F1000 FACULTY CRITIQUE

Should we use lung protective ventilation for non-ARDS patients? [version 1; peer review: not peer reviewed]

Manasi Singh, A. Murat Kaynar

Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA

V1 First published: 19 Nov 2015, 4:1293
<https://doi.org/10.12688/f1000research.6815.1>
Latest published: 19 Nov 2015, 4:1293
<https://doi.org/10.12688/f1000research.6815.1>

Not Peer Reviewed

This article is an F1000 Faculty Critique and has not been subject to external peer review.

Any comments on the article can be found at the end of the article.

Abstract

An evaluation of a recent study by Serpa Neto A, Cardoso SO & Manetta JA *et al*: **Association between Uses of Lung-Protective Ventilation with Lower Tidal Volume and Clinical Outcomes among Patients without Acute Respiratory Distress Syndrome a Meta-analysis**. JAMA, October 24/31, 2012—Vol 308, No. 16. PMID: 23093163.

This article is included in the **Critical care** collection.

Corresponding author: A. Murat Kaynar (kaynarm@upmc.edu)

Competing interests: The authors declare that they have no competing interests.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2015 Singh M and Kaynar AM. This is an open access article distributed under the terms of the **Creative Commons Attribution License**, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Singh M and Kaynar AM. **Should we use lung protective ventilation for non-ARDS patients? [version 1; peer review: not peer reviewed]** F1000Research 2015, 4:1293 <https://doi.org/10.12688/f1000research.6815.1>

First published: 19 Nov 2015, 4:1293 <https://doi.org/10.12688/f1000research.6815.1>

Critique of:

Citation

Serpa Neto A, Cardoso SO, Manetta JA, Pereira VG, Esposito DC, Pasqualucci Mde O, Damasceno MC, Schultz MJ. Association between Uses of Lung-Protective Ventilation with Lower Tidal Volume and Clinical Outcomes among Patients without Acute Respiratory Distress Syndrome a Meta-analysis. JAMA, October 24/31, 2012—Vol 308, No. 16. PMID: 23093163.

Background

Lung-protective mechanical ventilation with the use of lower tidal volumes has been found to improve outcomes of patients with acute respiratory distress syndrome (ARDS). It has been suggested that use of lower tidal volumes also benefits patients who do not have ARDS.

Methods

Objective

To determine whether use of lower tidal volumes is associated with improved outcomes of patients receiving ventilation who do not have ARDS.

Design

Data Sources. MEDLINE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up to August 2012.

Study Selection. Eligible studies evaluated use of lower vs. higher tidal volumes in patients without ARDS at onset of mechanical ventilation and reported lung injury development, overall mortality, pulmonary infection, atelectasis, and biochemical alterations.

Data Extraction. Three reviewers extracted data on study characteristics, methods and outcomes. Disagreement was resolved by consensus.

Results

Twenty articles (2822 participants) were included. Meta-analysis using a fixed-effects model showed a decrease in lung injury development (risk ratio [RR], 0.33; 95% CI, 0.23 to 0.47; P , 0%; number needed to treat [NNT], 11), and mortality (RR, 0.64; 95% CI, 0.46 to 0.89; P , 0%; NNT, 23) in patients receiving ventilation with lower tidal volumes. The results of lung injury development were similar when stratified by the type of study (randomized vs. nonrandomized) and were significant only in randomized trials for pulmonary infection and only in nonrandomized trials for mortality. The meta-analysis using a random-effects model showed, in protective ventilation groups, a lower incidence of pulmonary infection (RR, 0.45; 95% CI, 0.22 to 0.92; P , 32%; NNT, 26), lower mean (SD) hospital length of stay (6.91 [2.36] vs. 8.87 [2.93] days, respectively; standardized mean difference [SMD], 0.51; 95% CI, 0.20 to 0.82; P , 75%), higher mean (SD) PaCO₂ levels (41.05 [3.79] vs. 37.90 [4.19] mmHg, respectively; SMD, 0.51; 95% CI, -0.70 to -0.32; P , 54%), and lower mean (SD) pH values (7.37 [0.03] vs. 7.40 [0.04], respectively; SMD, 1.16; 95% CI, 0.31 to 2.02; P , 96%) but similar mean (SD) ratios of PaO₂ to fraction of inspired oxygen (304.40 [65.7] vs. 312.97 [68.13], respectively; SMD, 0.11; 95% CI, 0.06 to 0.27; P , 60%). Tidal volume gradients between the 2 groups did not have a significant influence on the final results.

Conclusions

Among patients without ARDS, protective ventilation with lower tidal volumes was associated with better clinical outcomes. Some of the limitations of the meta-analysis were the mixed setting of mechanical ventilation (intensive care unit or operating room) and the duration of mechanical ventilation.

Abstract adapted from the original provided courtesy of PubMed: A service of the National Library of Medicine and the National Institutes of Health.

Commentary

The use of lower tidal volume (V_T) was shown to reduce morbidity and mortality in patients with ARDS justifying the progressive decrease in V_T used by clinicians over the past decades¹⁻³. However, in critically ill patients without ALI, there is limited evidence regarding the benefits of ventilation with lower V_T , partly because of paucity of randomized controlled trials evaluating the best ventilator strategies in these patients^{4,5}.

It has been suggested that ventilator-induced lung injury (VILI) occurs even in patients without ARDS with an odds ratio of 1.3 for every milliliter above 6 ml/kg⁶. Many RCTs have studied the pattern of inflammatory cytokines in the broncho-alveolar lavage (BAL) and/or blood in patients with non-ARDS, when patients were ventilated at conventional V_T compared to protective V_T of 6 ml/kg PBW, studies showed that these markers had a sustained increase in the former group⁷. Experimentally, inflammatory markers increase as early as 1 hour after initiation of ventilation^{8,9}. It has also been shown in animal models that volume and not the high airway pressure is responsible for increasing the alveolar permeability¹⁰. Overall these studies point to conventional V_T causing a proinflammatory state in otherwise normal lungs. Therefore, ARDS could be an iatrogenic and hence a potentially preventable complication dependent upon how we ventilate our patients. A recent work among patients undergoing elective abdominal surgery suggested that a low V_T approach with intermittent sigh breaths does decrease pulmonary and extra-pulmonary complications within the first 7 days after the surgery⁵.

This meta-analysis of 2822 patients consisted of a mixture of operating room and intensive care patients and showed that using lower V_T reduces the risk of developing ARDS by almost three times in patients without lung injury at the onset of ventilation. It also decreases the mortality, incidence of pulmonary infections and atelectasis. Most of the patients were electively intubated for a scheduled surgery and ventilated for a few hours highlighting the importance of the initial set V_T – whether in the operating room or the intensive care unit.

For the reason mentioned above, high tidal volumes elicit an almost immediate increase in the inflammatory markers, even in cases with short duration of mechanical ventilation. The large number of patients analyzed is a major strength of this meta-analysis even though not all the studies were RCTs and the RCTs were of moderate quality.

In the study by Determann *et al.*, there were some concerns about the safety of the study in view of the general opinion that lung injury was more likely with the use of conventional tidal volumes necessitating a second interim analysis. The study had to be stopped after the analysis showed a *p* value of < 0.01 for lung injury using conventional tidal volumes. While not included in the meta-analysis, the work by Futier *et al.* also used relatively high V_T of 10–12 ml/kg without any positive end expiratory pressure (PEEP)⁵.

Recommendations

Most patients who need ventilation do not have lung injury and those who develop ARDS do so 48–72 hours after initiation of mechanical ventilation. Studies have shown a large tidal volume set on the first day post intubation is a risk factor for development of lung injury. Some studies point to possible harm by ventilating

patients at conventional V_T . Protective ventilation has been proven to be beneficial for lung injury patients and is not associated with an increased use of sedatives or vasopressors^{6,7}. Given these facts, and the findings of the impressive reduction in the risk of development of ARDS in this meta-analysis, ventilating all of the ICU patients, ARDS or not, with tidal volumes of 6 ml/kg PBW would seem most desirable. The use of appropriate PEEP needs to be further explored.

Competing interests

The authors declare that they have no competing interests.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References

- Amato MB, Barbas CS, Medeiros DM, *et al.*: **Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome.** *N Engl J Med.* 1998; **338**(6): 347–54.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med.* 2000; **342**(18): 1301–08.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Brun-Buisson C, Minelli C, Bertolini G, *et al.*: **Epidemiology and outcome of acute lung injury in European intensive care units. Results from the ALIVE study.** *Intensive Care Med.* 2004; **30**(1): 51–61.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Schultz MJ, Haitsma JJ, Slutsky AS, *et al.*: **What tidal volumes should be used in patients without acute lung injury?** *Anesthesiology.* 2007; **106**(6): 1226–31.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Futier E, Constantin JM, Paugam-Burtz C, *et al.*: **A trial of intraoperative low-tidal-volume ventilation in abdominal surgery.** *N Engl J Med.* 2013; **369**(5): 428–437.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Gajic O, Dara SI, Mendez JL, *et al.*: **Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation.** *Crit Care Med.* 2004; **32**(9): 1817–24.
[PubMed Abstract](#)
- Determann RM, Royakkers A, Wolthuis EK, *et al.*: **Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial.** *Crit Care.* 2010; **14**(1): R1.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Chiumello D, Pristine G, Slutsky AS: **Mechanical ventilation affects local and systemic cytokines in an animal model of acute respiratory distress syndrome.** *Am J Respir Crit Care Med.* 1999; **160**(1): 109–16.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Takata M, Abe J, Tanaka H, *et al.*: **Intraalveolar expression of tumor necrosis factor- α gene during conventional and high-frequency ventilation.** *Am J Respir Crit Care Med.* 1997; **156**(1): 272–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Hernandez LA, Peevy KJ, Moise AA, *et al.*: **Chest wall restriction limits high airway pressure-induced lung injury in young rabbits.** *J Appl Physiol (1985).* 1989; **66**: 2364–8.
[PubMed Abstract](#)

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research