomenon results when the ruptured plaque and fibrin clot create a sudden occlusion of the affected coronary artery, causing an acute decrease in coronary perfusion and ischemic cell death for a localized area of the myocardium. You may wonder why, if the blood is well oxygenated, the
administration of supplemental oxygen is routine practice for health care providers. A common medical view is that applying supplementary oxygen to patients experiencing ACS will increase coronary perfusion pressures, thereby increasing myocardial oxygenation and decreasing myocardial necrosis.8

A historical review appears to conclude that the medical view is primarily unproven.8,10,13 An exhaustive literature review of use of oxygen in persons with ACS finds many research examples highlighting the potential harm of supplemental oxygen in the absence of hypoxemia; however, few studies were found in support of its use. In the 1970s, 2 studies indicated a benefit with the use of oxygen in the situation of angina or myocardial infarction.10 One study10 reports that the threshold to pacing-induced angina is improved with oxygen therapy, although a similar benefit could not be demonstrated with exercise-induced angina. Another study suggested that the administration of oxygen therapy to patients experiencing a myocardial infarction may reduce ischemic injury, based on precordial ST segment mapping.10 The aforementioned studies represent the full extent of the clinical evidence for the benefits of oxygen therapy during myocardial infarction in the absence of hypoxemia. Unfortunately, the lack of a randomized controlled design, standardization of the duration of oxygen therapy, or blinding in the ST measurements limits the significance of these findings. The articles highlighting the potential harm for patients when applying supplemental oxygen to persons who are normoxic1,2,8,10,15 all acknowledge a need for more randomized control studies to accurately determine the risk for patients.

Discussion

We have determined that the conflict in recommendations related to the use of supplemental oxygen in the absence of hypoxemia appears to be centered around the following question: Can hyperoxia benefit the patient and reduce the potential harmful effects of the sudden coronary occlusion as history has claimed, or does hyperoxia lead to more harm than good? The benefits of oxygen are scientifically evident for patients presenting with complaints associated with hypoxemia and/or an oxyhemoglobin saturation <94%,1,15 but what about the patients for whom no evidence of hypoxemia exists?

Oxygen can have deleterious implications to ischemic myocardial tissue.1,2,6,15-17 High levels of blood oxygenation (partial pressure of oxygen, arterial [PaO2]) can be toxic to patients experiencing ACS. Levels of oxygenation are dependent on factors such as age, concentration, and length of time exposed to oxygen and barometric pressure. Implications related to hyperoxia are twofold for patients experiencing ACS. First, oxygen is a powerful vasoconstrictor that can reduce cardiac output and blood flow to the coronary arteries,2,15,17 and second, hyperoxia may exacerbate myocardial injury as the result of oxygen free radicals (OFRs).2,17

Hyperoxia has hemodynamic implications for patients experiencing ACS. Hyperoxia causes vasoconstriction and increases both peripheral and systemic vascular resistance, which can reduce cardiac output by decreasing stroke volume.2,15,17 An increase in systemic vascular resistance can increase myocardial oxygen demand, which may cause further damage to already stressed ischemic myocardial tissue. Coronary arteries also are affected by the vasoactive properties of oxygen.2,15 In a study involving 27 patients undergoing elective cardiac catheterization to evaluate chest pain, higher PaO2 levels (>250 mm Hg) decreased myocardial oxygen delivery and were associated with an approximately 40% increase in coronary resistance and an almost 30% decrease in coronary blood flow.17

The second major implication related to hyperoxia in patients experiencing ACS is related to OFRs. OFRs are normal by-products in aerobic cellular metabolism.16,18,19 OFRs are known to be cytotoxic and cardiotoxic, compounding the destruction of myocardial cells related to the inadequate perfusion caused by ACS.16,19,20 OFRs typically are managed by OFR scavengers, which help stabilize the toxic effects of OFRs and therefore minimize cardiac cell damage.16,18,20 In patients experiencing ACS, OFRs are thought to increase during the ischemic event and the reperfusion of the myocardium as damaged myocardial cells trigger a normal inflammatory response. This inflammatory response impairs the function of OFR scavengers, which can increase cardiac cell damage.16,19,20

In addition to the detrimental implications related to oxygenation, the 2010 Advanced Cardiac Life Support guideline changes also are related to respiratory physiology, specifically the oxyhemoglobin dissociation curve. The oxyhemoglobin dissociation curve describes the PaO2 and the arterial oxygen saturation (SpO2). The curve is utilized to understand hemoglobin’s affinity (binding power) for oxygen18-21 and essentially has 2 segments, a flat segment and a sloping segment (Figure).

The flat segment represents normoxemia with a PaO2 range of 60 to 100 mm Hg. In this segment a relatively
large change in $\text{PaO}_2$ causes relatively little change in $\text{SpO}_2$. If, for example, a patient’s $\text{PaO}_2$ drops from 100 to 60 mm Hg, the $\text{SpO}_2$ will reflect a small change from 97% to 90%. The sloping segment of the curve varies from the flat segment whereby a relatively small change in $\text{PaO}_2$ will cause a significant decrease in $\text{SpO}_2$ levels. If, for example, a patient is experiencing mild hypoxemia and $\text{PaO}_2$ levels drop from 60 to 40 mm Hg, a larger change is reflected in the $\text{SpO}_2$ readings from 90% to 70%. The affinity that oxygen has for hemoglobin can change with varying underlying health conditions; this change causes the curve to shift. A shift in the curve will either cause hemoglobin to hold onto oxygen and not release it to the body tissues, or it will cause it to release oxygen too easily to body tissues. Understanding these concepts of the oxyhemoglobin curve helps us to address treatment goals discussed later in this article (Table 1).

**Recommendations for Nurses Working in the Emergency Department**

It is important for ED nurses to understand the following elements when caring for patients with ACS: circumstances requiring supplementary oxygen, the concentration of oxygen required, and the most effective tool for monitoring oxygenation in the emergency department. Understanding these elements will ensure that we balance oxygen supply with oxygen demand for patients experiencing ACS and that we are not providing excess concentrations of oxygen to patients who do not require this treatment.

**TABLE 1**

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<tr>
<td>$\text{SpO}_2$: Clinical measure of oxygen bound to hemoglobin; reflects arterial oxygen saturation $^{21-23}$</td>
</tr>
<tr>
<td>$\text{PaO}_2$: Clinical measure of oxygen dissolved in blood plasma $^{21,23}$</td>
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<td>Hyperoxia: An increase in circulating blood oxygen tension or $\text{PaO}_2$. As per the American Heart Association, hyperoxia is a $\text{PaO}_2$ of $&gt;300$ mm Hg with an $\text{SpO}_2$ of 100%. $^{22}$</td>
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<td>Hyperoxygenation: The application of oxygen concentrations that exceed those required to prevent hypoxemia $^{15-22}$</td>
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<td>Hypoxemia: A decrease in circulating blood oxygen tension or $\text{PaO}_2$ (partial pressure of oxygen). $^{23}$ Hypoxemia is a $\text{PaO}_2$ of $&lt;60$ mm Hg or an $\text{SpO}_2$ (saturation of oxygen) $&lt;90%$.</td>
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Application of supplementary oxygen for patients presenting with symptoms suggestive of ACS should be based on clinical knowledge and judgment rather than tradition. Oxygen administration would be indicated when patients presenting with ACS have signs and symptoms of hypoxemia or pulmonary edema, or have a pulse oximetry reading of less than 94%. $^{11,22}$

According to the AHA, ED nurses have several options when administering oxygen to patients presenting with ACS, including a nasal cannula and a simple face mask (Table 2), if the patient has a patent airway, spontaneous respirations, satisfactory work of breathing (ie, rate, depth, and no accessory muscle use), minimal respiratory or oxygenation problems, and a normal arterial oxyhemoglobin saturation greater than 94%. $^{11,22}$ In cases in which patients with ACS have a normal ventilation rate and work of breathing, each liter per minute of nasal oxygen increases the fraction of inspired oxygen approximately 4%. $^{18}$

Non-rebreather face masks are recommended for patients who are seriously ill with a patent airway; spontaneous respirations have adequate depth of ventilation and require high concentrations of oxygen. $^{18}$

ED nurses must use assessment skills to determine if interventions related to oxygenation are balancing oxygen supply with demand. Frequent reassessment of patients experiencing ACS will be required to ensure that adequate oxygenation levels are achieved and hyperoxia and hypoxemia are avoided. Because of the invasive nature of arterial blood sampling, $\text{SpO}_2$ monitoring is the best tool ED nurses can use to assess the oxygenation status of patients experiencing ACS. $^{18}$ The targeted range should be an $\text{SpO}_2$
of greater than or equal to 94%. In a patient experiencing ACS, an SpO2 reading of 94% would indicate a probable PaO2 value of 70 mm Hg. With a PaO2 value of 70 mm Hg, the patient is normoxic and should be on the flat area of the oxyhemoglobin curve, indicating a normal oxygenation status. As previously discussed, small changes in oxygenation in this area of the curve will have little impact on SpO2. Therefore, the administration of oxygen to patients experiencing ACS with an SpO2 of greater than or equal to 94% will have very little impact on PaO2. The delivery of lower concentrations of oxygen (fraction of inspired oxygen) will have little impact in terms of harm or benefit to patients experiencing ACS if they have an SpO2 of equal to or greater than 94%. However, the evidence available indicates that the risks associated with the administration of high-flow oxygen (greater than 10 L) to patients with an SpO2 of greater than or equal to 94% appear to outweigh the potential benefit. More randomized controlled studies are needed to determine the extent of risk for patients.

Conclusion

The routine application of oxygen for all patients presenting with signs and symptoms suggestive of ACS is based on tradition and not scientific evidence. The historical recommendation by the AHA and others for the routine application of oxygen for “all ST-elevation myocardial infarction patients with UA/NSTEMI and uncomplicated STEMI within the first six hours of presentation” appears to have been based on 2 assumptions:

• Increasing arterial oxygen tension decreases the acute ischemic injury and the eventual infarct.
• Observations that some patients with uncomplicated myocardial infarction have hypoxemia due to fluid retention and a ventilation-perfusion mismatch (this is only 10% to 15% of those with acute myocardial infarction). In 2010, the International Liaison Committee on Resuscitation released a major update to the Cardiopulmonary Resuscitation and Emergency Cardiovascular Guidelines. The AHA and the European Resuscitation Council in turn released their interpretations. All these documents have amended the recommendations regarding the routine use of oxygen. Oxygen supplementation for uncomplicated ACS is no longer recommended with oxyhemoglobin saturation of ≥94% because of insufficient data to continue to support its use. In addition, the International Liaison Consortium on Resuscitation acknowledges that some data suggest that hyperoxia could result in oxygen toxicity. Although oxygen applied at nasal cannula may not cause any physiological harm, it also has not proved to lend to any improvement in myocardial perfusion in the absence of hypoxemia.

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REFERENCES


