Ventilator-induced Lung Injury

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KEYWORDS

• Ventilator-induced lung injury • Acute lung injury • Acute respiratory distress syndrome
• Mechanical ventilation • Respiratory mechanics

KEY POINTS

- Prevention of ventilator-induced lung injury (VILI) can attenuate multiorgan failure and improve survival in at-risk patients.
- Clinically significant VILI occurs from volutrauma, barotrauma, atelectrauma, biotrauma, and shear strain. Differences in regional mechanics play an increasingly recognized role in VILI pathogenesis.
- VILI occurs most readily in patients with concomitant physiologic insults (eg, sepsis, trauma, major surgery) that prime the immune system for a cascading response to mechanical lung injury.
- VILI prevention strategies must balance risk of lung injury with untoward side effects from the preventive effort, and may be most effective when targeted to subsets of patients at increased risk.

INTRODUCTION

As with most medical and pharmacologic interventions, mechanical ventilation must be titrated within a therapeutic window, providing the required life-sustaining support while minimizing unintended toxicity. The potential for mechanical ventilation to cause harm was first described in the mid–eighteenth century.[1,2] John Fothergill postulated that mouth-to-mouth resuscitation may be preferable to mechanical ventilation because "the lungs of one man may bear, without injury, as great a force as those of another man can exert; which by the bellows cannot always be determined."[1] More than 250 years later, ventilator-induced lung injury (VILI) was proved definitively to contribute to mortality in patients with acute respiratory distress syndrome (ARDS).[3]

Classically, 4 mechanisms of VILI have been described: barotrauma, volutrauma, atelectrauma, and biotrauma (**Table 1**).[4] Recent recognition that heterogeneous regional mechanics, stress frequency, and pulmonary capillary stress failure may also contribute to VILI has inspired a renewed line of investigation toward personalizing lung-protective ventilation.

CLASSIC MECHANISMS OF VENTILATOR-INDUCED LUNG INJURY

Barotrauma and Volutrauma

In 2000, the landmark ARDS Network trial showed definitively that limiting tidal volume (6 vs 12 mL/kg predicted body weight [PBW]) and plateau airway pressure ($\leq$30 vs $\leq$50 cm H_2O) improves survival in patients with ARDS.[3] This study and a small

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Table 1
Definitions of key terms frequently encountered in the literature

Term	Definition
Atelectrauma	Lung injury caused by high shear forces from cyclic opening and collapse of atelectatic but recruitable lung units
Baby lung	Conceptual model for the reduced volume of nonatelectatic aerated lung available for tidal insufflation and gas exchange in patients with ARDS
Barotrauma	Lung injury caused by high transpulmonary pressure. May occur even at lower airway pressure if pleural pressure is extremely negative (eg, forceful inspiratory effort)
Biotrauma	Additional lung and extrapulmonary organ injury caused by proinjurious inflammatory response to mechanical lung injury
Compliance	Change in volume for a given change in pressure. May refer to respiratory system compliance ($\Delta V/\Delta P_{airway}$), lung compliance ($\Delta V/\Delta P_{transpulmonary}$), or chest wall compliance ($\Delta V/\Delta P_{pleural}$). Respiratory system compliance reflects contributions of both the lung and chest wall, and is often incorrectly labeled as lung compliance in the literature
Elastance	Change in pressure for a given change in volume, also called stiffness. Inverse of compliance
Lung inhomogeneity	Differences in regional lung mechanics caused by mechanically interdependent interalveolar septae shared between aerated alveoli and adjacent fluid-filled or atelectatic alveoli. Results in high regional shear strain. Manifested on CT scan as regions of well-aerated lung adjacent to patchy ground-glass opacities and atelectasis
Shear strain	Angular deformation of an object relative to its resting conformation; eg, if resting object is square, shear strain produces an oblique-angled rhombus
Strain	Change in size/shape of an object relative to its resting size/shape, expressed as ratio of displacement magnitude divided by reference size. Calculation of lung strain in mechanically ventilated patients is controversial because ideal resting size/shape of the diseased lung is unclear
Stress	Internal forces per unit area that balance an external load. Lung stress is represented by the transpulmonary pressure
Transpulmonary pressure	Pressure difference inside vs outside the lung ($P_{TP} = P_{airway} - P_{pleural}$), which is the pertinent distending pressure of the lung. Airway and alveolar pressure are equal at points of zero flow
Volutrauma	Lung injury caused by alveolar overdistension

Abbreviation: Ptp, transpulmonary pressure.

preceding pilot trial[5] brought into clinical practice what had been suggested for decades by preclinical studies: that mechanical ventilatory support with high volumes and pressures can cause preventable morbidity and mortality in critically ill patients.

Lung volume and transpulmonary pressure

For much of the last 30 years, barotrauma (high inflation pressure–mediated lung injury) and volutrauma (overdistension-mediated lung injury) were viewed as distinct, albeit related, entities. In a classic study by Dreyfuss and colleagues,[6] rats were mechanically ventilated using one of 3 strategies: (1) high airway pressures and high tidal volumes, (2) high airway pressures and low tidal volumes, or (3) low airway pressures and high tidal volumes. The high-pressure low-volume strategy was achieved via thoracoabdominal strapping with rubber bands, decreasing chest wall compliance. In contrast, the low-pressure high-volume strategy was achieved via an iron lung (negative pressure ventilator). Animals supported with either high-volume strategy had markedly more severe lung injury compared with animals ventilated with the high-pressure low-volume strategy. Similar findings have been replicated in other animal models,[7–9] leading to the misleading conclusion that volutrauma is more important than barotrauma.[4,6,10]

It is true that high airway pressure per se does not cause VILI, as these studies confirmed. However, the pertinent distending pressure of the lungs is not simply the airway pressure but