Lung protective ventilation strategies in routine anaesthetic practice: ready for prime time?

P Toth-Tarsoly¹, T Szakmany¹,² *

Abstract
Introduction
The use of high tidal volumes, defined as tidal volume >10 ml/kg, in mechanically ventilated patients, was promoted as the standard after demonstrating the increased incidence of atelectasis in patients in whom low volume ventilation was used in the 1960s. However, in the 1970s, animal experiments suggested that high tidal volume ventilation leads to ventilator-induced lung injury, and this phenomenon was later confirmed by clinical studies.

Protective ventilation is a ventilation strategy where the patient’s lungs are ventilated with a low tidal volume (in the range of 4–8 ml/kg of predicted body weight), in order to protect the lungs from ventilator-induced lung injury. The benefits of using lung-protective ventilation strategies in patients with acute respiratory distress syndrome have been widely established and recommended. There is increasing evidence to prove that even in patients without acute respiratory distress syndrome, the use of high tidal volumes can cause injury to the lungs. Our aim was to review past literature regarding the use of lung-protective ventilation strategies, in patients mechanically ventilated with high VTs. However, in the 1970s, animal studies proved that high VT ventilation leads to ventilator-induced lung injury (VILI)²,³, and this finding was later confirmed by clinical studies⁴. VILI is initiated by high VTs which lead to high alveolar pressures, causing a wide range of local and systemic changes. High alveolar pressure results in barotrauma, and lung overdistention leads to volutrauma. The sheer stress of reopening and closing of the alveoli causes atelectrauma, leading to the generation of inflammatory cytokines that cause activation of the inflammatory cascade, resulting in biotrauma.

Protective ventilation is a ventilatory strategy where the patient is ventilated with a low VT (in the range of 4–8 ml/kg of predicted body weight [PBW]), in order to protect the lungs from VILI. The benefits of using lung-protective ventilation strategies in patients with acute respiratory distress syndrome (ARDS) has been widely established and recommended⁶-⁹. However, there is increasing evidence to prove that high VT ventilation can cause injury to the lungs and other organs¹⁰-¹². In addition, ventilated patients are at risk of developing hospital-acquired ARDS¹⁰-¹².

Our aim was to review past literature regarding the use of lung-protective ventilation strategies, in patients mechanically ventilated in the operating theatre for elective or emergency procedures. Our critical review is focussed on the prevention of lung injury using a prophylactic lung-protective ventilation strategy during anaesthesia as emerging new research shows that it can decrease the length of ventilation and help in the prevention of ARDS. However, the use of prophylactic lung-protective ventilation strategy is still not well established in patients without ARDS.

Discussion
Prophylactic lung-protective ventilation
ARDS can develop in patients after either direct (pulmonary pneumonia, lung contusion or toxic inhalation) or indirect, extrapulmonary (sepsis/systemic inflammation of non-lung origin, cardiopulmonary bypass or multiple transfusions) insult. Ventilation of the already injured lungs with high VT and consequently increased alveolar and transpulmonary pressures will further aggravate the problem, leading to VILI¹⁰-¹². It has

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### Critical review

#### Table 1. Studies comparing the effect of high and low VT ventilatory strategies during anaesthesia for surgery.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Patient population</th>
<th>Number of patients</th>
<th>Control settings</th>
<th>Experimental settings</th>
<th>Main findings</th>
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<tr>
<td></td>
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<td>VT (ml/kg)</td>
<td>PEEP (cm H2O)</td>
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<td></td>
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<td></td>
<td>VT (ml/kg)</td>
<td>PEEP (cm H2O)</td>
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<td>Wrigge et al.15</td>
<td>RCT</td>
<td>Elective non-thoracic</td>
<td>39</td>
<td>15</td>
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<td>Chaney et al.16</td>
<td>RCT</td>
<td>CABG</td>
<td>25</td>
<td>12</td>
<td>≥5</td>
<td>6</td>
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<td>Koner et al.17</td>
<td>RCT</td>
<td>CABG</td>
<td>44</td>
<td>10</td>
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<td>RCT</td>
<td>Abdominal and thoracic surgery</td>
<td>64</td>
<td>12–15</td>
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<td>Schilling et al.19</td>
<td>RCT</td>
<td>Thoracic surgery</td>
<td>32</td>
<td>10</td>
<td>3</td>
<td>5</td>
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<td>CABG</td>
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<td>12</td>
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<td>Reis Miranda et al.21</td>
<td>RCT</td>
<td>CABG</td>
<td>62</td>
<td>6–8</td>
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<td>Zupancich et al.22</td>
<td>RCT</td>
<td>CABG</td>
<td>40</td>
<td>10–12</td>
<td>2–3</td>
<td>8</td>
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<tr>
<td>Fernández-Pérez et al.23</td>
<td>OBS</td>
<td>Pneumonectomy</td>
<td>170</td>
<td>8.3 (mean)</td>
<td>6.7 (mean)</td>
<td>VT risk factor for acute respiratory failure</td>
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<tr>
<td>Choi et al.24</td>
<td>RCT</td>
<td>Elective abdominal surgery</td>
<td>40</td>
<td>12</td>
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<td>6</td>
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<td>Michelet et al.25</td>
<td>RCT</td>
<td>Oesophagectomy</td>
<td>52</td>
<td>9</td>
<td>0</td>
<td>5</td>
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<td>Licker et al.26</td>
<td>COH</td>
<td>Pneumonectomy</td>
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<td>7.1**</td>
<td>3.3**</td>
<td>5.3**</td>
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<td>Weingarten et al.27</td>
<td>RCT</td>
<td>Abdominal surgery</td>
<td>40</td>
<td>10</td>
<td>0</td>
<td>6</td>
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<tr>
<td>Yang et al.28</td>
<td>RCT</td>
<td>Pulmonary lobectomy</td>
<td>100</td>
<td>10</td>
<td>0</td>
<td>6</td>
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<td>Sundar et al.29</td>
<td>RCT</td>
<td>CABG and valves</td>
<td>149</td>
<td>10</td>
<td>≥5*</td>
<td>6</td>
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<tr>
<td>Lellouche et al.30</td>
<td>OBS</td>
<td>CABG and valves</td>
<td>3434</td>
<td>&lt;10 10–12 &gt;12</td>
<td>Less ITU stay and less organ dysfunction with low VT</td>
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</table>
been shown that VILI can worsen lung and systemic inflammatory mechanisms with a potential to cause iatrogenic ARDS. This mechanism is called the multiple-hit theory of ARDS\(^1\)\(^,\)\(^2\)\(^,\)\(^3\). Consequently, patients at a higher risk of developing lung injury could potentially benefit the most in protective ventilation with general anaesthesia during surgery, as this strategy may prevent the development of ARDS.

Studies that evaluate the effect of lung protective ventilation during general anaesthesia have been summarised in Table 1. Most of these studies involved patients undergoing cardiac or thoracic surgery, as these procedures generally take longer and patients are frequently admitted to intensive therapy units (ITU) postoperatively, requiring invasive ventilation for a longer duration. Postoperative respiratory complications occur relatively frequently in this patient population, hence, a better outcome can be expected using low VT ventilation. In general, the protective ventilation strategy involved VTs of 6–8 ml/kg with the use of positive end-expiratory pressure (PEEP). In the control groups, the practice was more varied from VTs of 15 ml/kg with no PEEP to 8 ml/kg with PEEP.

### Biochemical effects of lung-protective ventilation

Although some studies found no significant differences in the levels of inflammatory markers when comparing low and high intraoperative VTs\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^4\)\(^,\)\(^6\), others showed significant changes in favour of the lung-protective ventilation strategy. Schilling et al.\(^1\)\(^9\) showed a decrease in tumour necrosis factor-alpha (TNF-a) and soluble intercellular adhesion molecule 1 levels in the study population undergoing thoracic surgery. Wrigge et al.\(^2\)\(^0\) also found decreased TNF-a levels in the bronchoalveolar lavage samples of their coronary artery bypass graft (CABG) patients. Reis Miranda et al.\(^2\)\(^1\) found that the levels of pro-inflammatory cytokine levels decreased more rapidly in patients who were ventilated with low VT. Zupancich et al.\(^2\)\(^2\) also showed a reduced increase in pro-inflammatory cytokine levels (Interleukin-6 and Interleukin-8) after cardiopulmonary bypass, using lung-protective ventilation. Michelet et al.\(^2\)\(^3\) showed the same results in oesophagectomy patients. Choi et al.\(^2\)\(^4\) showed that after 5 hours of mechanical ventilation in abdominal surgical patients, the group receiving low VT ventilation had decreased activation in the coagulation system.

### Pathophysiological effects of intraoperative lung-protective ventilation

Although changes in the biochemical markers are crucially important, clinical outcome data provide more relevant information for the clinician involved in patient care. There are several randomised, controlled studies that have shown the beneficial effects of lung-protective ventilation. Chaney et al.\(^2\)\(^5\) investigated 25 patients undergoing CABG surgery. The patients were randomised into high VT (12 ml/kg) and low VT (6 ml/kg) groups, and they found that the low VT group showed improved respiratory mechanics. Michelet et al.\(^2\)\(^6\) studied 52 patients undergoing oesophagectomy. The patients in the low VT ventilation strategy group had improved oxygenation and shorter duration of mechanical ventilation. Although Weingarten et al.\(^2\)\(^7\) did not find any difference in the biomarker levels in their elderly, abdominal surgical patient population (40 patients, age >65), they found significant improvement in respiratory mechanics and oxygenation in the study group (PEEP: 12 cm H\(_2\)O, VT: 6 ml/kg) when compared with the control group (PEEP: 0 cm H\(_2\)O, VT: 10 ml/kg), without experiencing haemodynamic compromise. Yang et al.\(^2\)\(^8\) showed trend towards lesser pulmonary infections and lesser MV duration.

<table>
<thead>
<tr>
<th>Study</th>
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<th>Main findings</th>
</tr>
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<tr>
<td>Lee et al.(^3)(^1)</td>
<td>RCT</td>
<td>Mixed postoperative patients</td>
<td>103</td>
<td>VT (ml/kg)</td>
<td>PEEP (cm H(_2)O)</td>
<td>VT (ml/kg) PEEP (cm H(_2)O) Trend towards lesser pulmonary infections and lesser MV duration</td>
</tr>
<tr>
<td>Treschan et al.(^3)(^2)</td>
<td>RCT</td>
<td>Upper abdominal surgery</td>
<td>101</td>
<td>VT (ml/kg)</td>
<td>PEEP (cm H(_2)O)</td>
<td>VT (ml/kg) PEEP (cm H(_2)O) No difference in postoperative lung spirometry</td>
</tr>
</tbody>
</table>

**References:**

1. Lee et al.\(^3\)\(^1\) RCT Mixed postoperative patients.
2. Treschan et al.\(^3\)\(^2\) RCT Upper abdominal surgery.

**Study design** refers to the type of study design used, including RCT (randomised controlled trial) or OBS (observational study).

**Patient population** describes the type of surgical procedure and the patient demographics.

**Main findings** highlight the key outcomes of the studies, focusing on trends towards reduced pulmonary infections and shorter mechanical ventilation duration.

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**Further Reading:**


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randomised 100 patients undergoing pulmonary lobectomy. The patients who received low VT with PEEP had decreased incidence in pulmonary dysfunction in the first 72 hours postoperatively, as compared with conventional ventilation. Sundar et al. 29 randomised 149 patients undergoing elective cardiac surgery into low VT (6 ml/kg PBW) and high VT (10 ml/kg PBW) subgroups. PEEP settings were adjusted according to ARDS Network PEEP/FiO2 sliding scale, in both groups. They found that at 6 h and 8 h, significantly more patients were extubated in the low VT group. There was a significantly reduced reintubation rate in the study group as well. Lee et al. 31 randomised 103 mixed surgical patients into high and low VT groups. They found a trend towards less pulmonary infections and less time on mechanical ventilation in the low VT group. Tresch et al. 32 investigated 101 patients, undergoing upper abdominal surgery, in low VT and high VT groups and compared postoperative spirometry results. Both groups received the same PEEP (5 cm H2O) and both were ventilated to normocapnia. They did not find any significant differences in the postoperative lung function between the 2 groups. 32

In an observational study, Fernández-Pérez et al. 23 analysed the charts of 170 patients who underwent pneumonectomy. Of these, 18% of the patients developed acute respiratory failure, and 50% developed acute lung injury (ALI). They found that the patients who developed respiratory failure had higher intraoperative VT compared to those who did not (mean: 8.3 ml/kg vs 6.7 ml/kg; p < 0.001, odds ratio [OR]:1.56). Licker et al. 26 prospectively collected data from 1091 patients undergoing lung cancer resection over 10 years, comparing collected data from before and after implementation of the lung protective ventilation protocol. Baseline characteristics were the same in the two groups, except for a higher cardiovascular risk profile in the treatment group. After implementation of lung-protective ventilation, there was a decreased incidence of ALI (from 3.9% to 0.9%, p < 0.01) and atelectasis (from 8.8% to 5.0%, p = 0.018), fewer admissions to intensive care units (from 9.4% to 2.5%, p < 0.001) and shorter durations of hospital stay (from 14.5 ± 3.3 to 11.8 ± 4.1, p < 0.01). Implementation of the lung protective ventilation strategy was associated with a reduced risk for ALI (adjusted OR of 0.34). Lellouche et al. 30 prospectively recorded data from 3434 patients undergoing cardiac surgery. They defined three groups of patients based on VT on arrival to ITU: high VT (>12 ml/kg), traditional VT (10–12 ml/kg) and low VT (<10 ml/kg). They assessed the patients for risk factors associated with organ failure (prolonged mechanical ventilation, haemodynamic instability and renal failure) and for prolonged intensive care stay. The mean VT/actual body weight was 9.2 ml/kg, and mean VT/PBW was 11.5 ml/kg. Low, traditional and high VT was used in 21.1%, 45.6% and 33.3% of patients, respectively. Independent risk factors associated with high VT were body mass index ≥30 (OR: 6.25, p < 0.001) and female sex (OR: 4.33, p < 0.001). High and traditional VTs were independent risk factors for organ failure, multi organ failure and prolonged ITU stay. Organ failures were associated with longer ITU stay, higher hospital mortality and long-term mortality. Jaber et al. 31 conducted a multicentre, observational study to describe intraoperative ventilatory practices to determine the incidence of the use of large intraoperative VTs (>10 ml/kg of ideal body weight [IBW]) and to identify patient specific risk factors associated with this practice. They studied 2960 patients in 97 anaesthetic units in 49 hospitals. Of these, 85% of the cases were ventilated in the volume controlled mode; no patient was ventilated with synchronised intermittent mandatory ventilation. Pressure controlled ventilation (PCV) was used in 13% of cases, and only 15 patients received pressure support ventilation (9 from the same centre). In most of the cases, a tracheal tube was used (89%), 9% had a laryngeal mask inserted and 2% had their anaesthetic with a facemask. The mean VT was 533 ml, 7.7 ml/kg actual weight and 8.8 ml/kg IBW. In 18% of the cases, the lungs were ventilated with VT >10 ml/kg IBW, and 52 patients (2%) received a VT >12 ml/kg IBW. PEEP was applied in nearly 20% of the cases. Being female (OR: 5.58) and by logistic regression, underweight (OR: 0.06), overweight (OR: 1.98), obese (OR:5.02), severely obese (OR:10.12) and morbidly obese (OR:14.49) were the significant independent factors (p ≤0.005) for the use of large VTs during anaesthesia.

To overcome the potential effects of low VT ventilation on oxygenation, the use of regular recruitment manoeuvres (RM) has been advocated in ARDS. 7

At present, there are very few studies available on the effectiveness of alveolar recruitment, intraoperatively. Unzueta et al. 34 randomised 40 patients undergoing thoracotomies into recruitment and control groups. The recruitment group received 10 breaths of 40 cm H2O peak inspiratory pressure (PIP) over 20 cm H2O PEEP, immediately before commencing one-lung ventilation. They found that the recruitment not only decreased alveolar dead space but also improved oxygenation and the efficacy of ventilation.

In their meta-analysis, Aldenkortt et al. 35 compared results from 13 published, randomised, controlled trials testing intraoperative ventilation strategies in obese patients, and reporting on gas exchange, pulmonary mechanics or pulmonary complications. Six trials compared the effect of PEEP (5 or 10 cm H2O) with combined effects of PEEP and RM. They used four ways to recruit alveoli: PIP of 40 cm H2O for 40 s, PIP of 55 cm H2O for 10 s, PIP of 40 cm H2O with PEEP 20 cm H2O for 3 min, or incremental or sudden increase
in PEEP from 5 to 20 or 30 cm H2O. Using RM improved intraoperative PaO2/FiO2 ratio and increased respiratory system compliance, but did not affect intraoperative mean arterial pressure. Barotrauma was sought in two studies. In these studies, none of the 118 patients ventilated with PEEP, with or without RM, were reported to suffer from barotrauma after the operation. Four randomised, controlled trials compared PCV with volume controlled ventilation. They found no evidence showing any difference between ventilation modes in terms of PaO2/FiO2 ratio, intraoperative VTs or mean airway pressure. There was no evidence of any differences in cardiovascular parameters.

Implications for practice
Since the first publication on the benefits of lung protective ventilation in ARDS, many intensive care unit clinicians, working in the operating theatre, slowly adopted it in anaesthetic practice. The physiological rationale for the wider adoption of this approach hasn’t changed since then. Emerging data shows that low VT ventilation is not only feasible but also safe, and can potentially reduce postoperative morbidity, especially after long procedures. Low VT ventilation can significantly improve respiratory mechanics and reduce VILI even after a short exposure.

While the use of lower VTs can still lead to atelectasis and hypoxia as described in the Bendixen paper, it is now widely accepted that judicious application of PEEP can prevent these consequences. Although the optimal level of PEEP is undetermined at present, it has been repeatedly shown that the application of zero PEEP is associated with increased hypoxaemia, increased rate of health-care-associated infections and even hospital mortality. The presented data support findings suggesting that RM together with the application of 5–12 cm H2O PEEP can prevent and reverse this phenomena, even in the most affected obese patient populations. It has also been shown that high FiO2 levels, above 0.6, could be detrimental in ALI/ARDS, causing oxidative stress and denitrogenation atelectasis. While there is some evidence that hyperoxia during colorectal cancer surgery can improve wound healing, in most other procedures, SpO2 above 96% does not confer any clinical benefits. Moreover, predisposing hyperoxia and high VT mechanical ventilation, a common clinical scenario in emergency surgery, has been shown to play a pivotal role in inducing lung injury-mediated caspase activation and hence epithelial apoptosis leading to VILI.

Knowledge translation from research to daily clinical practice can take several years, and even the most highly convincing results from the ARDS trials suffered from this phenomena. One of the main barriers in the adoption of PBW-based VT settings is that it leads to ‘unconventionally low’ VTs. The evidence presented here suggests that VTs of 6–8 ml/kg PBW are safe to use and provide potential benefits during intraoperative ventilation, especially if the patients have risk factors for developing ALI/ARDS. This is easier in the intraoperative setting as literature suggests that surgical patients are more likely to have their height and weight measured than their medical counterparts. With the advent of electronic patient records and intelligent advisory systems it is not inconceivable that PBW and calculated ‘best’ VT could be incorporated into modern anaesthetic practice.

Conclusion
The use of lung protective ventilation strategy supplemented by intermittent RMs is recommended in the majority of patients who are ventilated during surgery. The use of 6–8 ml/kg PBW VT, together with at least 5 cm H2O PEEP and intermittent recruitment with PIP of approximately 40 cm H2O in prolonged procedures, could lead to significantly better outcomes in patients at risk of developing postoperative respiratory complications. Further investigations are needed on how these research findings could be implemented in everyday clinical practice.

Abbreviations list
ALI, acute lung injury; ARDS, acute respiratory distress syndrome; CABB, coronary artery bypass graft; IBW, ideal body weight; ITU, intensive therapy units; PBW, predicted body weight; PCV, pressure controlled ventilation; PEEP, positive end-expiratory pressure; PIP, inspiratory pressure; RM, recruitment manoeuvres; TNF-a, tumour necrosis factor-alpha; VILI, ventilator-induced lung injury; VT, tidal volumes.

References

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All authors abide by the Association for Medical Ethics (AME) ethical rules of disclosure.

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