recruitment, increases lung homogeneity, or alters dead space. The mechanical effects of PEEP on mortality hazard may be more complex. Indeed, although PEEP’s effect on total lung stress and strain will depend on multiple factors (e.g., baseline compliance, recruitability, and lung homogeneity), its amount is not indifferent to the outcome because PEEP can influence driving pressure (for a given VT) and dead space (and can indirectly influence the respiratory rate) as well as acting independently as a key component of the total mechanical energy delivered.

The relevance of PEEP in determining total stress and strain of the respiratory system is, in one sense, intuitive: omitting PEEP from a calculation of energy would imply that applying 30 cm H2O of PEEP to an individual patient adds no risk of VILI or other adverse outcomes. On the contrary, it is clear from the univariate, population-based models presented by Costa and colleagues (1) that PEEP, the static elastic component of mechanical power and of total power, impacts mortality with an effect size of similar magnitude as respiratory rate and driving pressure. There are not sufficient data available to fully elucidate the effect of PEEP on outcome, but there is already evidence—some from the same authors—that mechanical power is associated to outcome in the same populations (4).

Second, the simplicity of the bedside calculation of 4DPRR is not superior to the simplicity of the bedside calculation of mechanical power through simplified formulas (5). In addition, the 4DPRR formulation obscures the conceptual understanding of the delivered mechanical energy. Therefore, we argue that moving from the physical and physiological model of mechanical power to a contrived expression based on statistical models devoid of direct physical meaning may be a retrograde step.

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Reply to Camporota et al.

From the Authors:

We appreciate the authors’ interest in our work (1). Let us start by emphasizing what we agree on: Driving pressure and respiratory rate are important determinants of ventilator-induced lung injury (VILI). Irrespective of whether we reach an agreement on other issues below, this is a good take-home message. Now let us examine the points on which we diverge.

Based on physical and pathophysiological principles detailed below, we do not think that the elastic, static energy related to positive end-expiratory pressure (PEEP) should be included in the power computation, nor should the energy dissipated in the airways. Indeed, one of the goals of our study was to assess the role of the individual mechanical power components on mortality (1). We clearly demonstrated that the only component of power associated with outcome was the elastic, dynamic component related to driving pressure (see Figure 1 in Reference 1); the elastic static component (i.e., PEEP) and the resistive power (related to flow and airway resistance) had essentially a zero contribution to outcome.

Why should this be? PEEP can impact patient outcome through multiple mechanisms. PEEP, however, expands the lungs only once—when applied—and this expansion is sustained throughout the ventilatory support unless PEEP is changed. This single expansion can be tolerated by the lungs or can be excessive. In addition, there may be some further expansion if there is recruitment, but this is not linked to respiratory rate. Thus, it does not make sense to include PEEP in the...
Correspondence

mechanical power calculation, which multiplies PEEP (applied once) by the respiratory rate, as if there was tidal energy transfer related to PEEP. There is no such energy transfer.

The energy transferred to the lungs from the ventilator with each breath can be either stored in the form of elastic energy or can be dissipated (2). The stored fraction indicates energy conservation in the lung tissue compartment and presupposes that the lung can return to its previous state after the pressure release. In terms of potential lung damage, the focus should thus be on the dissipated energy fraction.

Most of the dissipation occurs because of friction during air flow through the endotracheal tube and airways (3). For obvious reasons, this component, which is captured in the equation for mechanical power, can hardly be considered the culprit for lung tissue damage. The focus concerning VILI should then be on energy dissipation in the surfactant system and in the lung tissue itself (2). This dissipation can be measured in quasistatic pressure–volume loops as the area between the expiratory and the inspiratory limbs, also called hysteresis. Elegant bench studies have demonstrated that large expansions of the surfactant film can lead to permanent changes to the surfactant system, which manifest as increased hysteresis (4). In vivo, surfactant function is continuously restored by many processes, including secretion of stored surfactant in lamellar bodies and production of new surfactant by type II pneumocytes. However, excessive and repeated lung deformations can exceed the lungs’ innate reparative abilities (4). Unfortunately, hysteresis is very difficult to measure at the bedside, making its clinical use unpractical. In their seminal paper in the 1970s, Horie and Hildebrandt showed that the driving pressure was the parameter more closely associated with the area of hysteresis, which supports its use at the bedside as a marker of potential VILI (5).

In addition, based on the principles of material fatigue, according to which not only strain and stress matter but also the rate at which they are imposed, we sought to investigate whether there was an interaction between driving pressure and respiratory rate. Our failure to show a significant interaction term suggests that within the stress range applied, the effect of respiratory rate is independent of driving pressure.

Finally, as highlighted by Beitler and Walkey, the editorialists for our paper, minimizing mechanical power at the bedside is challenging because the components of mechanical power move in opposite directions (6). We believe for the theoretical reasons outlined above, as well as these practical issues at the bedside, the concept of using $4 \times$ driving pressure + respiratory rate to quantify the impact of changes in ventilatory strategy on VILI is a rational and potentially very valuable approach.

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