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Higher initial tidal volumes associated with the subsequent development of acute lung injury in dose-response relationship

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Expanded Abstract

Citation

Gajic O, Dara SI, Mendez JL, Adesanya AO, Festic E, Caples SM, Rana R, St Sauver JL, Lymp JF, Afessa B, Hubmayr RD: Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. Crit Care Med 2004, 32:1817-1824 [1].

Objective

Although ventilation with small tidal volumes is recommended in patients with established acute lung injury, most others receive highly variable tidal volume aimed in part at normalizing arterial blood gas values. We tested the hypothesis that acute lung injury, which develops after the initiation of mechanical ventilation, is associated with known risk factors for ventilator-induced lung injury such as ventilation with large tidal volume.

Methods

Design: Retrospective cohort study.

Setting: Four intensive care units in a tertiary referral center.

Subjects: 332 patients who received invasive mechanical ventilation for ≥48 hrs between January and December 2001.

Intervention: None.

Measurements: The main outcome of interest, acute lung injury, was assessed by independent review of daily digital chest radiographs and arterial blood gases. Ventilator settings, hemodynamics, and acute lung injury risk factors were extracted from the Acute Physiology and Chronic Health Evaluation III database and the patients' medical records.

Results

Of 332 patients who did not have acute lung injury from the outset, 80 patients (24%) developed acute lung injury within the first 5 days of mechanical ventilation. When expressed per predicted body weight, women were ventilated with larger tidal volume than men (mean 11.4 vs. 10.4 ml/kg predicted body weight, $p<0.001$) and tended to develop acute lung injury more often (29% vs. 20%, $p=0.068$). In a multivariate analysis, the main risk factors associated with the development of acute lung injury were the use of large tidal volume (odds ratio 1.3 for each ml above 6 ml/kg predicted body weight, $p<0.001$), transfusion of blood products (odds ratio, 3.0; $p<0.001$), acidemia ($pH < 7.35$; odds ratio, 2.0; $p=0.032$) and a history of restrictive lung disease (odds ratio, 3.6; $p=0.044$).

Conclusion

The association between the initial tidal volume and the development of acute lung injury suggests that ventilator-associated lung injury may be an important cause of this syndrome. Height and gender should be considered when setting up the ventilator. Strong consideration should be given to limiting large tidal volume, not only in patients with established acute lung injury but also in patients at risk for acute lung injury.

Commentary

Numerous animal studies since the 1970s have shown that the lungs can be injured during mechanical ventilation. Ventilator-associated lung injury is thought to be caused by a variety of factors, including excess volume or pressure, surfactant inactivation, and shear stress from cyclic closing and reopening of lung units [2]. In 2000, an acute respiratory distress syndrome network (ARDSNet) trial showed that mortality was decreased when patients with

acute lung injury (ALI) or the acute respiratory distress syndrome (ARDS) were managed with low tidal volume ventilation [6 ml/kg predicted body weight (PBW)] as compared with higher tidal volume ventilation (12 ml/kg PBW) [3]. Despite the importance of the findings from the ARDSNet study, the trial did not address the following question, "Does the benefit of low tidal volume ventilation extend to patients without ALI at the onset of mechanical ventilation?" An early single-center prospective study by Lee and colleagues suggested that low tidal volume (6 ml/kg) ventilation significantly shortens ICU length of stay for critically ill patients without ALI [4], though this study did not specifically determine whether low tidal volumes results in less ALI.

The current study by Gadjic and colleagues begins to address this important issue. In a retrospective cohort study of 332 subjects without ALI at the initiation of mechanical ventilation, the authors found that the odds for developing ALI increased progressively for each 1.3 ml/kg above 6 ml/kg PBW. The authors concluded that strong consideration should be given to height and gender-based PBW when initially setting up the ventilator, not only for patients with established ALI but also for patients at risk for ALI.

Although the findings of the study by Gadjic and colleagues warrant the attention of intensivists, a few limitations also deserve consideration. By design this was an observational study, which means that the results are hypothesis generating and should not be viewed as definitive. Indication bias could have potentially affected the results, in that the clinician's choice of tidal volume may have been influenced by unmeasured factors that were also associated with poor outcome. Even so, the apparent dose-response relationship and the consistency of the findings with those of other animal and human studies are reassuring. As noted in the accompanying editorial [5], it is surprising that 30% of subjects in this study received very high tidal volumes (≥12 ml/kg PBW). Perhaps the physicians caring for these patients were using actual body weight instead of PBW when choosing tidal volumes. It is interesting to note that tidal volumes were highest in the two surgical ICUs, which leads one to wonder how care may have differed in other ways across the different ICUs in the study. Including treating ICU as a covariate in the multivariable models could have, at least partially, adjusted for such differences.

Despite these limitations, the Gadjic study seems to provide strong evidence for using lower tidal volumes in patients at risk for ALI. However, the question of "what is the lowest beneficial tidal volume?" remains unanswered. Few subjects in the study received tidal volumes <6 ml/kg, making it impossible to determine the tidal volume at which trauma due to atelectasis, derecruitment, and repeated opening and closing of lung units becomes problematic. Furthermore, because only a small number of subjects received positive end expiratory pressure (PEEP) >5 cm H_2O, the study does not address the issue of whether certain PEEP-based strategies can mediate the potential risks of low tidal volume ventilation.

Recommendation

Based on the results of this study and the earlier work by Lee and colleagues [4], a prospective randomized and (ideally) multicentric trial of low tidal volume ventilation in patients without ALI is warranted. Such a trial should address the safe lower tidal volume limit and the role of PEEP in low tidal volume strategies. Until data from a well-designed trial are available, we cannot recommend universal application of this strategy.

Competing interests

The authors declare that they have no competing interests.

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