CHEST

Mechanical Ventilatory Support in Potential Lung Donor Patients

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Lung transplantation reduces mortality in patients with end-stage lung disease; however, only approximately 21% of lungs from potential donor patients undergo transplantation. A large number of donor lungs become categorized as unsuitable for lung transplantation as a result of lung injury around the time of brain death. Limiting this injury is key to increasing the number of successful lung procurements and subsequent transplants. This narrative review by a working group of pulmonologists, respiratory therapists, and lung transplant specialists elucidates principles of mechanical ventilatory support that can be used to limit lung injury in potential lung donor patients and examines the implementation of protocolized strategies in enhancing the procurement of donor lungs for transplantation. CHEST 2014; 146(1):220-227

ABBREVIATIONS: APRV = airway pressure release ventilation; IBW = ideal body weight; NPE = neurogenic pulmonary edema; PCV = pressure-control ventilation; PEEP = positive end expiratory pressure; Phigh = high airway pressure; PIP = peak inspiratory pressure; Plow = low airway pressure; SALT = San Antonio Lung Transplant; VCV = volume-control ventilation; V_T = tidal volume

Lung transplantation has proven to be a lifesaving procedure and an established therapeutic option for patients with end-stage lung disease. Until recently, the demand for lung transplantation greatly exceeded the supply of donor lungs. Although the gap between donors and those waiting for transplant has narrowed, further advancements in lung donation could result in reductions in both time and mortality on the waiting list. In 2011, only about 21% of lungs from donors were transplanted.[1] However, the majority of donor lungs (64.4%) were deemed incompatible because of the lung damage that generally predates but in some instances supervenes following brain death.[1] This effect may be compounded by complications emanating during the treatment of potential lung donor patients, including the mechanical ventilation strategies selected. Advances in lung donor patient management may obviate these detrimental effects and thereby enhance the procurement of donor lungs for transplantation.

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Pathophysiologic Changes Affecting the Lungs After Brain Death

Prior to brain death, donor lungs may have been damaged from trauma, resuscitation

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maneuvers, mechanical ventilation, aspiration of blood or gastric content, or pneumonia.[2,3] After brain death, lungs are at a risk for the development of lung injury resulting from the onset of neurogenic pulmonary edema (NPE).[2,3] Although well recognized as a sequela to CNS injury, NPE remains poorly understood and underdiagnosed.[4]

The manner in which brain death leads to NPE is postulated to involve complex hemodynamic and inflammatory pathophysiologic mechanisms,[4,5] triggered by a transient sympathetic storm,[2,3] as well as an alteration in pulmonary capillary permeability also resulting from direct sympathetic stimulation.[2,3] The overall degree of pulmonary edema that can occur has been demonstrated in animal studies, revealing that up to 72% of the circulating blood volume may be redistributed within the lungs and left side of the heart following brain death.[6]

A secondary cardiovascular collapse may also follow the aforementioned sympathetic storm due to a loss in sympathetic tone.[7,8] Because of the preexisting NPE, hemodynamic management becomes challenging, as fluid loading to correct hypotension carries the risk of worsening oxygenation.[9] Furthermore, brain death is also believed to induce various inflammatory and immunologic responses, which in turn trigger a systemic inflammatory response syndrome associated with the release of cytokines. This further stimulates neutrophilic infiltration that can incite damage to the lung parenchyma, potentially increasing the risk of the development of the ARDS and consequently primary graft dysfunction.[2,3,7]

Prevention of Lung Injury in the Potential Lung Donor Patient

By the time the lungs are ready to be harvested, potential lung donor patients may have developed pulmonary edema as a result of systemic inflammatory responses occurring in the periods before and after brain death pronouncement. This may predispose the donor lungs to ventilator-induced lung injury, which in turn may further compound the problem of hypoxemic respiratory failure. Donor gas exchange before procurement has been shown to be associated with early and long-term outcomes; furthermore, a steep increase in the relative risk of death occurred with donor $Pao_2/Fio_2 < 350$ mm Hg.[10] It is unclear how low the Pao_2/Fio_2 can be without affecting transplant outcome, as ratios < 300 mm Hg have been reported.[11,12] Nonetheless, appropriate oxygenation in potential lung donor patients is believed to be the most important indicator for the functional quality of the lung[8] and is, therefore, a required criterion in most transplant programs.[13-15] It is, therefore, no surprise that for many years, the majority of lungs were deemed unsuitable for transplantation, having not met the ideal criteria of oxygenation set forth by expert panel recommendations.[7] These criteria include a clear chest radiograph, a $Pao_2 > 300$ mm Hg on an Fio_2 of 1.0, and a positive end-expiratory pressure (PEEP) equal to 5 cm H_2O.[7]

Use of low tidal volume (Vt) ventilation has been shown to decrease mortality by 9% in patients with ARDS[16]; however, the vast majority of potential lung donor patients do not have ARDS at the time of intubation.[17] Nonetheless, the use of higher Vt ventilation has been associated with an increased likelihood of developing lung injury in patients with normal lung function at the onset of mechanical ventilation[18-21] and in patients with acute brain injury.[22] In a meta-analysis of patients without ARDS, the use of low as opposed to high Vt ventilation was associated with a lower risk of developing ARDS, fewer pulmonary infections, less atelectasis, and reduced mortality.[23] This suggests that low Vt ventilation may be protective in patients with normal lungs following intubation.[24] Consequently, the use of aggressive lung-protective ventilatory management strategies may obviate or reverse conditions such as ventilator-induced lung injury, NPE, and atelectasis in potential lung donor patients.[25] To achieve these goals, the principles of mechanical ventilation are proposed in Table 1.[3]

Lung Transplant Protocols

Studies have shown that with the implementation of a specific and aggressive lung donor patient management protocol, many of the lungs that were previously deemed unsuitable may be salvageable. A few pertinent studies depicting this are summarized.[26-28]

TABLE 1] Principles of Mechanical Ventilation in Potential Lung Donor Patients

Objective	Parameters Adjusted
Prevention of overdistention	Tidal volume 6-8 mL/kg IBW, plateau pressure < 30 cm H_2O
Maintain alveolar recruitment	Adequate PEEP 8-10 cm H_2O
Prevention of oxygen toxicity	Lowest Fio_2 (≤ 0.5) to keep Spo_2 92%-95%

IBW = ideal body weight; PEEP = positive end-expiratory pressure; Spo_2 = oxygen saturation by pulse oximetry.