Permissive Hypoxemia
Is It Time To Change Our Approach?

To the Editor:

Ahmed et al1 reported an interesting case of Wegener granulomatosis with diffuse alveolar hemorrhage in a 26-year-old woman. The patient was urgently intubated, sedated, paralyzed, and maintained on 100% oxygen and a positive end-expiratory pressure as high as 18 cm H2O. Despite the use of different modes of ventilation, including volume control, pressure control with inverse inspiratory/expiratory ratio, and high-frequency oscillatory ventilation, refractory hypoxemia persisted (arterial oxygen saturation [SaO2] < 80%), and the decision was made to start extracorporeal membrane oxygenation (ECMO). The patient seems to have fulfilled the blood gas criteria for ECMO. However, I am interested to know if there was any evidence of tissue hypoxia prior to the initiation of ECMO.

In general, criteria for ECMO are the existence of severe hypoxemia not responding to maximal conventional therapy. Most if not all ventilatory and nonventilatory strategies, including ECMO, focus primarily on the maintenance of satisfactory arterial oxygenation (often defined as an SaO2 > 90%), regardless of the adequacy of tissue oxygenation. It is often assumed that acute hypoxemia is poorly tolerated by critically ill patients because of increased risk of tissue hypoxia and death. It must be emphasized however, that tissue oxygenation is determined not only by SaO2 but also by hemoglobin concentration, cardiac output, oxygen affinity of hemoglobin, oxygen extraction, and metabolic demand of the body.2,3 Therefore, because of the presence of several factors that determine oxygen delivery and consumption, SaO2 alone cannot be expected to be a sensitive index of tissue oxygenation. To date, no large prospective randomized trial has been published to evaluate the relationship between acute hypoxemia, tissue oxygenation, and clinical outcome in critically ill patients and to demonstrate to what extent could such a relationship be modified by other parameters of oxygen delivery and consumption such as hemoglobin affinity and oxygen demand of the body.

As a result of the widely used lung protective ventilation, many patients with ARDS are now prone to hypercapnia and respiratory acidosis that can promote oxygen delivery and improve tissue oxygenation (due to right shift of oxyhemoglobin dissociation curve),4 although the SaO2 may be relatively low. In addition, oxygen demand and consumption are often reduced in patients who receive mechanical ventilation because of sedation, muscle paralysis, and decreased oxygen cost of breathing.5 The beneficial effects of permissive hypercapnia, sedation, and muscle paralysis on oxygen delivery and consumption may partly explain why arterial hypoxemia is not necessarily associated with tissue hypoxia. In 1984, Lund et al6 reported a case of severe hypoxemia (PaO2 < 30 mm Hg) in a patient with ARDS who had no evidence of tissue hypoxia. Therefore, it may be difficult to determine a critical value of SaO2 that can define tissue hypoxia in all ICU patients, irrespective of the other parameters of tissue oxygenation. Instead, it may be more appropriate to assess tissue hypoxia in each individual patient (with blood lactate or mixed venous oxygen saturation) rather than using SaO2 as a surrogate marker of tissue oxygenation.

The concept that hypoxemia is probably well tolerated by ICU patients is further supported by the fact that multiorgan failure rather than tissue hypoxia is the leading cause of death in patients with ARDS. Interestingly, although refractory hypoxemia is the hallmark of ARDS, only a minority of patients who die do so because of respiratory failure.7-10 Ventilator-induced lung injury (including oxygen toxicity, volutrauma, and biotrauma) rather than hypoxemia may therefore explain the high incidence of multiorgan failure and death in patients with ARDS. The mortality rate from ARDS is approximately 40 to 50%.11-13 However, in a recent study,14 the mortality rate as low as 26% was reported. In the ARDS Network trial, lung-protective ventilation with low tidal volume has been shown to result in substantial reduction in mortality in patients with ARDS.15 It may be of interest to mention that improved outcome in the low tidal volume group was not due to improved arterial oxygenation. However, the higher mortality in patients who received large tidal volume ventilation did not result from hypoxemia and tissue hypoxia but probably from multiorgan failure induced by alveolar overdistension and biotrauma.

An important lesson to learn from the ARDS Network trial is that clinical outcome in ARDS is probably determined by the ability to avoid ventilator-induced complications rather than to improve arterial oxygenation. Over many years, maintenance of adequate arterial oxygen content (by improving oxygen saturation and optimizing hemoglobin concentration) has been a mainstay of supportive management of critically ill patients. In a large multicenter randomized controlled trial16 that compared restrictive transfusion strategy (hemoglobin, 7 to 9 g/dL) vs a liberal strategy (10 to 12 g/dL), it has been demonstrated that RBC transfusion used to augment oxygen delivery did not offer any survival benefit in critically ill patients with normoemia when the hemoglobin concentration was > 7 g/dL. The Canadian trial has clearly shown that "permissive anemia" can be remarkably tolerated by critically ill patients. I think the most important lesson from the Canadian trial is the recognition that lowering of arterial oxygen content, as a result of anemia, is not necessarily associated with tissue hypoxia and death. However, it is not clear whether a reduction of oxygen content due to mild-to-moderate hypoxemia can also be well tolerated. Therefore, more studies are needed to compare a restrictive strategy of arterial oxygenation or permissive hypoxemia (SaO2 maintained between 82% and 86%) to a liberal oxygenation strategy (SaO2 maintained between 88% and 92%) in patients with ARDS and other diseases characterized by refractory hypoxemia.

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To the Editor:

Preferences in COPD Patients

On Depression, Antidepressant Medications, and Resuscitation Preferences in COPD Patients

To the Editor:

In their excellent article (January 2005),1 Dr. Stapleton and colleagues described the association of high depressive symptoms on the Center for Epidemiologic Studies-Depression (CES-D) scale with a lower preference for cardiopulmonary resuscitation (CPR) in patients with COPD. Approximately 36% of their study subjects reported a history of clinical depression as a current coexisting illness. It is not clear why the authors did not examine the association between end-of-life preferences and the presence of self-reported depression given that clinical depression was already diagnosed; the presence of high depressive symptoms measured by the CES-D indicates possible depression. I thus wonder if the authors would have had similar results if self-reported clinical depression was used as a predictor of treatment preferences for CPR and mechanical ventilation. Reanalyzing their data using self-reported depression may also help in explaining the discrepancy in their finding of a lower preference for CPR and a similar preference for mechanical ventilation by subjects with CES-D scores ≥ 16 when compared to those with scores CES-D < 16.

In their discussion, the authors rightly suggest that patients responding to antidepressant medications might change their end-of-life preferences as their moods improved. In view of this suggestion, it would also be important if the authors could analyze their data examining whether the preference rates for CPR among the depressed COPD patients might change with adjustment for antidepressant medication use in the multivariate analyses. Adjustment for antidepressant medication use might lend further support to the need for end-of-life preferences reassessment after an adequate trial of antidepressants. In addition to improving mood, antidepressant medications may have additional benefits for other common COPD comorbidities: reduction of tobacco craving, palliation of subjective dyspnea, improvement of appetite with weight loss reversal, and lowering of anxiety symptoms.2–4 The nihilistic attitude fostered by depressive symptoms and other common psychological comorbidities in COPD patients may dissipate with antidepressant use, possibly leading to a more informed decision regarding end-of-life care preferences. Given the high prevalence of depression in the COPD population, screening for (and early treatment of) depression in these patients should be part of routine care, as antidepressant use might improve their overall quality and quantity of life. A controlled trial of the impact of antidepressants on overall well-being and survival of COPD patients with depression is long overdue.

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REFERENCES


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