Could dynamic ventilation waveforms bring about a paradigm shift in mechanical ventilation?

Samir D. Amin and Béla Suki
Department of Biomedical Engineering, Boston University, Boston, Massachusetts

TODAY, MECHANICAL VENTILATORS are the primary life-support systems routinely used in every intensive care unit around the world. Mechanical ventilators first reached widespread use in the United States during the poliomyelitis epidemic in the 1940–1950s. Initial devices, known as “iron lungs,” provided negative pressure external to the body to support breathing for patients in respiratory failure. By the 1960s, mechanical ventilators were available in most intensive care units, and the era of the iron lung diminished as the more practical, positive pressure ventilation approach gained popularity.

Positive pressure mechanical ventilation has been applied to patients suffering from a variety of disease conditions, including acute lung injury, infant respiratory distress syndrome, and acute respiratory distress syndrome (ARDS). In the early days, mortality rates following prolonged periods of mechanical ventilation were high, reaching 90% in the most severe ARDS cases (17), apparently due to ventilator-induced lung injury (VILI). In 1974, a study by Webb et al. (16) demonstrated that high ventilation pressures were associated with pulmonary edema, as well as injury. Over the next two decades, studies repeatedly found that VILI could be reduced by limiting end-inspiratory plateau pressure and adding a positive end-expiratory pressure (8, 9). This simple mechanical factor profoundly reduced mortality rates to between 50 and 60% (13). In parallel, efforts to elucidate the causes of VILI attributed injury to tissue overdistention at high pressures and atelectrauma at low pressures (7, 11). Consequently, the Consensus Conference on Mechanical Ventilation in 1993 set up standardized practices for mechanical ventilation (14). In 1998, the introduction of protective low tidal volume ventilation (2) triggered a second profound transition in ventilation strategy, reducing mortality rates to around 30% in ARDS patients (1). Since then, however, mortality rates in ARDS patients have been stagnant (12), indicating that the maximal benefit from current protocols has been reached. One reason for the lack of further improvement may be that mechanical ventilation has been considered as a stable and static mode of aerating the lung. As we strive toward reducing mortality rates, it is time to turn to more complex modes of ventilation that take into account the dynamic nature of airway reopening, one of the main contributors to VILI (6, 11).

In a new study published in the journal by Glindmeyer et al. (9a), the authors present an intriguing combination of experimental results with computational modeling in an effort to establish that a pulsatile waveform during inspiration substantially improves endogeneous surfactant transport and efficacy, thus potentially reducing the likelihood of VILI. In a model system consisting of a rigid tube lined with epithelial cells, they examine the effects on cell death of an air bubble propagating through the tube mimicking airway reopening in the presence of minimal surfactant. Their experiments show that cell death is reduced when the constant flow bubble propagation is replaced with a dynamic flow pattern consisting of temporary flow reversals superimposed on a steady flow. Their computational model provides a possible mechanism for these results, including the production of surfactant multilayers in the vicinity of the air-liquid interface, which reduces the injury-inducing gradient of normal forces acting on epithelial cells during the reopening process (5). These results convincingly demonstrate that the dynamic characteristics of the air-liquid interface can affect the underlying cell viability and hence the development of VILI.

Before the findings of Glindmeyer et al. (9a) can be transferred to clinical practice, several aspects of the study should be investigated using more physiological constructs. For example, the influence of non-rigid airway walls as well as bifurcations needs to be elucidated to fine tune the amplitude and frequency of the superimposed cyclic flow. Furthermore, these wave forms should also be tested in animal models of ARDS.

Nevertheless, the above results could well be the first steps toward new approaches to mechanical ventilation that incorporate certain intra-breath dynamics such as cyclic flow reversal during inspiration. The benefits of dynamic ventilation pattern at the level of multiple breaths have already been demonstrated. Indeed, breath-to-breath variation in tidal volumes, called variable ventilation, increases compliance and improves gas exchange in various animal models of ARDS (10, 15). More importantly, variability in stretch pattern delivered to the epithelium during variable ventilation has been shown to enhance surfactant release (3, 4). Combining the intra-breath cyclic flow reversal with the inter-breath variability in tidal volume could simultaneously maximize surfactant release and minimize epithelial injury related to airway reopening and hence synergistically reduce the likelihood of VILI. These concepts link molecular scale biophysics of surfactant function to organ scale ventilation protocols and may lead to the next paradigm shift in ventilation strategy, perhaps also opening avenues toward a new reduction in mortality rate of ARDS patients requiring mechanical ventilation.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS
Author contributions: S.D.A. and B.S. drafted manuscript; B.S. approved final version of manuscript.

REFERENCES
1. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung


