Ventilation with low tidal volumes during upper abdominal surgery does not improve postoperative lung function

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Patients who are mechanically ventilated during surgery experience varying degrees of postoperative lung function impairment, including decreased forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1). Risk factors for severe postoperative lung function impairment include the duration, site, and technique of surgery. In contrast, the type of anaesthesia and the choice of anaesthetics can help to minimize postoperative lung function impairment. Whether intraoperative tidal volume (VT) influences postoperative lung function is unknown. Previous trials found that high VT during abdominal surgery maintained better intraoperative lung mechanics and gas exchange than low VT. Relatively high VT is thus routinely used for intraoperative mechanical ventilation. However, high airway pressures, lung overdistention, or both may aggravate or even induce lung injury. Based on results from acute respiratory distress syndrome (ARDS) and critically ill patients, there is a growing trend to favour low VT for patients without lung injury who require intraoperative ventilation. Of note, there are no robust data on the proper application of PEEP in this context. Low VT combined with moderate PEEP is nonetheless increasingly used for intraoperative ventilation without an adjustment of PEEP. This thus remains unclear whether a reduction in VT per se is beneficial compared with traditional high VT with similar PEEP for patients undergoing intraoperative ventilation.

If low intraoperative VT combined with moderate PEEP is protective, patients at high risk for postoperative pulmonary complications might benefit from improved postoperative lung function including earlier recovery of FVC and FEV1. We therefore tested the hypothesis that intraoperative...
ventilation with low $V_T$ improves postoperative time-weighted average (TWA) FVC and FEV$_1$ in patients undergoing elective upper abdominal surgery.

**Methods**

Our study was approved by the local ethics committee (Ethics committee of the Medical Faculty, Heinrich-Heine-University Düsseldorf, Germany, study number 2974 and registered at ClinicalTrials.gov number 00795964). We studied 101 patients (age $\geq$ 50 yr, ASA $\geq$ II) undergoing elective upper abdominal surgery lasting at least 3 h with combined general and epidural anesthesia. Exclusion criteria were impaired mental state, increased intracranial pressure, or neuromuscular disease.

Patients were premedicated with midazolam 0.1 mg kg$^{-1}$ orally up to a maximal total dose of 7.5 mg. Before general anaesthesia, arterial and epidural catheters were inserted [epidural catheter level T$_7$–T$_{12}$; loading dose: 10–15 ml ropivacaine 0.75%, continuous infusion: ropivacaine 0.375% (6–8 ml h$^{-1}$)]. General anaesthesia was induced with sufentanil 0.4 $\mu$g kg$^{-1}$, thiopental 4–5 mg kg$^{-1}$, or propofol 1–2 mg kg$^{-1}$. It was maintained with sevoflurane in oxygen/air and sufentanil. Tracheal intubation was facilitated by succinylcholine (1 mg kg$^{-1}$), cis-atracurium (0.2 mg kg$^{-1}$), or rocuronium (0.6 mg kg$^{-1}$). High-volume, low-pressure cuffs with an internal diameter of 7.5 mm for women and 8.0 mm for men (Mallinkrodt$^\text{TM}$ Hi-Contour tube) were inflated with air and cuff pressure maintained below 20 mbar. A central venous catheter and a nasogastric tube were inserted. An additional non-depolarizing neuromuscular blocking agent and vasopressors were given as deemed necessary by the attending anaesthesiologist.

Anaesthetic administration was adjusted to maintain arterial pressure and heart rate within 20% of preoperative values. We aimed to maintain normothermia. The primary criteria were impaired mental state, increased intracranial pressure, or neuromuscular disease.

The patients were randomly assigned to (i) the high $V_T$ (12 ml kg$^{-1}$ predicted body weight (PBW)) group or (ii) the low $V_T$ (6 ml kg$^{-1}$ PBW) group. Computer-generated randomization codes (permuted blocks of 10, allocation ratio 1:1) were kept in sequentially numbered sealed opaque envelopes until shortly before induction of general anaesthesia. PBW was calculated as follows:

Men : \[ \text{PBW in kg} = 50.0 + 0.91 \times (\text{height in cm} - 152.4) ; \]

Women : \[ \text{PBW in kg} = 45.5 + 0.91 \times (\text{height in cm} - 152.4) . \]

After intubation, $V_T$ was set to the designated values. The initial breathing rate of 14 (low $V_T$) or 7 (high $V_T$) min$^{-1}$ was subsequently adjusted to maintain end-tidal $P_{CO_2}$ of 4.6–5.4 kPa (35–40 mm Hg). Other ventilator settings were identical in both groups, including an initial fresh gas flow of 10 litre min$^{-1}$ with an inspired oxygen fraction ($F_{IO_2}$) of 1.0, PEEP 5 cm H$_2$O, and inspiratory-to-expiratory ratio 1:2. $F_{IO_2}$ was reduced to 0.5 shortly after intubation, and fresh gas was provided by a ZEUS anaesthesia machine in the autotitration mode (Dräger, Lübeck, Germany).

If deemed necessary by the attending physician, $F_{IO_2}$ or PEEP was increased to maintain $P_{A_{O_2}}$ within 20% of preoperative values or $S_{P_{O_2}} \geq 95\%$.

Before weaning, $F_{IO_2}$ was increased to 1.0 for 15 min. The neuromuscular blocking agent was antagonized if necessary at the discretion of the attending anaesthesiologist. When spontaneous breathing began, support was achieved with a continuous positive airway pressure of 5 cm H$_2$O and assisted spontaneous breathing adjusted so as to maintain end-tidal $P_{CO_2}$ 4.6–5.4 kPa (35–40 mm Hg) with pressure support levels of 3–10 cm H$_2$O. All patients received a lung expansion manoeuvre consisting of three manual bag ventilations with a maximum pressure of 40 cm H$_2$O shortly before extubation. Mechanical ventilation of patients who were transferred intubated to the intensive care unit (ICU) was continued according to group assignment under the discretion of the intensivist in charge. After operation, all patients received standard institutional care, including regular visits and treatment by our pain service and personal physiotherapy with respiratory exercises, mobilization, and incentive spirometry.

**Measurements**

Patients and postoperative investigators were blinded to intraoperative group assignment; thus, all postoperative data were collected in a double-blinded fashion.

Blood loss and fluid administration including allogenic blood, vital signs, core temperature, ventilator settings, $F_{IO_2}$, end-tidal $CO_2$, and airway pressures were recorded at 15 min intervals throughout surgery, and blood gas analyses were performed hourly or more often as clinically indicated.

**Spirometry**

Preoperative spirometry was performed after the patient had received a detailed instruction. Measurements were performed in accordance with the American Thoracic Society’s standards$^8$ using a single pneumotachograph (SpiroPro, Jaeger, Würzburg, Germany). We made all measurements in the supine position with 30° upper body elevation. After operation, measurements were taken at 1–2, 24, 72, and 120 h after extubation. We aimed to measure FEV$_1$ and FVC three times at each time point with the highest values selected for analysis. Patients were requested to rate their pain at rest in the supine position with 30° upper body elevation on a numeric rating scale of 0–10 (0, no pain; 10, maximum pain). Spirometric testing was only performed if pain scores at rest were $\leq$ 3. Otherwise, pain therapy was optimized before spirometric measurements.

**Blood gas analysis**

Before and after operation, blood was sampled for gas analysis just after each spirometric measurement. If an arterial
catheter was in place, blood was withdrawn from it; otherwise, arterialized blood gases [pre-treatment of the ear lobe with a nonivamid- and nicobool-containing cream (finalgon®)] were sampled from the patient's ear lobe. Supplemental oxygen, if being used, was withdrawn 15 min before each postoperative spirometry and blood gas analysis.

Chest radiographs
Immediate postoperative chest radiographs were performed as part of the clinical routine after central line placement and prolonged surgery. Anteroposterior X-rays were taken with the patients in the supine position using a portable X-ray machine. Results were scored by a radiologist unaware of group assignment using a Radiological Atelectasis Score: 0, clear lung field; 1, plate like atelectasis or slight infiltration; 2, partial atelectasis; 3, lobar atelectasis; 4, bilateral lobar atelectasis.9

Others
The Sequential Organ Failure Assessment score was calculated on the fifth postoperative day.10 The duration of hospitalization, ICU stay, and mortality were recorded from the patients’ charts and the hospital data management system. Severe postoperative complications (acute heart failure, myocardial infarction, ARDS, renal insufficiency, venous embolism, and wound infections) were assessed using a checklist during the daily visits until postoperative day 5. Information until hospital discharge was obtained from the hospital data management system. The incidence of postoperative pulmonary complications was defined as: (i) respiratory failure: $P_{aO_2} \leq 6.7$ kPa while breathing ambient air or $P_{aCO_2} \geq 6.7$ kPa while breathing spontaneously,11 (ii) reintubation for respiratory distress during hospital stay; (iii) pneumonia; (iv) unplanned mechanical ventilation >24 h for pulmonary reasons; or (v) pneumothorax. Impaired oxygenation was defined by a $P_{aO_2}/FIO_2$ ratio of <40 kPa.

Statistical analysis
Our primary outcome variables were TWAs of postoperative FVC and FEV₁.

The sample-size estimate indicated that a minimum of 48 patients per group would provide an 80% chance of detecting a 20% relative increase in FVC from a presumed postoperative FVC of 2.0 (0.7) litre with a corresponding FEV₁ of 1.5 (0.5) litre.

Data are presented as absolute values, mean (SD), or percentages on an intention-to-treat basis. Two-tailed Fishers’ exact test, Student’s t-test, or Wilcoxon rank-sum tests were used as appropriate. Because there were two primary outcomes, time-weighted FVC and FEV₁, a P-value of <0.025 was considered statistically significant. For secondary outcomes, which were exploratory, a P-value of <0.05 was accepted. We used ‘R’ software (R Foundation for Statistical Computing, Vienna, Austria, http:www.R-project.org).

Results
Over a 2 yr period, 101 patients were enrolled (Fig. 1) and randomized to high or low $V_T$. The two groups had similar preoperative and intraoperative characteristics, except for the randomly assigned ventilatory parameters (Table 1). Chronic medications and doses of anaesthetics, including neuromuscular blocking agents, did not differ significantly between the groups (data not shown).

Spirometry
TWA FVC was 1.8 (0.7) litre for the 6 ml group vs 1.6 (0.5) litre for the 12 ml group ($P=0.12$) and TWA FEV₁ 1.4 (0.5) litre for the 6 ml group vs 1.2 (0.4) litre for the 12 ml group ($P=0.15$). FVC and FEV₁ also did not differ significantly between groups at any postoperative time point (Fig. 2). Spirometry was performed in 58 patients immediately after surgery and in 54 patients on day 1. The measurement could not be performed as planned in the missing cases due to ventilatory support, reduced consciousness and lack of willingness, or high pain scores. On postoperative days 3 and 5, measurements were possible in 70 and 75 patients, respectively.

Intraoperative respiratory parameters
Intraoperative $P_{aO_2}/FIO_2$ ratios, compliance, resistance, and airway pressures of the 12 ml group were significantly higher (Figs 3 and 4). One patient in the 12 ml group suffered from severe bronchospasm immediately after intubation and received extensive bronchospasmolytic therapy. Two patients received neostigmine to antagonize muscle relaxation; both of them were in the 12 ml group.

Other postoperative parameters
The majority of the patients was extubated immediately after surgery (6 ml group, $n=41$; 12 ml group, $n=44$;...
Table 1  Patient characteristics and intraoperative data. Data are presented as absolute values and percentage or mean (sd). A P-value of < 0.05 was considered statistically significant; n, number of patients. * Represent values averaged over anaesthesia duration

<table>
<thead>
<tr>
<th></th>
<th>6 ml group (n=50)</th>
<th>12 ml group (n=51)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender (n)</td>
<td>36 (72%)</td>
<td>39 (76%)</td>
<td>0.654</td>
</tr>
<tr>
<td>Age (yr) (range)</td>
<td>68 (52 - 87)</td>
<td>68 (51 - 86)</td>
<td>0.905</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173 (8)</td>
<td>175 (10)</td>
<td>0.306</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79 (16)</td>
<td>77 (22)</td>
<td>0.319</td>
</tr>
<tr>
<td>Current smoker (n)</td>
<td>15 (30%)</td>
<td>12 (24%)</td>
<td>0.610</td>
</tr>
<tr>
<td>ASA class (II/III/IV)</td>
<td>15/34/1</td>
<td>14/35/2</td>
<td>0.851</td>
</tr>
<tr>
<td>Forced vital capacity (litre)</td>
<td>3.04 (1.0)</td>
<td>3.02 (0.9)</td>
<td>0.464</td>
</tr>
<tr>
<td>Forced expiratory volume in 1 s (litre)</td>
<td>2.30 (0.8)</td>
<td>2.37 (0.6)</td>
<td>0.310</td>
</tr>
<tr>
<td>Haemoglobin (g dl(^{-1}))</td>
<td>10.8 (1.9)</td>
<td>10.8 (2.6)</td>
<td>0.220</td>
</tr>
<tr>
<td>Preoperative PO(_2) (kPa)</td>
<td>10.9 (1.8)</td>
<td>11.1 (1.7)</td>
<td>0.640</td>
</tr>
<tr>
<td>Preoperative PC(_O_2) (kPa)</td>
<td>4.9 (0.5)</td>
<td>4.9 (0.5)</td>
<td>0.588</td>
</tr>
<tr>
<td>Type of operation (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver resection</td>
<td>18 (36%)</td>
<td>24 (47%)</td>
<td>0.365</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>8 (16%)</td>
<td>8 (16%)</td>
<td></td>
</tr>
<tr>
<td>Whipple</td>
<td>24 (48%)</td>
<td>17 (33%)</td>
<td></td>
</tr>
<tr>
<td>Others: hemicolectomy, rectum resection</td>
<td>0</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Type of anaesthesia (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General and epidural anaesthesia</td>
<td>39 (78%)</td>
<td>44 (86%)</td>
<td>0.650</td>
</tr>
<tr>
<td>General anaesthesia alone</td>
<td>11 (22%)</td>
<td>7 (14%)</td>
<td></td>
</tr>
<tr>
<td>Reasons for missing epidural (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulation disturbance</td>
<td>5</td>
<td>4</td>
<td>0.407</td>
</tr>
<tr>
<td>Technical difficulties</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Discretion of attending</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (h)</td>
<td>6.1 (2.7)</td>
<td>6.1 (2.1)</td>
<td>0.617</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (h)</td>
<td>8.7 (5.2)</td>
<td>8.7 (5.9)</td>
<td>0.661</td>
</tr>
<tr>
<td>Patients extubated in the operating theatre (n)</td>
<td>41 (82%)</td>
<td>44 (86%)</td>
<td>0.157</td>
</tr>
<tr>
<td>Ventilatory parameters averaged over anaesthesia duration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute tidal volume (ml)</td>
<td>448 (88)</td>
<td>834 (194)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relative tidal volume (ml kg(^{-1}) PBW)</td>
<td>6.7 (1.1)</td>
<td>12.0 (2.3)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minute ventilation (litre)</td>
<td>7.8 (2.1)</td>
<td>6.2 (1.9)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Breaths per minute</td>
<td>17 (4)</td>
<td>8 (4)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P(_max) (cm H(_O_2))</td>
<td>15 (3)</td>
<td>17 (3)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P(_mean) (cm H(_O_2))</td>
<td>9 (3)</td>
<td>10 (3)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oxygenation with F(_O_2) 0.5, PEEP 5 cm H(_O_2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum P(_O_2) (kPa)</td>
<td>29.7 (5.5)</td>
<td>35.3 (5.7)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum P(_O_2) (kPa)</td>
<td>21.6 (6.4)</td>
<td>26.6 (7.5)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjustments of F(_O_2) or PEEP, total (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase in F(_O_2) only (n)</td>
<td>6</td>
<td>3</td>
<td>0.234</td>
</tr>
<tr>
<td>Increase in PEEP only (n)</td>
<td>2</td>
<td>3</td>
<td>0.322</td>
</tr>
<tr>
<td>Increase in F(_O_2) and PEEP (n)</td>
<td>2</td>
<td>0</td>
<td>0.243</td>
</tr>
<tr>
<td>F(_O_2) &gt; 0.5 throughout surgery (n)</td>
<td>5</td>
<td>0</td>
<td>0.027</td>
</tr>
<tr>
<td>Intraoperative fluids and transfusions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total fluid balance (litre)</td>
<td>4.0 (2.3)</td>
<td>4.2 (2.2)</td>
<td>0.622</td>
</tr>
<tr>
<td>Crystalloids (litre)</td>
<td>3.4 (1.3)</td>
<td>3.2 (1.4)</td>
<td>0.431</td>
</tr>
<tr>
<td>Hetastarch (litre)</td>
<td>0.9 (0.4)</td>
<td>0.9 (0.6)</td>
<td>0.809</td>
</tr>
<tr>
<td>Gelatin (litre)</td>
<td>1.5 (1.0)</td>
<td>1.8 (1.0)</td>
<td>0.098</td>
</tr>
<tr>
<td>Urine output (litre)</td>
<td>0.9 (0.7)</td>
<td>1.0 (0.7)</td>
<td>0.800</td>
</tr>
<tr>
<td>Blood loss (litre)</td>
<td>1.7 (2.2)</td>
<td>1.3 (1.1)</td>
<td>0.278</td>
</tr>
<tr>
<td>Packed red blood cells (units)</td>
<td>4.5 (3.0)</td>
<td>4.4 (3.4)</td>
<td>0.878</td>
</tr>
<tr>
<td>FFP (litre)</td>
<td>1.7 (0.9)</td>
<td>1.4 (1.2)</td>
<td>0.511</td>
</tr>
</tbody>
</table>

Continued
Postoperative disposition (post-anaesthetic care unit, ICU, or normal ward), the need for mechanical ventilation, requirement for supplemental oxygen via a mask, and pain scores did not differ significantly between the groups at any postoperative time point. Immediate postoperative chest X-ray examinations revealed significantly more patients with atelectasis in the 6 ml group (88% vs 68%, \( P = 0.017 \)). However, the severity of radiological atelectasis did not differ significantly between groups.

The postoperative \( P_{aO_2} \) values for patients’ breathing room air were comparable between groups until day 3. On day 5, oxygenation was significantly higher in the 12 ml group [\( P_{aO_2} 10.4 (1.7) \text{ vs } 9.2 (1.3) \text{ kPa, } P = 0.005 \)].

Other secondary outcomes did not differ between groups (Table 2). There was one unplanned postoperative mechanical ventilation of more than 24 h: a patient in the 12 ml group had myocardial infarction at the end of surgery. Per definition, this was not counted as a pulmonary complication.
Another patient from the 12 ml group was reintubated on day 3 due to respiratory distress. His X-ray showed significant atelectasis and mediastinal shift. In the 6 ml group, three patients were admitted to the critical care unit after 5, 8, and 11 days—one after a planned second surgical intervention and two due to sepsis.

**Discussion**

Intraoperative mechanical ventilation with low $V_t$ of 6 ml kg$^{-1}$ PBW when compared with high $V_t$ of 12 ml kg$^{-1}$ PBW—with a PEEP of 5 cm H$_2$O in both groups—did not significantly improve postoperative lung function in patients undergoing major upper abdominal surgery. There was no significant difference in FVC or FEV$_1$ values between groups over the first 5 postoperative days.

Postoperative pulmonary dysfunction after upper abdominal surgery results from reduced ventilatory muscle activity, diaphragmatic dysfunction, and decreased lung compliance. As might therefore be expected, lung function was significantly impaired for 5 days, regardless of intraoperative $V_t$. Thus, despite a manual recruitment manoeuvre before

![Fig 3](image1) Pre- and intraoperative oxygenation in the two groups. The $P_{aO2}/FIO2$ ratio was significantly higher in the 12 ml group during the intraoperative period.

![Fig 4](image2) Intraoperative respiratory mechanics. (A) Dynamic respiratory system compliance. (B) Airway resistance. (C) Maximum airway pressure. (D) Mean airway pressure. Data are expressed as mean (SD). *$P<0.05$ at individual time points. The $P$-value at the corner of each panel shows the overall statistical difference between the groups.
extubation, the reductions in FVC and FEV\textsubscript{1} in our patients were higher than expected\textsuperscript{13} and in fact comparable with values reported from patients after cardiac surgery.\textsuperscript{14} This is in line with findings from a recent large prospective multicentre study, which found upper abdominal and intrathoracic surgeries to have equal impact on lung function and introduced them into a new individual risk score to predict postoperative pulmonary complications.\textsuperscript{15} Pulmonary dysfunction after major surgery thus remains an important clinical problem, and one that is not ameliorated by intraoperative ventilation with low tidal volumes. In contrast, prophylactic chest physiotherapy\textsuperscript{13} and optimal pain control\textsuperscript{16} have been shown to significantly improve postoperative pulmonary function and to reduce the incidence of postoperative pulmonary complications.

Our trial was designed to show a difference in spirometric lung function of 20\% between groups, a difference we defined as clinically relevant, because comparable effects on lung function have been shown after modifications of surgical and anaesthesiological techniques.\textsuperscript{4, 17} With the observed variance, we had 80\% power to detect a 25\% difference. We thus cannot rule out smaller differences between the groups. Our lung function measurements ended on postoperative day 5 and differences between the groups could have potentially occurred afterwards. We collected clinical outcome parameters until hospital discharge, but our trial was not powered to detect significant differences for secondary outcomes.

As in previous trials,\textsuperscript{5} intraoperative lung mechanics and gas exchange were better and atelectasis less with high V\textsubscript{T}. Using a higher PEEP in the low V\textsubscript{T} group could have influenced the results in favour of lower V\textsubscript{T}. We did not do so for several reasons. First, differences between groups, if any, could then not be attributed to low V\textsubscript{T} alone, and our trial was specifically designed to study effects of intraoperative low V\textsubscript{T}. Secondly, the ideal PEEP is just high enough to keep the lungs open at end-expiration. Individual patients’ “ideal-PEEP” can be identified by PEEP trials. However, they are time-consuming and difficult to implement into the intraoperative setting. Thirdly, the use of high PEEP (≥10 cm H\textsubscript{2}O) may be limited in the surgical setting. To address the latter issue, a large multicentre trial is currently underway.\textsuperscript{18}

Even low V\textsubscript{T} without PEEP induces significant pulmonary inflammation.\textsuperscript{19} Previous trials of intraoperative mechanical ventilation which reported higher levels of proinflammatory cytokines or more pulmonary coagulation activation with high V\textsubscript{T} nonetheless compared high V\textsubscript{T} without PEEP to low V\textsubscript{T} plus PEEP.\textsuperscript{20–22} We used a minimum PEEP of 5 cm H\textsubscript{2}O in both groups in order to counterbalance this component of cyclic airway opening and closing. However, cyclic airway opening and closing also depends on the V\textsubscript{T} and respiratory rate. Using a lower V\textsubscript{T} inevitably increases dead space fraction. Per protocol, we kept our patients normocapnic. Therefore, a significantly higher minute ventilation and a two-fold higher respiratory rate were used in the low V\textsubscript{T} group, which may contribute to ventilator-induced lung injury.\textsuperscript{23} Additionally, there were more atelectases in the low V\textsubscript{T} group and more venous admixture which resulted in significantly lower intraoperative Pa\textsubscript{O\textsubscript{2}}/Fi\textsubscript{O\textsubscript{2}} ratios. Thus, potential benefits from mechanical ventilation with low tidal volumes could have been out-weighted by the higher minute ventilation and frequency and the lower intraoperative Pa\textsubscript{O\textsubscript{2}}/Fi\textsubscript{O\textsubscript{2}} ratio in those patients. Alternatively, to achieve similar minute ventilation in both groups, we would have had to accept permissive hypercapnia in our low V\textsubscript{T} patients, a practice that is

\begin{table}
\centering
\caption{Postoperative pulmonary complications and other clinical outcomes. Data are presented as absolute values or mean (SD). There were no statistically significant differences between groups. SOFA, sequential organ failure assessment; n, number of patients. *One patient in the 6 ml group fulfilled two criteria for postoperative pulmonary complications.}
\begin{tabular}{|c|c|c|c|}
\hline
 & 6 ml group (n=50) & 12 ml group (n=51) & P-value \\
\hline
Postoperative pulmonary complications & & &  \\
Total number of patients & 13* & 11 & 0.966  \\
Respiratory failure within first 5 days (n) & 7 & 3 & 0.200  \\
Unplanned MV > 24 h (n) & 0 & 0 & 1.0  \\
Reintubation due to respiratory distress within first 5 days (n) & 0 & 1 & 1.0  \\
Pneumonia (n) & 5 & 6 & 0.776  \\
Pneumothorax (n) & 2 & 1 & 0.617  \\
Incidence of PaO\textsubscript{2}/FiO\textsubscript{2} < 40 kPa (%) & 20 & 19 & 0.839  \\
Primary postoperative ICU admission (n) & 31 & 30 & 0.744  \\
Duration of primary ICU stay (days) & 4 (10) & 3 (4) & 0.218  \\
Readmission to ICU (n) & 7 & 7 & 1.0  \\
Secondary ICU admission only (n) & 3 & 0 & 0.118  \\
Total duration of ICU stay (days) & 9 (17) & 5 (8) & 0.313  \\
Duration of hospitalization (days) & 30 (15) & 25 (15) & 0.259  \\
SOFA Score on day 5 & 2.8 (2.1) & 2.4 (2.1) & 0.826  \\
Acute heart failure (n) & 2 & 2 & 1.0  \\
Myocardial infarction (n) & 0 & 2 & 0.492  \\
Acute respiratory distress syndrome (n) & 1 & 0 & 0.495  \\
Renal insufficiency (n) & 5 & 3 & 0.487  \\
Venous embolism (n) & 4 & 1 & 0.205  \\
Delayed wound healing/wound infections (n) & 12 & 17 & 0.380  \\
In-hospital deaths (n) due to & 3 & 5 & 0.715  \\
Septic multiorgan failure & 3 & 1 & 0.362  \\
Cardiac decompensation & 0 & 2 & 0.495  \\
Bleeding & 0 & 1 & 1.0  \\
Progression of malignancy & 0 & 1 & 1.0  \\
\hline
\end{tabular}
\end{table}
uncommon in patients with healthy lungs. However, protective effects of hypercapnia on pulmonary function have been suggested. Whether these apply to the setting of intraoperative ventilation in patients with healthy lungs was beyond the scope of our trial. Furthermore, to minimize atelectasis and venous admixture and to optimize $P_{A\text{O}_2}/F_{I\text{O}_2}$ ratios with low $V_T$, a PEEP higher than 5 cm H$_2$O is needed.

Although few data exist, it seems that in clinical routine, $V_T$ rarely exceeds 10 ml kg$^{-1}$. For ventilation of healthy lungs in the surgical setting, the rationale behind this common practice is not quite obvious. Positive effects of $V_T$ as high as 15 ml kg$^{-1}$ on intraoperative gas exchange are well documented. In this trial, we looked at the so far unreported consequences of different $V_T$ at a similar PEEP on postoperative lung function and used 12 ml kg$^{-1}$ as the higher volume for comparison. Based on available data, we did not see a reason to consider this $V_T$ per se as harmful for healthy lungs. Gattinoni and colleagues estimated that $V_T$ must exceed 17 ml kg$^{-1}$ to induce injury in otherwise healthy lungs.

We found no substantive difference in postoperative pulmonary function. It is thus quite unlikely that a comparison of 10 vs 6 ml kg$^{-1}$ would have revealed differences.

We present a single-centre trial with a small sample size on a specific group of patients undergoing a selected type of surgery. Thus, our data cannot be generalized to other groups of patients or types of surgery. We did not titrate PEEP levels individually. The duration of mechanical ventilation was substantial (i.e. an average of 8.5 h), but it remains possible that differences in lung function as a function of tidal volume only develop after longer periods. In summary, intraoperative mechanical ventilation with low $V_T$ when compared with high $V_T$ applied over a mean of 8.5 h in patients with healthy lungs did not result in spirometric or other lung function differences during the first 5 days after major abdominal surgery. However, intraoperative parameters suggest poorer pulmonary mechanics and gas exchange with low $V_T$ at a PEEP of 5 cm H$_2$O. Thus, further evaluation of potential outcome benefits of low $V_T$ and the adequate PEEP setting for intraoperative ventilation of healthy lungs are needed.

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