



## UvA-DARE (Digital Academic Repository)

### Lung-protective ventilation in intensive care unit and operation room

*Tidal volume size, level of positive end-expiratory pressure and driving pressure*

Serpa Neto, A.

**Publication date**

2017

**Document Version**

Other version

**License**

Other

[Link to publication](#)

**Citation for published version (APA):**

Serpa Neto, A. (2017). *Lung-protective ventilation in intensive care unit and operation room: Tidal volume size, level of positive end-expiratory pressure and driving pressure*. [Thesis, fully internal, Universiteit van Amsterdam].

**General rights**

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

**Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

## Chapter 5

### Optimizing the settings on the ventilator settings: High PEEP for all?

Serpa Neto A, Schultz MJ

*JAMA* 2017; 317:1413-4

Mechanical ventilation is an incredibly effective life support technique widely deployed across a variety of clinical settings in the care of many millions of patients each year worldwide. However, it is not a panacea. A central issue is that artificial ventilation works by pushing air into the lungs via positive pressure, whereas physiologic respiration works by generating negative pressure to suck air into the lungs. Pushing air into the lungs is tricky because not all lung areas distend and collapse at the same driving pressure. Thus, a positive pressure breath may overstretch one area while failing to open another one, compromising gas exchange and causing direct mechanical injury to the lung (so-called 'ventilator-induced lung injury' [VILI]). Both the volume and pressure settings on a ventilator have been implicated in VILI, with tidal volumes that are 'too large' implicated in overdistension and positive end-expiratory pressure (PEEP) settings that are 'too low' implicated in alveolar collapse. Thus, current guidelines endorse a 'low' tidal volume and a 'high', or at least avoidance of 'low' PEEP level. But, these 'one size fits all' recommendations may not be optimal for all patients.

There is convincing evidence for benefit of using a low tidal volume in patients with acute respiratory distress syndrome (ARDS),<sup>1</sup> a syndrome characterized by coexistence of open and closed lung areas. Because even a low tidal volume is still able to cause overdistension of open lung areas in patients with extensive lung collapse,<sup>2</sup> there is a noticeable trend towards extracorporeal support allowing the use of an even lower, or so-called 'ultra-low' tidal volume.<sup>3</sup> While it is still unclear whether a low tidal volume should be used in all patients receiving mechanical ventilation,<sup>4</sup> evidence for harm from ventilation with a too large tidal volume is rapidly emerging in other patient groups, including critically ill patients without ARDS,<sup>5</sup> emergency department patients,<sup>6</sup> and even surgery patients who receive intraoperative ventilation only for a very short period of time.<sup>7</sup>

There is also clear evidence for benefit of using a high PEEP level in patients with ARDS;<sup>8</sup> however this benefit has only been observed in patients with moderate or severe ARDS. Among patients with milder forms of this life-threatening complication of critical illness, the use of a high PEEP level does not appear to be associated with an improved

survival and even appears to be associated with a longer duration of invasive ventilatory support.<sup>8</sup> However, it still remains unclear whether a high PEEP level should be considered in other patient categories, as investigators continue to generate new evidence. For example, a recent meta-analysis suggested absence of evidence for benefits of ventilation with a high PEEP level in critically ill ventilated patients without ARDS.<sup>9</sup> This meta-analysis did not even show benefit of the commonly used PEEP level of '5 cm H<sub>2</sub>O', which usually is considered to be the minimum level to be used during invasive positive pressure ventilation.

This same finding of lack of benefit is true for patients undergoing surgery who receive intraoperative ventilation.<sup>7</sup> Even though the results of randomized clinical trials suggest benefit of use of a high PEEP level during intraoperative ventilation,<sup>7</sup> the majority of these trials did not simply compare different PEEP levels, but instead 'bundles of ventilation' consisting of a low tidal volume with a high PEEP level versus a high tidal volume with a low PEEP level. Indeed, the question is whether benefit resulted from tidal volume reduction, PEEP level increase, or both. In addition, a recently published randomized trial of intraoperative ventilation that compared ventilation with a low PEEP level versus one with a high PEEP level demonstrated no benefit from a high PEEP level.<sup>10</sup>

In this issue of JAMA, Leme *et al.*<sup>11</sup> present the results of a single center randomized clinical trial of postoperative ventilation comparing a low PEEP level with a high PEEP level added to a lung protective ventilator strategy in hypoxemic patients after cardiac surgery. In this trial, postoperative ventilation with a high PEEP level (157 patients) compared to a lower PEEP level (163 patients) resulted in a significant shift toward less severe pulmonary complications and was associated with a shorter length of stay in intensive care unit (3.8 versus 4.8 days) and hospital (10.9 versus 12.34 days). These results are intriguing and could be important for advancing current understanding of the role of PEEP in postoperative ventilation. Furthermore, the findings also may help determine which patients may benefit from ventilation using a high PEEP level.

The results of the trial by Leme *et al.*<sup>11</sup> are, at least in part consistent with those from two previous studies of postoperative ventilation.<sup>12,13</sup> The first, a 'physiological' study in

patients following cardiac surgery, showed that the lung and chest wall were stiffer in the first postoperative hours.<sup>12</sup> This could be a potential reason for consideration of using a high PEEP level in these patients, at least for some hours. The second report, a before–after study in patients following cardiac surgery, showed that a ventilation strategy using a high level of PEEP for 4 hours was associated with improved oxygenation lasting days after surgery.<sup>13</sup> In contrast to the trial by Leme *et al.*<sup>11</sup> the investigators of that study failed to show a positive association with other clinical outcomes.<sup>13</sup> Important, patients in this earlier study of cardiac surgery patients differed from those included in the randomized trial by Leme *et al.*<sup>11</sup> The trial by Leme *et al.*<sup>11</sup> included only patients who presented with hypoxemia, whereas the earlier study had no restrictions with regard to whether the patient was hypoxemic.<sup>13</sup>

Could it be hypothesized that patients included in the randomized trial by Leme *et al.*<sup>11</sup> were not ‘simple’ postoperative patients with ‘healthy’ lungs, but instead were patients with ‘injured’ lungs after cardiac surgery? Patients included in the trial by Leme *et al.*<sup>11</sup> were not only having oxygenation problems, but also had stiff lungs, as seen by their low respiratory system compliance. Also, electrical impedance tomography showed a misdistribution of ventilation, a typical finding in patients with severe alveolar collapse. Considering this information is it possible that these patients could have had a type of ‘postoperative ARDS’? For patients with this clinical profile, there is proven evidence for benefit of ventilation with a high PEEP level.<sup>8</sup>

Thus, the question remains as to whether a high PEEP level should be used in all patients. However, high PEEP not only recruits collapsed lung tissue, but can also lead to lung overdistension. If lung collapse is extensive, as in patients with ARDS, and maybe also in patients with ‘postoperative ARDS’, the balance between benefit, i.e., recruitment of lung tissue, and harm, i.e., lung overdistension, tips towards the first. If there is very little lung collapse, as in critically ill patients without ARDS or patients during surgery, this balance could go in the other direction.

Finally, postoperative ventilation with high PEEP in the randomized trial by Leme *et al.*<sup>11</sup> resulted in a lower driving pressure. A recent meta–analysis showed that a change in

the PEEP level resulting in a lower driving pressure level during intraoperative ventilation was associated with a lower incidence of postoperative pulmonary complications.<sup>14</sup> This raises the issue of whether it is best to select a 'fixed' high PEEP level, or whether PEEP level should be titrated, trying to reach a low driving pressure level. Leme *et al.*<sup>11</sup> could do an additional analysis to see whether there is a relation between the driving pressure level and the occurrence of postoperative complications. Could it be that in some patients ventilated with a high PEEP level, the driving pressure level did not change, or even increased? To put it differently, could it be that in some patients it could have been better to 'accept' some lung collapse, as the price for opening them was a higher driving pressure level?<sup>15,16</sup>

In conclusion, the clinical trial by Leme and colleagues in this issue of JAMA provides another brick in the wall of 'lung-protection'. However, it remains unclear which patients benefit most from ventilation with a high PEEP level.

### **Funding**

Support was provided solely from institutional and/or departmental source.

## References

1. Putensen C, Theuerkauf N, Zinserling J, Wrigge H, Pelosi P. Meta-analysis: ventilation strategies and outcomes of the acute respiratory distress syndrome and acute lung injury. *Ann Intern Med* 2009; 151:566-76.
2. Terragni PP, Rosboch G, Tealdi A, et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2007; 175:160-6.
3. Bein T, Weber-Carstens S, Goldmann A, et al. Lower tidal volume strategy ( $\approx 3$  ml/kg) combined with extracorporeal CO<sub>2</sub> removal versus 'conventional' protective ventilation (6 ml/kg) in severe ARDS: the prospective randomized Xtravent-study. *Intensive Care Med* 2013; 39:847-56.
4. Ferguson ND. Low tidal volumes for all? *JAMA* 2012; 308:1689-90.
5. Neto AS, Simonis FD, Barbas CS, et al. Lung-Protective Ventilation With Low Tidal Volumes and the Occurrence of Pulmonary Complications in Patients Without Acute Respiratory Distress Syndrome: A Systematic Review and Individual Patient Data Analysis. *Crit Care Med* 2015; 43:2155-63.
6. Fuller BM, Ferguson IT, Mohr NM, et al. A Quasi-Experimental, Before-After Trial Examining the Impact of an Emergency Department Mechanical Ventilator Protocol on Clinical Outcomes and Lung-Protective Ventilation in Acute Respiratory Distress Syndrome. *Crit Care Med* 2017; 45:645-52.
7. Serpa Neto A, Hemmes SN, Barbas CS, et al. Protective versus Conventional Ventilation for Surgery: A Systematic Review and Individual Patient Data Meta-analysis. *Anesthesiology* 2015; 123:66-78.
8. Briel M, Meade M, Mercat A, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA* 2010; 303(9):865-73.
9. Serpa Neto A, Filho RR, Cherpanath T, et al. Associations between positive end-expiratory pressure and outcome of patients without ARDS at onset of ventilation: a

systematic review and meta-analysis of randomized controlled trials. *Ann Intensive Care* 2016; 6:109.

10. The PROVE Network Investigators. Higher versus lower positive end-expiratory pressure during general anaesthesia for open abdominal surgery: the PROVHILO trial. *Lancet* 2014; 384:495–503.

11. Leme AC, Hajjar LA, Volpe MS, et al. Effect of Intensive vs Moderate alveolar Recruitment Strategies Added to Lung-Protective Ventilation on Postoperative Pulmonary Complications: A Randomized Clinical Trial in Hypoxemic Patients after Cardiac Surgery. *JAMA* 2017; 317:1422-32.

12. Ranieri VM, Vitale N, Grasso S, et al. Time-course of impairment of respiratory mechanics after cardiac surgery and cardiopulmonary bypass. *Crit Care Med* 1999; 27:1454-60.

13. Dongelmans DA, Hemmes SN, Kudoga AC, Veelo DP, Binnekade JM, Schultz MJ. Positive end-expiratory pressure following coronary artery bypass grafting. *Minerva Anesthesiol* 2012; 78:790-800.

14. Neto AS, Hemmes SN, Barbas CS, et al. Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: a meta-analysis of individual patient data. *Lancet Respir Med* 2016; 4:272-80.

15. Gldner A, Kiss T, Serpa Neto A, et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *Anesthesiology* 2015; 123:692-713.

16. Chu EK, Whitehead T, Slutsky AS. Effects of cyclic opening and closing at low- and high-volume ventilation on bronchoalveolar lavage cytokines. *Crit Care Med* 2004; 32:168-74.