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UNDERSTANDING THE DISEASE

Understanding preoxygenation and apneic oxygenation during intubation in the critically ill

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The most common adverse event encountered during the intubation of critically ill patients is oxygen desaturation, which is often a harbinger of serious complications such as cardiovascular collapse, anoxic brain injury, and death. It is imperative to attenuate this risk by optimizing preoxygenation prior to intubation. This paper explores the physiology and challenges related to preoxygenation and maintenance of oxygenation during intubation in these high-risk patients.

The purpose of preoxygenation is to maintain hemoglobin saturation despite ongoing oxygen consumption during apnea. This is accomplished in principle by denitrogenating the alveoli so that the functional residual capacity (FRC) serves as an oxygen reservoir, the efficacy of which can be evaluated by the fraction of expired O_2 (FeO_2) (Fig. 1).

The FeO_2 achieved using several methods of denitrogenation has been studied in healthy volunteers and elective surgical patients. Masks that create a tight seal provide the most effective denitrogenation with mean single-breath FeO_2 around 80 % after 3 min, compared to a non-rebreather mask (NRB), which achieves an FeO_2 of 52 % [1, 2]. Interestingly, adding a nasal cannula only improved the FeO_2 in the presence of a mask leak [1, 2]. Maximum exhalation prior to denitrogenation, or taking eight deep breaths in 60 s can accelerate the denitrogenation process [3, 4]. Preoxygenation with high O_2 concentrations in the absence of positive end-expiratory pressure (PEEP) increases the risk of atelectasis due to alveolar denitrogenation. High-flow nasal oxygen during the apneic period, termed apneic oxygenation (ApOx), can augment the efficacy of preoxygenation and theoretically prolongs the time to desaturation by continuously replenishing the oxygen consumed from the FRC. Additionally, high-flow nasal oxygen creates a flow-dependent positive pharyngeal pressure, which prevents the atelectasis associated with denitrogenation [5].

While in healthy individuals preoxygenation and denitrogenation may be synonymous, in critically ill patients preoxygenation must involve more than denitrogenation. First, increased oxygen consumption leads to faster hemoglobin desaturation and reduces the safe apnea time. Second, as the alveolar-arterial [A-a] gradient increases, the oxygen reservoir stored in the FRC is less efficient at saturating hemoglobin. Thus, as the A-a gradient increases, preoxygenation involves addressing arterial oxygen content and delivery rather than denitrogenation alone. This is particularly evident in patients with acute respiratory distress syndrome (ARDS), where extensive alveolar filling results in a functionally smaller area of lung available for gas exchange. The high shunt fraction limits the ability to continuously saturate hemoglobin despite maximal denitrogenation, reflected clinically as a high FeO_2, appropriate oxygen saturation (SpO_2), and a partial pressure of arterial O_2 (PaO_2) near the upper inflection of the oxygen–hemoglobin dissociation curve. While the PaO_2 does not significantly contribute to O_2 content, it is an indication of the efficiency of the alveolar–capillary interface, and thus time to desaturation. In this case the FeO_2 and SpO_2 could both be high, with a PaO_2 indicating the time to desaturation will be short as the reservoir of oxygen in the lungs is effectively inaccessible.

In these patients, 4 min of denitrogenation with a bag-valve mask (BVM) to an FeO_2 of 87 % has been shown

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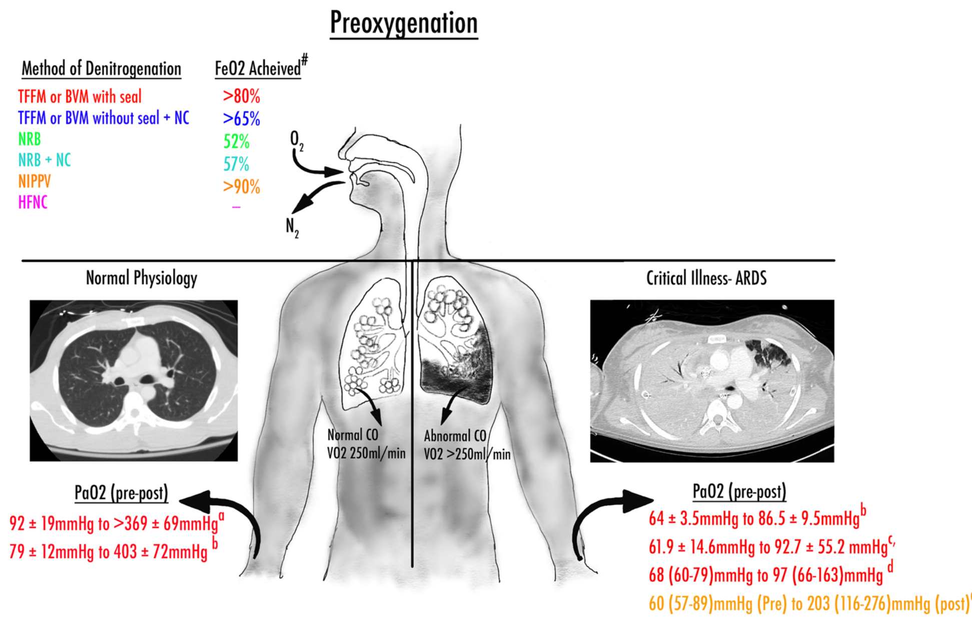

Fig. 1 [#]FeO_2 data from Groombridge et al. [1], Hayes-Bradley [2], Mort [6], and Hanouz et al. [15]. [a]Data from Baraka et al. [4]. [b]Data from Mort [6], [c]Mort et al. [7], and [d]Baillard et al. [8]. *Top panel* preoxygenation prior to intubation includes the process of denitrogenation, the effectiveness of which can be monitored by the fraction of exhaled oxygen (FeO_2). Several methods of denitrogenation have been evaluated, and methods that provide a seal such as a tight-fitting face mask (TFFM) on an anesthesia circuit or bag-valve mask (BVM) perform best, achieving an $FeO_2 > 80$ %. The addition of positive end-expiratory pressure (PEEP) with non-invasive positive pressure ventilation (NIPPV) can achieve an $FeO_2 > 90$ % and additionally prevent the atelectasis associated with denitrogenation with a high fraction of inspired O_2 and zero PEEP. When a leak is present, or when using devices that do not create a seal, such as a non-rebreather mask (NRB), nasal cannula (NC), or a combination of both, denitrogenation is less effective. Denitrogenation and continuous oxygen supplementation through the apneic period (apneic oxygenation, ApOx) with high-flow nasal cannulas (HFNC) have not been studied for FeO_2 achieved, but have resulted in prolonged time to desaturation. HFNCs can be used either in combination with other methods of preoxygenation and left in place during the apneic period, placed after preoxygenation, or used in isolation for both preoxygenation and apneic oxygenation. The partial pressure of arterial oxygen (PaO_2) can assess the degree of shunt physiology and thus the efficiency of the interface between the oxygen reserve in the denitrogenated lung and the alveolar capillary circulation. *Bottom left* In healthy volunteers or in patients undergoing elective surgeries, denitrogenation alone results in adequate preoxygenation. Because of the anatomic redundancy in ventilation-perfusion units, denitrogenating the functional residual capacity (FRC) provides a reservoir of oxygen to continually saturate hemoglobin throughout the apneic period. This is evident by the large changes in the PaO_2 prior to preoxygenation (95 ± 22 mmHg) to after preoxygenation (392 ± 72 mmHg), which can be accelerated by 8 deep breaths in 60 s (92 ± 19 mmHg → 369 ± 69 mmHg). *Bottom right* In critically ill patients, derangements in oxygen consumption, cardiac output, and hemoglobin all contribute to faster desaturation of hemoglobin. In patients with airspace disease, such as acute respiratory distress syndrome (ARDS), the formation of the "baby lung" results in an overall decrease in FRC, and shunt physiology results in inadequate maintenance of hemoglobin saturation during apnea. The FRC can be denitrogenated effectively, achieving a high FeO_2; whereas, physiologic shunt results in poor interface between the smaller FRC and the alveolar capillary blood flow. Alveolar recruitment with PEEP can increase FRC size, resulting in reduced shunt fraction and significantly improved preoxygenation, reflected as an increased PaO_2. Pulmonary vasodilators, such as inhaled nitric oxide, may be useful to improve ventilation–-perfusion mismatch in patients with refractory hypoxemia

to result in poor overall preoxygenation with only minimal PaO_2 change [6]. Doubling the time to 8 min resulted in no significant improvement in preoxygenation, with only 22 % achieving a PaO_2 greater than 100 mmHg and 24 % worsening their PaO_2 [7]. In a study in patients with hypoxemic respiratory failure comparing a non-rebreathing BVM for 3 min to non-invasive positive pressure ventilation (NIPPV) with 5 cmH_2O of PEEP, NIPPV achieved a higher mean PaO_2 (Fig. 1) [8]. The improved PaO_2 reflects a decreased shunt fraction from alveolar recruitment thus improving the alveolar–capillary interface.

The addition of ApOx in emergency department patients has been shown to increase first-pass success without hypoxemia, presumably by increasing the duration of the first attempt without desaturation [9]. In ICU patients with hypoxemia, data have been more variable. Denitrogenation with 60 L/min by high-flow nasal cannula (HFNC) with the cannula left in place for ApOx was compared to an NRB mask at 15 L/min and a higher median lowest saturation was found with HFNC [10]. However, a second randomized study found no difference with the same comparison (NRB at 15 L/min or HFNC at

60 L/min for 4 min) in patients with more severe hypoxemia [11]. In a randomized trial in the ICU, there was no difference in desaturation when using ApOx, although the flow rate used was only 15 L/min and preoxygenation techniques were variable [12]. In a porcine model of ARDS, ApOx maintained saturations greater than 60 % in most animals for 10 min while without ApOx they desaturated to less than 60 % in under 2 min [13]. However, the more severe the shunt fraction was, the faster the desaturation occurred.

Interpretation of preoxygenation data in critically ill patients is difficult for multiple reasons. First, performing the intubation precludes evaluating the physiologic endpoint, time to desaturation. Second, the surrogate outcome of desaturation during intubation does not have a standard definition. Additionally, there are no data to indicate what saturation can be tolerated by the brain and cardiovascular system during intubation, and for what duration. Third, in patients with a high A-a gradient, neither FeO_2 nor SpO_2 indicates the duration of safe apnea, yet these are the most commonly reported outcomes. On the basis of the available data, we offer the following recommendations:

1. "Preoxygenation" should be defined as the initiation of denitrogenation to the initiation of mechanical ventilation and thus includes the apneic period.
2. Denitrogenation should begin with maximum exhalation followed by high-flow oxygen administration with a tight-fitting mask for at least 3 min. In the presence of a mask leak, a nasal cannula should be added.
3. In patients with a high A-a gradient, preoxygenation with NIPPV should be performed for at least 3 min for alveolar recruitment. Promising pilot data suggest that HFNC may be useful as well [14].
4. ApOx efficacy depends on denitrogenation adequacy, the A-a gradient, and the degree of shunt. ApOx performed with an HFNC capable of 40–60 L/min may be effective and, if not available, a nasal cannula at greater than 15 L/min could be added after adequate denitrogenation. NIPPV by nasal mask can provide similar flows and the addition of positive pressure when the mouth is closed.

All airway mangers intubating the critically ill should be intimately familiar with these concepts and understand their application to optimize oxygenation before and during intubation to maximize the safety of the procedure.

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Compliance with ethical standards

Conflicts of interest

None for all authors.

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