Reviewer's report

Title: High tidal volume mechanical ventilation-induced lung injury in rats is greater after acid instillation than after sepsis-induced acute lung injury, but does not increase systemic inflammation: an experimental study.

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Reviewer: Chun-Jen Huang

Reviewer's report:

In this manuscript (High tidal volume mechanical ventilation-induced lung injury in rats is greater after acid instillation than after sepsis-induced acute lung injury, but does not increase systemic inflammation: an experimental study), the author investigated the effect of high tidal volume mechanical ventilation on lung injury induction in rats receiving intra-tracheal acid instillation or cecal ligation and puncture. Their data revealed that the levels of lung injury in rats receiving high tidal volume mechanical ventilation plus acid instillation were worse than those receiving high tidal volume mechanical ventilation plus cecal ligation and puncture. They therefore concluded that high tidal volume mechanical ventilation causes lung injury after acid instillation but not during sepsis. These data are of certain clinical implications. However, several flaws in study design and data interpretation have prevented this reviewer from recommending this manuscript for publication consideration with its present format.

Major comments:

1. The effects of mechanical ventilation (i.e., low tidal volume and high tidal volume) per se on inducing lung injury were not investigated in this study. The data would be more complete if two groups of rats receiving sham instrumentation plus low tidal volume mechanical ventilation and sham instrumentation plus high tidal volume mechanical ventilation were included.

2. Arterial blood gas data and data regarding inflammation response in lung tissues are lacking. The data would be more complete if these data were included.

3. The authors frequently withdrew arterial blood for analysis during the experiment. Considering the relative small amount of blood volume, it is likely that this manipulation per se may cause significant amount of blood loss and, therefore, induce hemorrhage or hemorrhagic shock. If so, then the effects observed in this study should be considered as the effects of acid instillation plus hemorrhage and sepsis plus hemorrhage. The authors should justify their decision for frequent blood drawing during the experiment and report how they control the effects of this manipulation.

4. Data presentation and data interpretation requires major revision. For instance, the authors stated that “Acid instillation increased IL-6 plasma concentrations as compared to sepsis (p=0.002)”. However, this data
interpretation was not supported by their data, as data shown in table 2 revealed comparable plasma IL-6 concentrations (321 ± 13 vs. 312 ± 8). In addition, the plasma IL-6 concentration in rats receiving low tidal volume mechanical ventilation plus acid instillation seemed higher than those receiving high tidal volume mechanical ventilation plus acid instillation (1113 ± 387 vs. 758 ± 209). These data seem to suggest that low tidal volume mechanical ventilation may induce more significant systemic inflammation response than high tidal volume mechanical ventilation in rats receiving acid instillation. What was the statistical analysis result? Was the difference not statistically significant? The authors should report the results in the text.

5. Abundant data have indicated that high tidal volume mechanical ventilation could aggravate lung injury in septic animals (Nin et al., Shock 2009; 31:429-34; Yang et al., J Surg Res 2011; 167:e273-81; Hu et al., Crit Care Med 2010; 38:194-201; etc.). However, data reported in this study seemed to indicate otherwise, as the authors reported that the levels of lung injury in rats receiving high tidal volume mechanical ventilation plus cecal ligation and puncture were comparable to those receiving low tidal volume mechanical ventilation plus cecal ligation as well as cecal ligation and puncture alone. Any explanation or speculation?

Minor comments:
1. The symbols of figure 2 were not labeled.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.