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Is Mechanical Power the One Ring to Rule Them All?

Mechanical power has been proposed as the "unifying currency" to quantify risk of lung injury from the mechanical ventilator. Specifically, it has been suggested that the transmission of energy from the ventilator to the lung as potential, kinetic, and heat energy may cause structural changes at both the cellular and tissue levels (1–3). Tidal volume, one key element of the power equation, has been studied extensively; however, although there is physiologic rationale for mechanical power as an integrated measure (flow, pressure, repetitive cycling) (3, 4), there are currently only associations (5–7) between high mechanical power and poor clinical outcomes.

In this issue of the *Journal*, von Wedel and colleagues (pp. 553–562) report on 2,103 surgical patients (2008–2020) transitioning from the operating room (last hour of surgery) to the ICU (first 6 h) (8). Tidal volume and dynamic driving pressures decreased (median: 8.4 to 7.3 ml/kg and 18.5 to 14.0 cm H_2O, respectively), whereas the respiratory rate increased (12 to 17/min), resulting in increased mechanical power. In adjusted analyses, ventilator adjustments yielding a higher mechanical power were associated with a higher 28-day mortality (9.2% with stable mechanical power during transition compared with 12.9% when mechanical power increased). In a secondary analysis, only changes in respiratory rate were significantly associated with 28-day mortality. These findings are tantalizing. First, they reveal the growing usage of lower tidal volumes (and higher respiratory rate) both in the operating room and the ICU, in line with evidence that protective ventilation is associated with reduced postoperative respiratory complications (9, 10). Second, and perhaps more important, they question whether respiratory rate, or cycle frequency, is a critical contributor to ventilator-induced lung injury, an association that has previously been observed in patients with acute respiratory distress syndrome (7).

Taken at face value, these findings challenge the current paradigm of lung-protective ventilation and suggest that ventilator adjustments associated with lower tidal volumes, such as increased respiratory rate, convey risk that must be balanced with the benefit of conventional lung protection. Lung injury after pharmacologically induced increases in minute ventilation also suggests a link with high respiratory rate; however, this was confounded by concomitant increases in tidal volume (11).

As it would require robust data to discard the focus on lower tidal volumes and lower driving pressure, we should interpret this study cautiously and with a full understanding of its limitations. These include the unique characteristics and clinical circumstances of this cohort of patients, the lack of data on other potential contributors such as inspiratory flow, and the inherent limitations of retrospective and observational data.

Although the cohort is large and relatively well characterized, it represents a unique clinical state: the transition from the operating room to the ICU setting. The estimated minute ventilation increased from 6.4 L to 7.7 L, yet Pa_{CO_2} was similar, which is consistent with an increase in CO_2 production once patients reached the ICU, perhaps because of the inflammatory response postsurgery. The transition to ICU is often associated with changes in the usage of neuromuscular blockers and opiates, which may affect end-expiratory lung volume (12). Resulting complex pathophysiologic effects such as maldistribution of aeration and ventilation, end-tidal derecruitment, and increased spontaneous respiratory effort could contribute to lung injury. The observed association may also reflect over distention during the perioperative period with the expected downstream sequelae. Last, these patients have relatively preserved compliance and gas exchange, unlike many patients who are intubated with acute lung injury, which may limit the benefit of further reduction of tidal volumes and plateau pressure (13).

The authors have used a previously validated equation (14) to estimate mechanical power from tidal volume, respiratory rate, peak inspiratory pressure, and positive end-expiratory pressure. However, it is surprising that even a small increase in respiratory rate within a clinically modest range would have a significant impact on mortality, particularly despite a decrease in driving pressure. A commonly used simplified formula of 4 × driving pressure + respiratory rate (7) suggests that driving pressure should be the dominant determinant of outcomes. Perhaps there is less benefit decreasing driving pressure in less injured lungs, or,

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alternatively, respiratory rate may not mediate the association. There are no data presented on ventilator mode, inspiratory flow rate, or flow profile during the study period, despite potentially injurious effects (15, 16). In some calculations, the percent increase in mechanical power is independent of whether the parameter increase is tidal volume, driving pressure or inspiratory flow rate (a 20% parameter increase causing a 37% power increase), but smaller (27% and 5.7%) with either respiratory rate or positive end-expiratory pressure (1). Thus, inspiratory flow changes that accompany changes in respiratory rate may be equally or more important. The authors have also had to utilize peak inspiratory pressure rather than plateau pressure, which was not routinely measured in the perioperative period. Although the authors have done an extensive investigation with recalculation of mechanical power using measured and imputed plateau pressures, these are important limitations.

Finally, the unavoidable limitation of observational studies is the potential for residual confounding. The authors have made admirable attempts to adjust for potential confounders, but unfortunately it is not possible to fully do so in these data and many comparisons are made without the benefit of randomization.

With these limitations, this study is best utilized as motivation for future clinical trials targeting mechanical power rather than an impetus for change in clinical practice. It again raises the important question of whether long-neglected variables such as respiratory rate should be given more attention, and it highlights how much is unknown: What is the optimal way to calculate mechanical power? Is there a safe threshold or an acceptable level of mechanical power? Is the effect of mechanical power or its individual elements linear? What are the mechanisms of harm outside of our traditional understanding of ventilator-induced lung injury? And, perhaps most important, what of all of this is meaningful clinically?

Observational science has brought us this far, but clinical trials are now required. This will require careful design and a pre-specified understanding of potential confounders. Additionally, the small effect size seen in cohort studies such as this, the number of variables contributing to mechanical power, and complex clinical cohorts suggest that clinical trials may need to be sizable to identify a meaningful impact.

In summary, although many are looking to mechanical power as the "One Ring" that will unify the risk of ventilator-induced lung injury, it remains to be seen whether it will rule us all—whether the Gandalf recitation was incorrect or whether we are looking in the wrong Gollum lair! ■

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Neuromuscular Blockade Improves Results in Acute Respiratory Distress Syndrome

A Mechanism May Be Prevention of Expiratory Muscle Activity, Which Allows More Lung Expansion

Neuromuscular blockers are now used in ∼40% of patients with severe acute respiratory distress syndrome (ARDS) (1). Evidence for their use is not unambiguous, however. One large trial found that continuous neuromuscular block for the first 48 hours of the ICU stay improved 90-day mortality in patients with severe ARDS (2), whereas a more recent trial found no survival benefit (3). Possible mechanisms by which neuromuscular blockers improve outcome are preventing vigorous patient effort and thus limiting tidal lung distension, limiting patient–ventilator interactions and improving oxygenation, direct anti-inflammatory effects, or reducing total body oxygen consumption (4–6). Further elucidating these possible mechanisms would help determine which patients might benefit most from neuromuscular block.

Summary of Findings by the Authors

Fortuitously, in this issue of the *Journal*, Plens and colleagues (pp. 563–572) noted that end-expiratory lung volume, estimated with electrical impedance tomography, increased in some patients with ARDS when they were administered muscle relaxants (7). Plens and colleagues hypothesized that this increase was caused by preventing expiratory muscle activity, and they systematically studied the prevalence and mechanisms of this phenomenon. They cleverly exploited the clinical requirement to provide "windows" in neuromuscular block: In this period, they made before-and-after measurements in each patient.

They found that responses to neuromuscular blockade were highly variable. In half of the patients, end-expiratory lung volume increased by more than 10% after reinstating neuromuscular blockers. Impedance measurements of regional ventilation suggested that these "responders" were using their expiratory muscles during the windows in neuromuscular block, whereas the "non-responders" were not. This was confirmed in a further patient sample by measuring esophageal pressure, which assesses respiratory muscle effort directly.

Pathophysiology of Expiratory Muscle Recruitment in ARDS: The "Anti-PEEP" Effect

Some studies suggest that moderate respiratory effort improves ICU outcomes (8), which contradicts findings that neuromuscular blockers can be advantageous. However, respiratory effort in early respiratory failure should not cause excessive lung stretch. Controlling respiratory effort is often difficult when ventilatory drive is excessive, which is often the case in critical illness: Reduced efficiency of gas exchange, hypercapnia and hypoxia, neural reflexes from pulmonary inflammation, and increased metabolism may all contribute. In patients in whom respiratory effort is difficult to control, neuromuscular blockade may be the only solution.

An almost universal method to reduce lung damage and improve gas exchange is to increase lung volume with positive end-expiratory pressure (PEEP). An increase in end-expiratory lung volume should prevent collapse of lung regions where the distending transpulmonary pressure is small. Moving the lung to a less harmful part of its pressure–volume relationship may also reduce elastic stress. However, the final effect of PEEP depends on the mechanical properties of the chest wall and the presence of expiratory muscle activity (Figure 1). Action of expiratory muscles will decrease lung volume, causing possible local collapse, and might thus contribute to lung injury by several pathways: greater lung elastance requiring increased driving pressures, impaired gas exchange, cyclic recruitment of alveoli, and increased lung inhomogeneity. It had been suspected in earlier studies that improved oxygenation after neuromuscular block might be caused by lung recruitment after cessation of abdominal muscle recruitment (9), but the effects of neuromuscular block on lung volumes had not been demonstrated as elegantly as in this paper. Plens and colleagues call the reduction in end-expiratory lung volume by expiratory activity an "anti-PEEP" effect, which is an insightful moniker, but it might be better to think that PEEP can restore the diminished lung volumes caused by active expiration.

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