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Update in Management of Severe Hypoxemic Respiratory Failure

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Mortality related to severe-moderate and severe ARDS remains high. We searched the literature to update this topic. We defined severe hypoxemic respiratory failure as Pao_2/Fio_2 < 150 mm Hg (ie, severe-moderate and severe ARDS). For these patients, we support setting the ventilator to a tidal volume of 4 to 8 mL/kg predicted body weight (PBW), with plateau pressure (Pplat) ≤ 30 cm H_2O, and initial positive end-expiratory pressure (PEEP) of 10 to 12 cm H_2O. To promote alveolar recruitment, we propose increasing PEEP in increments of 2 to 3 cm provided that Pplat remains ≤ 30 cm H_2O and driving pressure does not increase. A fluid-restricted strategy is recommended, and nonrespiratory causes of hypoxemia should be considered. For patients who remain hypoxemic after PEEP optimization, neuromuscular blockade and prone positioning should be considered. Profound refractory hypoxemia (Pao_2/Fio_2 < 80 mm Hg) after PEEP titration is an indication to consider extracorporeal life support. This may necessitate early transfer to a center with expertise in these techniques. Inhaled vasodilators and nontraditional ventilator modes may improve oxygenation, but evidence for improved outcomes is weak.

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ARDS, a life-threatening condition, is an important cause of acute hypoxemic respiratory failure and accounts for approximately 10% of ICU admissions and 25% of patients who require mechanical ventilation.[1] Currently, there is controversy about the management of severely hypoxemic patients, both in the selection of rescue strategies and the sequence in which they are used. To provide greater clarity in the management of such patients, we conducted a PubMed search (severe hypoxemic respiratory failure, prevention of ARDS, ventilator management, recruitment

ABBREVIATIONS: APRV = airway pressure release ventilation; ΔP = driving pressure; ECMO = extracorporeal membrane oxygenation; HFOV = high-frequency oscillatory ventilation; HFPV = high-frequency percussive ventilation; NIV = noninvasive ventilation; NMBA = neuromuscular blocking agent; PBW = predicted body weight; PEEP = positive end-expiratory pressure; PP = prone positioning; Pplat = plateau pressure; P-SILI = patient self-inflicted lung injury; RCT = randomized controlled trial; RHC = right heart catheterization; RV = right ventricular; VV ECMO = venovenous extracorporeal membrane oxygenation

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maneuver, ECMO, prone positioning, neuromuscular blocking agents, inhaled prostaglandins, nitric oxide, nutrition, and ARDS), limited to the past 6 years to provide an update for our previously published papers.[2,3] This search was supplemented by appropriate cross-references and our individual familiarity with the topic. Through this narrative review, we aim to provide a concise overview of the definition, diagnosis, recognition, prevention, and treatment of severe hypoxemic respiratory failure.

Definition of Severe Hypoxemic Respiratory Failure

The Berlin definition incorporates the timing and origin of pulmonary edema and categorizes severity based on the degree of hypoxemia with a minimum positive end-expiratory pressure (PEEP) of 5 cm H_2O.[4] Severe ARDS is defined as a $Pao_2/Fio_2 \leq 100$ mm Hg, and moderate ARDS is defined as a Pao_2/Fio_2 of 100 to 200 mm Hg.[2] Several recent studies[5,6] have focused on patients with ARDS in whom the Pao_2/Fio_2 is < 150 mm Hg (severe-moderate and severe ARDS) as the population most likely to respond to interventions such as prone positioning (PP) and neuromuscular blockade. Consistent with these trials and for the purpose of this review, we define severe hypoxemic respiratory failure as a Pao_2/Fio_2 of < 150 mm Hg.

Impact of Severe ARDS

Increased ventilator days, length of ICU stay, and mortality as high as 52% have been reported in severe ARDS.[4] Among patients with ARDS, the prevalence of severe hypoxemic respiratory failure ($Pao_2/Fio_2 <$ 100 mm Hg) is about 23%, with a 46% mortality.[7] Conversely, many patients with mild ARDS go unrecognized and therefore fail to receive appropriate lung-protective ventilation.[7] In such cases, ventilator-induced lung injury may perpetuate lung damage.

Prevention of ARDS

Strategies to prevent ARDS should be used whenever possible. The Lung Injury Prediction Score was developed to stratify patients at high risk for ARDS. Sepsis and pneumonia are two high-risk conditions that predispose to ARDS.[8,9] The Checklist for Lung Injury Prediction[8] was developed to allow earlier recognition of patients at high risk for the development of lung injury for the purpose of instituting early preventive measures. This includes restrictive blood transfusions, appropriate and timely antimicrobial agents, diligent perioperative care, adherence to lung-protective ventilation, aspiration precautions, and appropriate management of shock, pancreatitis, and trauma.

The term patient self-inflicted lung injury (P-SILI) was recently introduced.[10] In spontaneously breathing patients with a high respiratory drive, there may be large tidal volumes and potentially injurious transpulmonary pressure swings. This can occur with pressure control, pressure support, airway pressure release ventilation (APRV), and even with noninvasive ventilatory support. Due to pendelluft, a strong effort can induce intrapulmonary redistribution of gas, even before the start of inflation.[11] Due to the potential for P-SILI, clinicians must be cognizant of adverse effects from excess spontaneous breathing in patients with moderate and severe ARDS and consider remedial measures such as sedation and paralysis.[12]

Ventilatory Strategies

Ventilator-Induced Lung Injury and Prevention

For patients with severe hypoxemic respiratory failure, invasive ventilation is preferred over noninvasive ventilation (NIV), as poor outcomes have been reported in patients treated with NIV.[13] Provided that the tenets of lung-protective ventilation are followed, usually volume-control or pressure-control ventilation can be used.[14,15] Setting limits to tidal volume and to alveolar distending pressure should be routinely performed.[16] Specifically, the tidal volume target should be 4 to 8 mL/kg predicted body weight (PBW)[17] and reduced to as low as 4 mL/kg PBW if plateau pressure (Pplat) targets are not achieved. Pplat should not exceed 30 cm H_2O provided that chest wall effects are normal. When the chest wall exerts a collapsing effect on the lungs (eg, morbid obesity, abdominal hypertension, chest wall deformity), Pplat $>$ 30 cm H_2O might be safe provided that transpulmonary pressure is acceptable. Gattinoni et al[18] proposed that transpulmonary pressure (stress) should not exceed 22 to 23 cm H_2O. Given the inhomogeneity in the lungs of patients with ARDS and the magnifying effect of stress raisers, a conservative approach of limiting transpulmonary pressure to $<$ 20 cm H_2O seems reasonable. In the setting of elevated pleural pressure, esophageal manometry might be useful to establish a safe ventilating pressure. The authors of recently published evidence-based clinical practice guidelines recommend that patients with ARDS receive mechanical ventilation with strategies that limit tidal volumes (4-8 mL/kg PBW) and Pplat ($<$ 30 cm H_2O)

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