Driving Pressure: The Road Ahead

Mechanical ventilation has long been the cornerstone of treatment for acute respiratory failure to facilitate gas exchange while allowing time for the underlying lung injury to heal. However, ventilator-induced lung injury (VILI) may contribute to the morbidity and mortality associated with acute respiratory failure. In recent years, mechanical ventilation strategies have focused on limiting tidal volume and end-inspiratory plateau pressure to prevent VILI from alveolar overdistention.[1] Nevertheless, even patients receiving mechanical ventilation according to these guidelines may remain at high risk for VILI.[2-4] Driving pressure has recently been proposed as a new target for lung-protective ventilation based on numerous observational studies that showed associations between lower driving pressure and lower mortality in subjects with ARDS.[5-10]

Driving pressure is easily calculated at the bedside as the plateau pressure minus PEEP, and it reflects the ratio of the tidal volume to the compliance of the respiratory system. Driving pressure is a strong independent predictor of mortality and may be a key mediator of current lung-protective ventilation strategies.[5,7-10] Reductions in tidal volume or increases in PEEP are only associated with improved survival if they concomitantly result in decreases in driving pressure.[5] Although there is robust physiologic rationale for targeting driving pressure over traditional surrogates of VILI and now a plethora of observational studies that demonstrate an association between driving pressure and mortality, many questions still need to be answered before driving pressure-targeted ventilation can be prospectively evaluated. Especially before embarking on phase III randomized controlled trials of reducing driving pressure, we must know if there are sufficient numbers of patients who could potentially benefit, if driving pressure is an adequate surrogate for lung stress and subsequent VILI, and if a mechanical ventilation strategy that lowers driving pressure can be feasibly tested.

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In this issue of Respiratory Care, Baldomero et al[11] took the first step in answering these questions by defining the natural range and temporal variability of driving pressure in patients who receive traditional lung-protective ventilation. In a retrospective review of 125 mechanically ventilated subjects, ~60% of the participants had driving pressures that exceeded a proposed safety limit of 15 cm H_2O[5,12] within the first 8 h of mechanical ventilation. They also noted temporal driving pressure variability over the first 24 h of mechanical ventilation, with gradually decreasing driving pressure presumed secondary to progressive lung recruitment from positive pressure ventilation improving lung compliance and treatment of the underlying illness.[11] Also, they noted intriguing findings regarding driving pressure differences related to sex, body mass index, and the presence of spontaneous respiratory efforts.

Driving pressure is physiologically and mathematically coupled with tidal volume, plateau pressure, and respiratory system compliance. Thus, reductions in tidal volume may be a powerful mechanism for reducing driving pressure.[13] In the modern low-tidal volume era, the clinical range of driving pressure is not as wide as the ranges found in studies that used higher tidal volumes.[12,14] Despite this, the results from Baldomero et al[11] suggest that a majority of patients on mechanical ventilation may be eligible for interventions that attempt to reduce driving pressure, especially important because trial recruitment in critical care can be notoriously difficult.[15-17] Furthermore, although Baldomero et al[11] picked a safety threshold of 15 cm H_2O, results of other studies suggested a threshold effect closer to 13 cm H_2O, which suggests even more patients than suspected may benefit from a driving pressure-limited strategy.[8,9] The true safe upper limit of driving pressure is unknown, and different cutoffs should continue to be evaluated prospectively. In reality, driving pressure is a continuous variable, and the lowest driving pressure that can be achieved without consequences from the strategies necessary to achieve it (eg, respiratory acidosis or the need for increased sedation) will

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Correspondence: Sarina K Sahetya MD MHS, Division of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, 1830 E. Monument St, Suite 503, Baltimore MD 21287; e-mail: ssahety1@jhmi.edu.

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likely be optimal. Also, the timing and duration for which strict adherence to a driving pressure-limited strategy would continue to lead to benefits, as opposed to potential risks required to maintain a low driving pressure target, remains to be determined.

The investigators also noted a consistently higher driving pressure for participants who were passively breathing than participants who were actively breathing. Active breathing was ascertained retrospectively, but the findings raise important questions regarding the validity of driving pressure as a surrogate for cyclic lung stress and the contribution of patient effort to measurement of driving pressure and VILI in general. As described above, driving pressure represents the stress applied to the respiratory system (lung and chest wall combined) from end-inspiration to end-expiration. In contrast, transpulmonary driving pressure more directly represents the stress applied to the lung and eliminates the variable effects of chest-wall compliance. The interpretation of airway driving pressure as a marker of VILI assumes that alterations in airway pressure are driven primarily by the lung rather than chest-wall mechanics.

However, in some patients with ARDS, chest-wall compliance is decreased due to obesity,[18,19] fluid loading,[20] or increased intra-abdominal pressures.[19] In these patients, changes in driving pressure could represent changes in the compliance of the lung or the chest wall. In addition, in patients with decreased chest-wall compliance, a high driving pressure may overestimate the potential for VILI due to the contribution of the chest wall to high airway pressures. Indeed, in this study by Baldomero et al,[11] there was a general trend to increased driving pressure that correlated with increased body mass index, which reflected the increased contribution from the altered chest wall rather than more severe lung injury.

Although measuring transpulmonary driving pressure might be preferable to assess lung stress, an estimation of pleural pressure by using esophageal manometry is required, which is not routinely performed in most ICUs due to its laborious nature, as well as several assumptions and limitations associated with the technique.[21] Alternatively, airway driving pressure is easily and quickly measured at the bedside, without the need for additional equipment or software. Post hoc analyses of 2 previous studies indicate that, for most patients, airway driving pressure adequately correlates with transpulmonary driving pressure and is an adequate surrogate for lung stress.[7,8] However, further studies that prospectively evaluate the validity of driving pressure as a surrogate for transpulmonary driving pressure and lung stress are essential.

In the past 19 years, mortality from acute respiratory failure and ARDS has declined substantially with the implementation of lung-protective ventilation. However, personalized mechanical ventilation tailored to an individual's underlying lung physiology or phenotype remains a key research priority for the critical care community.[22] Unfortunately, in recent years, numerous physiologic approaches to mechanical ventilation have not demonstrated superiority over current practices despite encouraging observational or pilot studies, such as in the most recent study of esophageal pressure-guided PEEP titration.[23-25] However several important differences existed between the pilot study[26] and the larger, phase II study[23] with regard to the study population and comparator group, which may explain the difference in the results. Nevertheless, the disappointment in these promising ventilation strategies after translation to larger randomized controlled trials is perhaps the most replicable finding in critical care research to date.

Consequently, we strongly advocate for a deliberate approach to evaluating driving pressure as a target for lung-protective ventilation by starting with high-quality pilot studies designed and refined through prospective qualitative work to optimize a complex mechanical ventilation strategy intended to limit driving pressure.[27,28] Rather than attempting to determine preliminary effect sizes, pilot studies should be conducted to determine the feasibility and acceptability of a driving pressure-limited mechanical ventilation strategy before progressing to other phases (Fig. 1). Notably, the preliminary phases of testing should be iterative, which al-

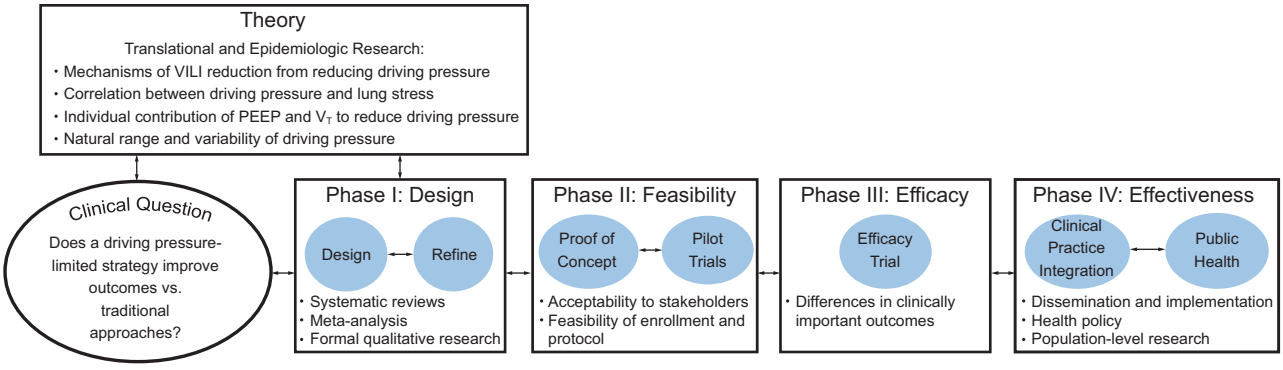

Fig. 1. The continuum of research proposed for evaluating driving pressure as a target for lung protective ventilation strategies in acute respiratory failure. VILI = ventilator-induced lung injury. Adapted from Reference 29.

lows for bidirectional movement between phases as the intervention is refined and optimized before efficacy testing. The cumulative insights generated from these rigorous pilot studies will be critical to the ultimately successful design and implementation of future efficacy trials.[27]

The road to personalized lung-protective ventilation strategies is currently paved with numerous observational studies that suggest a driving pressure-limited mechanical ventilation strategy could improve outcomes in patients with acute respiratory failure and ARDS. Unfortunately, few prospective studies that target driving pressure as a primary goal for mechanical ventilation have been published at this moment. Perhaps now it is time for the rubber to meet the road.

Sarina K Sahetya
Division of Pulmonary and Critical Care Medicine
Johns Hopkins School of Medicine
Baltimore, Maryland

Eddy Fan
Interdepartmental Division of Critical Care Medicine
and the Institute of Health Policy Management
and Evaluation
University of Toronto
Toronto, Ontario, Canada

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