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Editorial

Exhaled CO_2, a guide to ARDS management during lung-protective ventilation?

The assessment of respiratory function is a common part of the decision-making process in the care of critically ill patients. Evaluation of carbon dioxide (CO_2) elimination is critical for the determination of adequacy of ventilation in any patient breathing spontaneously or requiring mechanical ventilation. Over the years, while examining approaches to manage patients with the acute respiratory distress syndrome (ARDS), dead space (V_D) to tidal volume (V_T) ratios have been used to determine optimal positive end-expiratory pressure (PEEP) level [1-5] and predict prognosis [6-9]. Since the late 1950's, the V_D/V_T has been used as an index of distribution of ventilation and pulmonary blood flow [10]. V_D/V_T describes inefficiency of the lung to eliminate CO_2. In patients with ARDS, either too little or too much PEEP increases V_D/V_T. Although the selection of optimal PEEP following a recruitment maneuver has commonly been based on best respiratory system compliance [11] or best oxygenation and more recently on a PEEP level that maintains a positive end-expiratory transpulmonary pressure [12], equivalent determinations of optimal PEEP can be achieved by calculating V_D/V_T [1-5]. Numerous authors have reported that elevated V_D/V_T (>60%) determined during the first week of ARDS is a predictor of survival [6-9].

Before the advent of the modern capnography technology, the assessment of V_D/V_T required the invasive measurement of arterial PCO_2. The dead space fraction (V_D/V_T) was calculated from the Enghoff modification of the Bohr equation [$V_D/V_T = (PaCO_2 - P_{\bar{E}}CO_2) / PaCO_2$], where $P_{\bar{E}}CO_2$ is the partial pressure of mixed exhaled CO_2, and $PaCO_2$ was used instead of alveolar PCO_2 (P_ACO_2). We know today that the inflection point of phase II of the exhaled volumetric capnograph identifies the volume of anatomic dead space, and the midpoint of phase III of the volumetric capnograph identifies the P_ACO_2 [13]. Although end-tidal PCO_2 approximates to $PaCO_2$ in normal individuals, $PaCO_2$ is usually affected by the level of intrapulmonary shunt in critically ill patients. Thus, a better evaluation of V_D/V_T in critically ill patients can easily be performed at the bedside in a completely non-invasive manner using the original Bohr equation [$V_D/V_T = (P_ACO_2 - P_{\bar{E}}CO_2) / P_ACO_2$]. Thus, V_D/V_T ratios can be determined on a breath to breath basis and easily used to assess severity of acute lung injury and to determine optimal PEEP.

In this issue of the Journal, Gogniat et al. [14] adds another piece to the puzzle of using V_D/V_T as an adjunct to manage patients with ARDS. They performed a physiological study in a small cohort of 14 ARDS patients with different degrees of severity according to the Berlin criteria (7 mild, 4 moderate, 3 severe) and explored the relationship between V_D/V_T, driving pressure, and plateau pressure and four levels of PEEP (zero, 6, 10 and 16 cmH_2O). When the impact of PEEP was evaluated in this small and mixed study population, they found that as PEEP increased, plateau pressure significantly decreased at 6 and 10 cmH_2O PEEP but increased at 16 cmH_2O. However, none of the indices of CO_2 elimination or dead space were significantly affected across all PEEP levels. When the study population was stratified into patients who responded with a >15% increase in driving pressure ($n = 7$) vs. a ≤15% increase in driving pressure ($n = 7$) at 16 cmH_2O PEEP, the interpretation of their findings markedly changed. The authors found that all indices of CO_2 elimination and calculations of V_D/V_T became significantly different between the two groups. The ≤15% change group showed the most positive effects when increasing PEEP. The group with the least change in driving pressure had a lower V_D/V_T fraction based on both the Bohr equation and the Enghoff modification. CO_2 elimination was also greater in the group with minimal driving pressure change. In addition, plateau pressure, driving pressure and compliance minimally changed from zero PEEP to 16 cmH_2O PEEP. There was a trend of increasing plateau pressure, driving pressure and decreasing compliance in the group where driving pressure increased >15%.

There are, however, several important concerns with their study design and interpretation of their findings. First, this is a physiological study and not an outcome study. Thus, mortality figures are impossible to interpret, especially because of the small sample size, the mixture of patients with distinct degrees of severity, and the authors did not provide the cause of death. Second, there is no information regarding the response to PEEP in each category of severity. In general, patients with mild ARDS do not require PEEP > 12 cmH_2O; those levels of PEEP in mild ARDS would be expected to increase V_D/V_T. Third, the authors did not remove the mechanical dead space of the ventilator circuit before making measurements. Leaving a heat and moisture exchanger (V_D of approximately 40 ml) in the circuit during these measurements increased the airway dead space at baseline and at each PEEP level. Thus, potentially negating some of the increases seen in the overall V_D/V_T ratios at each PEEP settings, especially in the >15% driving pressure increase group. Fourth, the selection of 15% driving pressure increase to separate patients into 2 groups was completely arbitrary. Clinically, as we titrate PEEP we expect the driving pressure to decrease as we approach on optimal level of PEEP. Paradoxically, the authors indicated that the study was not designed to determine optimal PEEP; however, any specific PEEP level that increases driving pressure should be of concern. Finally, based on reported data at baseline, most patients had a $PaCO_2 < 45$ mm Hg with a respiratory rate of about 20 breaths/min and a minute ventilation of ≤10 L/min, suggesting ARDS patients in this series did not have an excessive V_D/V_T.

How do we use these results? Simply increasing PEEP without a recruitment maneuver makes it difficult to identify the PEEP level

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resulting in the best lung mechanics and gas-exchange, although this approach is used by many clinicians. The data from Gogniat et al. [14] reinforces the fact that regardless of whether you use lung mechanics or gas exchange as PEEP is titrated, an increased V_D/V_T, plateau pressure, driving pressure or a decrease in compliance or CO_2 elimination identifies an excessive PEEP level under the specific measurement circumstances. However, as this group of investigators has shown in previous publications [3,4], in the appropriate patient, a decremental PEEP titration following a recruitment maneuver using any of the methods to determine the optimal PEEP setting, results in a PEEP level most effective in improving lung mechanics and gas exchange. Therefore, yes, you can use V_D/V_T to assess ventilator management in ARDS patients but this should be additive to the other variables readily available to assess these patients: plateau pressure, driving pressure, compliance, and oxygenation. The greater the number of variables indicating an appropriate setting, the greater the likelihood that the setting chosen is the most appropriate!

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