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Reply to Tobin

From the Authors:

We thank Professor Tobin for his thoughtful letter regarding our findings. We share his concern that the application of a low V_T in patients with acute respiratory distress syndrome (ARDS) with low respiratory system elastance may sometimes result in an unnecessary risk of dyspnea, respiratory distress, patient–ventilator dyssynchrony, and needless use of sedation and neuromuscular blockade, although this has not been consistently demonstrated (1).

Dr. Tobin suggests that V_T should be titrated according to a plateau pressure limit of 32 cm H_2O, rather than according to driving pressure (ΔP). Although plateau pressure is an important parameter to monitor, we argue that there are several reasons to prioritize ΔP over plateau pressure. First, experimental studies have demonstrated that the magnitude of injury is more closely linked to the magnitude of dynamic (tidal) strain than the peak static strain (2, 3). Second, owing to variability in chest wall mechanics (e.g., rightward shift of the chest wall pressure–volume curve common in ARDS and obesity), absolute values of airway pressure may be unreliable measures of alveolar distention (4). For example, a patient with morbid obesity may have an airway plateau pressure well above 32 cm H_2O without risk of alveolar hyperdistention because of high pleural pressure (5), provided ΔP is kept sufficiently low. On the other hand, some patients with a small "baby lung" volume exhibit substantial alveolar hyperdistention even when plateau pressure is kept below 30 cm H_2O (6). The relation between ΔP and dynamic lung stress is relatively unaffected by a rightward shift in chest wall pressure–volume curve. Third, most of the trials included in the analysis (including the largest) targeted a plateau airway pressure of 30 cm H_2O or less in the intervention arm, and yet we found substantial heterogeneity of treatment effect related to elastance (7). Attending only to plateau pressure while ignoring ΔP may therefore fail to adequately protect the lung and increase mortality.

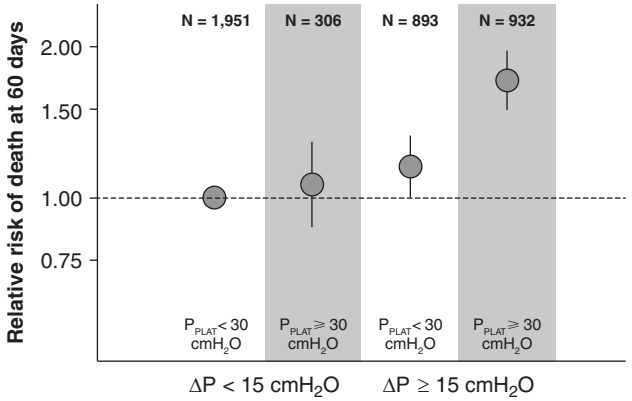

Figure 1. Association between Pplat and mortality varies according to ΔP. Error bars represent 95% confidence intervals. The association between Pplat and mortality varied according to ΔP; higher Pplat was associated with a substantially increased risk of death only when ΔP was increased ($P = 0.015$ for interaction). Data are adjusted for age, APACHE/SAPS risk, arterial pH, P/F ratio, and study trial. APACHE = Acute Physiology and Chronic Health Evaluation; P/F ratio = Pa_{O_2}/FI_{O_2}; ΔP = driving pressure; Pplat = plateau pressure; SAPS = Simplified Acute Physiology Score.

To further substantiate our position, we present additional analysis of the comparative associations of ΔP and plateau pressure with mortality in ARDS (Figure 1). This analysis was performed in the same data set used for a previously published report examining ΔP and mortality in ARDS (8), updated to include ART (the Alveolar Recruitment Trial) ($n = 4{,}090$) (9). A plateau pressure ⩾30 cm H_2O was associated with a higher risk of mortality, but *only* in patients in whom ΔP was ⩾15 cm H_2O (relative risk, 1.47; 95% confidence interval [CI], 1.27–1.70). In patients in whom ΔP was <15 cm H_2O, a plateau pressure ⩾30 cm H_2O was not associated with a higher risk of death (relative risk, 1.09; 95% CI, 0.90–1.33; $P = 0.015$ for interaction). Very similar results were obtained when using a plateau pressure threshold of 32 cm H_2O. Note that the use of a ΔP threshold of 15 cm H_2O for this analysis is not intended to imply that this is the definitively confirmed safe limit for ΔP, although we found that lowering V_T was unlikely to improve mortality when ΔP is <15 cm H_2O (7).

Although we are unaware of a process for issuing a codicil to a published guideline, we believe that these findings should be considered in future guidelines for management of mechanical ventilation in ARDS. For the present, we believe it would be prudent for clinicians to incorporate limitation of ΔP in the ventilatory strategy for patients with ARDS. ■

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Asthma and Chronic Obstructive Pulmonary Disease: Just Old Friends or Relatives?

To the Editor:

There is broad consensus that asthma and tobacco smoke–related chronic obstructive pulmonary disease (COPD) are clinically, immunologically, and histopathologically distinct. However, recent evidence identified different trajectories that lead to chronic airflow limitation at different times of one's life, starting from childhood (1). It is now well established that prenatal, perinatal, and early childhood factors affect lung development and function (2). The more we learn about these common etiologies, the more studies aimed at digging into the first years of life are needed to shed light on the roots of the structural and functional changes associated with airflow limitation.

We have read with great interest the study from Izadi and colleagues. By further analyzing the Childhood Asthma Management Program, an initial drug trial turned to a well-defined, long-term, ongoing cohort study. Izadi and colleagues unravel some knowledge gaps in the nature of childhood factors associated with persistent severe asthma in adult life (3). These authors reported that only two determinants among more than 22 explored, namely, reduced lung growth in childhood and maternal smoking during pregnancy, were predictors of persistent severe asthma later in life. Interestingly, this association was not maintained if the subjects had normal lung growth in childhood even in the presence of early lung function decline, suggesting that lung function in the first years of life is a major determinant of chronic airflow limitation regardless of how the lung function is going to develop and/or decline. These findings shed light on the gray transition area in which patients with asthma become progressively irreversible until they meet the spirometric criteria for COPD. Large cohort studies had previously found irreversible airflow obstruction to be associated with low lung function at birth, especially when modifiable early-life exposure such as first- or second-hand smoke, including maternal exposures, are present (4). Also, irreversible airflow obstruction compatible with COPD is common in those with severe asthma (5). Thus, this study serves as a bridge between early origins of asthma and COPD.

From a pathobiological standpoint, inflammatory processes contribute to small airway obstruction in both asthma and COPD. The nature of these processes and the extent to which they overlap in both conditions or evolve into each other are not well understood (6). We have missed for years the opportunity to explore, especially by longitudinal imaging, the lungs from younger subjects before they develop any spirometric criteria for COPD and/or after they surpassed the critical age to be studied as patients with asthma.

Altogether, these studies aimed at profiling the causes and the evolution of airflow obstruction are slowly shifting the focus toward younger individuals who have been so far overlooked, as COPD was wrongly considered a disease of the elderly. These long-term (life-long?) cohorts are crucial to further understand the determinants of lung function from birth; how small airway obstruction shapes into asthma, COPD, or both; and the potential long-term implications of these factors for the development of COPD later in life.

Here and now, there is a brand new window of opportunity to tackle the multifaceted aspects of airflow limitation. Let's keep this window wide open to promote lung health starting from birth. ■

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