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RESPIRATION AND THE AIRWAY

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

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Editor's key points

- In the intensive care unit, low tidal volume ventilation has been shown to preserve lung function.
- The authors aimed to study whether low intraoperative tidal volume ventilation would preserve postoperative lung function.
- Postoperative lung function was similar, irrespective of whether the patients received high or low tidal volume ventilation.

Background. Prolonged postoperative decrease in lung function is common after major upper abdominal surgery. Evidence suggests that ventilation with low tidal volumes may limit the damage during mechanical ventilation. We compared postoperative lung function of patients undergoing upper abdominal surgery, mechanically ventilated with high or low tidal volumes.

Methods. This was a double-blind, prospective, randomized controlled clinical trial. One hundred and one patients (age ≥50 yr, ASA ≥II, duration of surgery ≥3 h) were ventilated with: (i) high [12 ml kg^{-1} predicted body weight (PBW)] or (ii) low (6 ml kg^{-1} PBW) tidal volumes intraoperatively. The positive end-expiratory pressure was 5 cm H_2O in both groups and breathing frequency adjusted to normocapnia. Time-weighted averages (TWAs) of forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) until 120 h after operation were compared ($P<0.025$ considered statistically significant). Secondary outcomes were oxygenation, respiratory and non-respiratory complications, length of stay and mortality.

Results. The mean (SD) values of TWAs of FVC and FEV_1 were similar in both groups: FVC: 6 ml group 1.8 (0.7) litre *vs* 12 ml group 1.6 (0.5) litre ($P=0.12$); FEV_1: 6 ml group 1.4 (0.5) litre *vs* 12 ml group 1.2 (0.4) litre ($P=0.15$). FVC and FEV_1 at any single time point and secondary outcomes did not differ significantly between groups.

Conclusions. Prolonged impaired lung function after major abdominal surgery is not ameliorated by low tidal volume ventilation.

Keywords: lung protection; mechanical ventilation; respiratory function tests; tidal volume

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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 (FEV_1).[1] Risk factors for severe postoperative lung function impairment include the duration, site, and technique of surgery.[2 3] In contrast, the type of anaesthesia[4] and the choice of anaesthetics[1] can help to minimize postoperative lung function impairment. Whether intraoperative tidal volume (V_T) influences *post*-operative lung function is unknown. Previous trials found that high V_T during abdominal surgery maintained better *intra*operative lung mechanics and gas exchange than low V_T.[5] Relatively high V_T is thus routinely used for intraoperative mechanical ventilation. However, high airway pressures, lung overdistention, or both may aggravate or even induce lung injury.[6] Based on results from acute respiratory distress syndrome (ARDS) and critically ill patients, there is a growing trend to favour low V_T for patients without lung injury who require intraoperative ventilation.[7] Of note, there are no robust data on the proper application of PEEP in this context. Low V_T is nonetheless increasingly used for intraoperative ventilation without an adjustment of PEEP. It thus remains unclear whether a reduction in V_T *per se* is beneficial compared with traditional high V_T with similar PEEP for patients undergoing intraoperative ventilation.

If low intraoperative V_T 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 FEV_1. 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 ≥50 yr, ASA ≥II) undergoing elective upper abdominal surgery lasting at least 3 h with combined general and epidural anaesthesia. 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 μg 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 (Mallinckrodt™ 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 fluid was Ringer's lactate solution. Up to 500 ml was given with induction of anesthesia and subsequently at a rate of 2–4 ml kg^{-1} h^{-1}. Blood loss was replaced with Ringer's solution at a 3:1 ratio, with colloids at a 2:1 ratio, or with red blood cells at a 1:1 ratio.

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:

$$\text{Men}: \quad \text{PBW in kg} = 50.0 + 0.91 \times (\text{height in cm} - 152.4);$$
$$\text{Women}: \quad \text{PBW in kg} = 45.5 + 0.91 \times (\text{height in cm} - 152.4).$$

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 ($F_{I_{O_2}}$) of 1.0, PEEP 5 cm H_2O, and inspiratory-to-expiratory ratio 1:2. $F_{I_{O_2}}$ was reduced to 0.5 shortly after intubation, and fresh gas was provided by a ZEUS anaesthesia machine in the autoflow mode (Dräger, Lübeck, Germany).

If deemed necessary by the attending physician, $F_{I_{O_2}}$ or PEEP was increased to maintain Pa_{O_2} within 20% of preoperative values or $S\,p_{O_2} \geq 95\%$.

Before weaning, $F_{I_{O_2}}$ 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_2O 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_2O. All patients received a lung expansion manoeuvre consisting of three manual bag ventilations with a maximum pressure of 40 cm H_2O 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, $F_{I_{O_2}}$, 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 ≤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 nicoboxil-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: $Pa_{O_2} \leq 6.7$ kPa while breathing ambient air or $Pa_{CO_2} \geq 6.7$ 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 $Pa_{O_2}/F_{I_{O_2}}$ ratio of <40 kPa.

Statistical analysis

Our primary outcome variables were TWAs of postoperative FVC and FEV_1.

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 FEV_1 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 FEV_1, 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 FEV_1 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 FEV_1 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 $Pa_{O_2}/F_{I_{O_2}}$ 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, $n=44$;

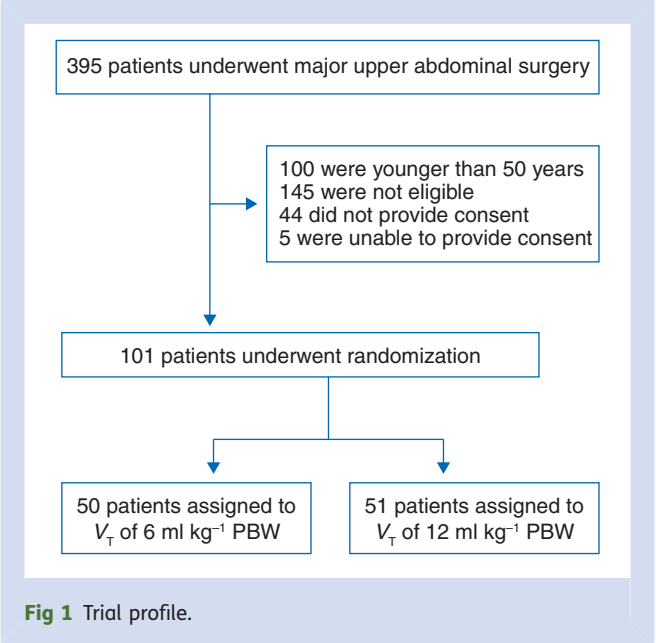

Fig 1 Trial profile.

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

	6 ml group (*n*=50)	12 ml group (*n*=51)	*P*-value
Male gender (*n*)	36 (72%)	39 (76%)	0.654
Age (yr) (range)	68 (8) (52–87)	68 (9) (51–86)	0.905
Height (cm)	173 (8)	175 (10)	0.306
Weight (kg)	79 (16)	77 (22)	0.319
Current smoker (*n*)	15 (30%)	12 (24%)	0.610
ASA class (II/III/IV)	15/34/1	14/35/2	0.851
Forced vital capacity (litre)	3.04 (1.0)	3.02 (0.9)	0.464
Forced expiratory volume in 1 s (litre)	2.30 (0.8)	2.37 (0.6)	0.310
Haemoglobin (g dl^{-1})	10.8 (1.9)	10.8 (2.6)	0.220
Preoperative P_{O_2} (kPa)	10.9 (1.8)	11.1 (1.7)	0.640
Preoperative P_{CO_2} (kPa)	4.9 (0.5)	4.9 (0.5)	0.588
Type of operation (*n*)			
Liver resection	18 (36%)	24 (47%)	0.365
Gastrectomy	8 (16%)	8 (16%)	
Whipple	24 (48%)	17 (33%)	
Others: hemicolectomy, rectum resection	0	2 (4%)	
Type of anaesthesia (*n*)			
General and epidural anaesthesia	39 (78%)	44 (86%)	0.650
General anaesthesia alone	11 (22%)	7 (14%)	
Reasons for missing epidural (*n*)			
Coagulation disturbance	5	4	0.407
Technical difficulties	5	1	
Discretion of attending	1	2	
Duration of surgery (h)	6.1 (2.7)	6.1 (2.1)	0.617
Duration of mechanical ventilation (h)	8.7 (5.2)	8.7 (5.9)	0.661
Patients extubated in the operating theatre (*n*)	41 (82%)	44 (86%)	0.157
Ventilatory parameters averaged over anaesthesia duration			
Absolute tidal volume (ml)	448 (88)	834 (194)*	<0.001
Relative tidal volume (ml kg^{-1} PBW)	6.7 (1.1)	12.0 (2.3)*	<0.001
Minute ventilation (litre)	7.8 (2.1)	6.2 (1.9)*	<0.001
Breaths per minute	17 (4)	8 (4)*	<0.001
P_{max} (cm H_2O)	15 (3)	17 (3)*	<0.001
P_{mean} (cm H_2O)	9 (3)	10 (3)*	<0.001
Oxygenation with $F_{I_{O_2}}$ 0.5, PEEP 5 cm H_2O			
Maximum Pa_{O_2} (kPa)	29.7 (5.5)	35.3 (5.7)*	<0.001
Minimum Pa_{O_2} (kPa)	21.6 (6.4)	26.6 (7.5)*	<0.001
Adjustments of $F_{I_{O_2}}$ or PEEP, total (*n*)	10	6	0.176
Increase in $F_{I_{O_2}}$ only (*n*)	6	3	0.234
Increase in PEEP only (*n*)	2	3	0.322
Increase in $F_{I_{O_2}}$ and PEEP (*n*)	2	0	0.243
$F_{I_{O_2}}>0.5$ throughout surgery (*n*)	5	0	0.027
Intraoperative fluids and transfusions			
Total fluid balance (litre)	4.0 (2.3)	4.2 (2.2)	0.622
Crystalloids (litre)	3.4 (1.3)	3.2 (1.4)	0.431
Hetastarch (litre)	0.9 (0.4)	0.9 (0.6)	0.809
Gelatin (litre)	1.5 (1.0)	1.8 (1.0)	0.098
Urine output (litre)	0.9 (0.7)	1.0 (0.7)	0.800
Blood loss (litre)	1.7 (2.2)	1.3 (1.1)	0.278
Packed red blood cells (units)	4.5 (3.0)	4.4 (3.4)	0.878
FFP (litre)	1.7 (0.9)	1.4 (1.2)	0.511

Continued

Table 1 *Continued*

	6 ml group ($n=50$)	12 ml group ($n=51$)	*P*-value
Thrombocyte transfusion (units)	0.12 (0.6)	0.17 (0.6)	0.632
Cumulative catecholamines (mg)	3.4 (2.5)	3.2 (2.4)	0.903
End of operation core body temperature (°C)	36.9 (0.6)	36.7 (0.6)	0.356

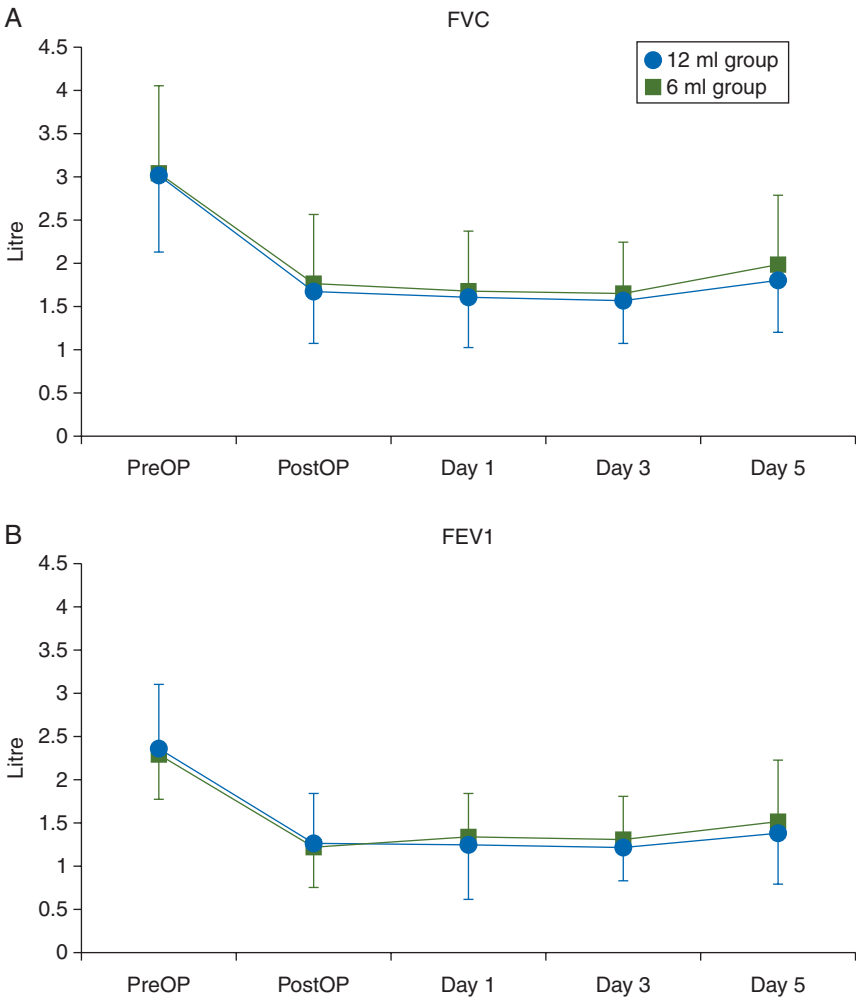

Fig 2 Spirometry results in the two groups. Data are expressed as mean (SD). (A) Forced vital capacity. (B) Forced expiratory volume in 1 second. There were no statistically significant differences between groups, or between the groups.

P=0.556). 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 Pa_{O_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 [Pa_{O_2} 10.4 (1.7) *vs* 9.2 (1.3) 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.

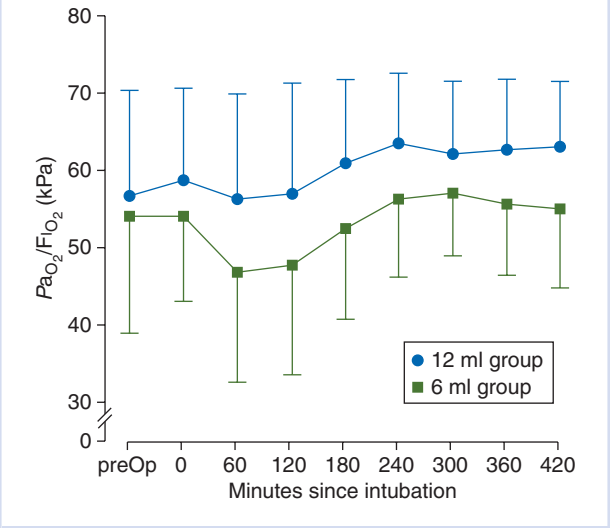

Fig 3 Pre- and intraoperative oxygenation in the two groups. The Pa_{O_2}/FI_{O_2} ratio was significantly higher in the 12 ml group during the intraoperative period.

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_2O 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.[12] 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

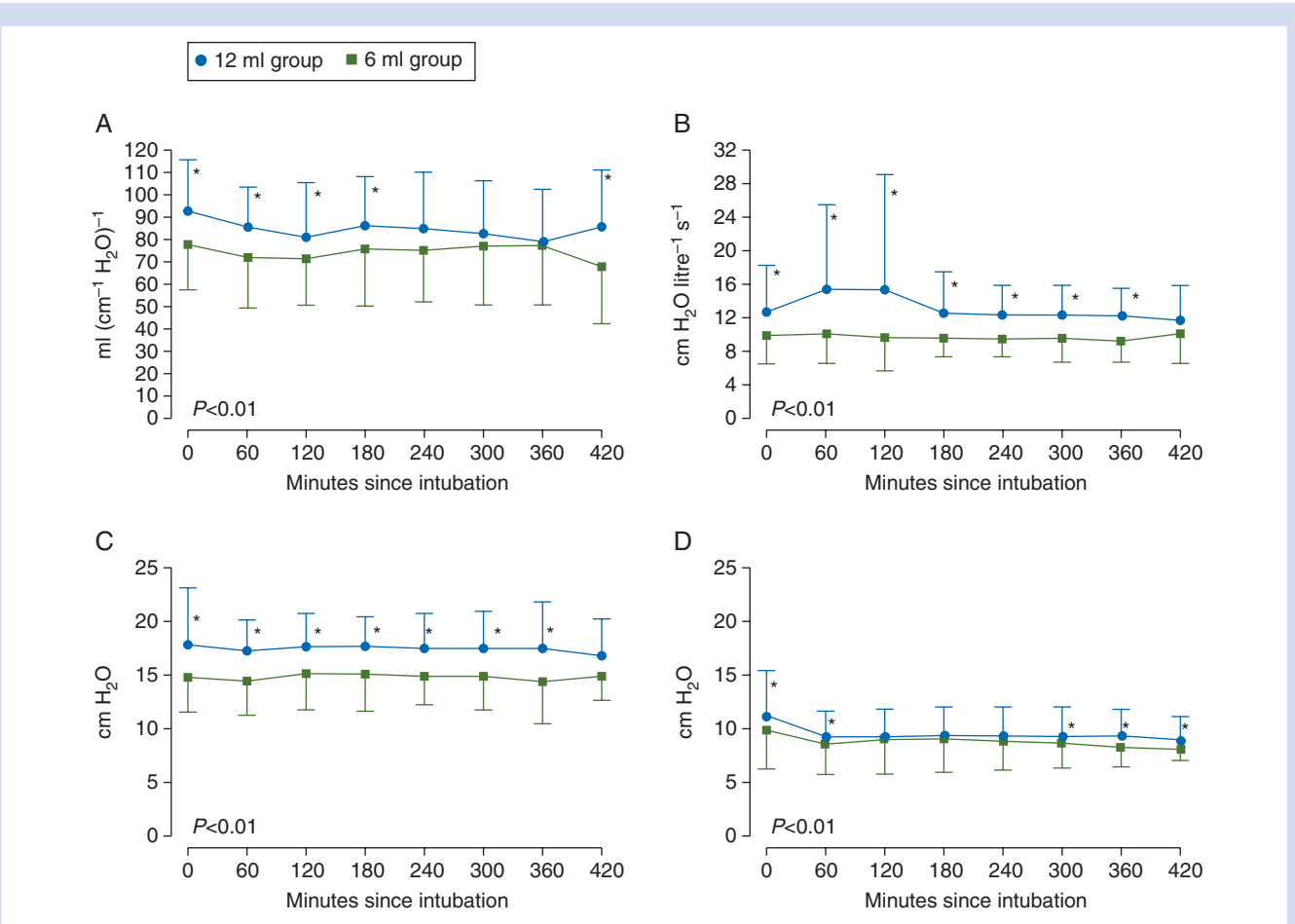

Fig 4 Intraoperative respiratory mechanics. (A) Dynamic respiratory system compliance. (B) Airway resistance. (C) Maximum airway pressure. (D) Mean airway pressure. Data are expressed as mean (SD). *$P<0.05$ at individual time points. The P-value at the corner of each panel shows the overall statistical difference between the groups.

Table 2 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

	6 ml group (*n*=50)	12 ml group (*n*=51)	*P*-value
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 $P_{O_2}/F_{I_{O_2}}$ <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

extubation, the reductions in FVC and FEV_1 in our patients were higher than expected[13] and in fact comparable with values reported from patients after cardiac surgery.[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.[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[13] and optimal pain control[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.[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,[5] intraoperative lung mechanics and gas exchange were better and atelectasis less with high V_T. Using a higher PEEP in the low V_T group could have influenced the results in favour of lower V_T. We did not do so for several reasons. First, differences between groups, if any, could then not be attributed to low V_T alone, and our trial was specifically designed to study effects of intraoperative low V_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 ($\geq$10 cm H_2O) may be limited in the surgical setting. To address the latter issue, a large multicentre trial is currently underway.[18]

Even low V_T without PEEP induces significant pulmonary inflammation.[19] Previous trials of intraoperative mechanical ventilation which reported higher levels of proinflammatory cytokines or more pulmonary coagulation activation with high V_T nonetheless compared high V_T without PEEP to low V_T plus PEEP.[20–22] We used a minimum PEEP of 5 cm H_2O 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_T and respiratory rate. Using a lower V_T inevitably increases dead space fraction. Per protocol, we kept our patients normocapnic. Therefore, a significantly higher minute ventilation and a two-fold higher respiration rate were used in the low V_T group, which may contribute to ventilator-induced lung injury.[23] Additionally, there were more atelectases in the low V_T group and more venous admixture which resulted in significantly lower intraoperative $Pa_{O_2}/F_{I_{O_2}}$ ratios. Thus, potential benefits from mechanical ventilation with low tidal volumes could have been out-weighed by the higher minute ventilation and frequency and the lower intraoperative $Pa_{O_2}/F_{I_{O_2}}$ 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_T patients, a practice that is

uncommon in patients with healthy lungs. However, protective effects of hypercapnia on pulmonary function have been suggested.[24] 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 $Pa_{O_2}/F_{I_{O_2}}$ ratios with low V_T, a PEEP higher than 5 cm H_2O 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.[5] 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[6] 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_2O. 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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Declaration of interest

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