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Original Article

The association of postoperative pulmonary complications in 109,360 patients with pressure-controlled or volume-controlled ventilation

A. Bagchi,[1] M. I. Rudolph,[2] P. Y. Ng,[3] F. P. Timm,[2] D. R. Long,[4] S. Shaefi,[5] K. Ladha,[6] M. F. Vidal Melo[7] and M. Eikermann[8,9]

1 Staff Anaesthesiologist, 2 Research Assistant, 3 Research Fellow 4 Anaesthesiology resident, 7 Professor of Anaesthesiology Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
5 Staff Anaesthesiologist, 8 Vice Chair, Department of Anesthesia, Critical Care, and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA
6 Staff Anaesthesiologist, Department of Anesthesia and Pain Medicine, University of Toronto and Toronto General Hospital, Toronto, ON, Canada
9 Adjunct Associate Professor Klinik für Anästhesiologie und Intensivmedizin, Universität Duisburg-Essen, Essen, Germany

Summary
We thought that the rate of postoperative pulmonary complications might be higher after pressure-controlled ventilation than after volume-controlled ventilation. We analysed peri-operative data recorded for 109,360 adults, whose lungs were mechanically ventilated during surgery at three hospitals in Massachusetts, USA. We used multivariable regression and propensity score matching. Postoperative pulmonary complications were more common after pressure-controlled ventilation, odds ratio (95%CI) 1.29 (1.21–1.37), $p < 0.001$. Tidal volumes and driving pressures were more varied with pressure-controlled ventilation compared with volume-controlled ventilation: mean (SD) variance from the median 1.61 (1.36) $ml.kg^{-1}$ vs. 1.23 (1.11) $ml.kg^{-1}$, $p < 0.001$; and 3.91 (3.47) cmH_2O vs. 3.40 (2.69) cmH_2O, $p < 0.001$. The odds ratio (95%CI) of pulmonary complications after pressure-controlled ventilation compared with volume-controlled ventilation at positive end-expiratory pressures < 5 cmH_2O was 1.40 (1.26–1.55) and 1.20 (1.11–1.31) when ≥ 5 cmH_2O, both $p < 0.001$, a relative risk ratio of 1.17 (1.03–1.33), $p = 0.023$. The odds ratio (95%CI) of pulmonary complications after pressure-controlled ventilation compared with volume-controlled ventilation at driving pressures of < 19 cmH_2O was 1.37 (1.27–1.48), $p < 0.001$, and 1.16 (1.04–1.30) when ≥ 19 cmH_2O, $p = 0.011$, a relative risk ratio of 1.18 (1.07–1.30), $p = 0.016$. Our data support volume-controlled ventilation during surgery, particularly for patients more likely to suffer postoperative pulmonary complications.

Correspondence to: M. Eikermann
Email: meikerma@bidmc.harvard.edu
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Introduction

Mortality and morbidity are reduced in patients with acute respiratory distress syndrome by ventilating their lungs with a combination of relatively small tidal volumes, positive end-expiratory pressure (PEEP) and low plateau pressures [1]. Similar intra-operative ventilatory strategies might reduce postoperative pulmonary complications in populations without acute respiratory distress, whose lungs are often ventilated with higher volumes with little or no end-expiratory pressure [2–8].

Pulmonary ventilation, controlled by volume rather than pressure, might modify the rate of postoperative pulmonary complications, even though studies in patients with acute lung injury have not shown significant differences [9, 10]. Postoperative pulmonary complications are associated with intra-operative PEEP, ventilatory driving pressure and oxygen partial pressure [2, 11–15]. Studies have reported effects of pressure-controlled vs. volume-controlled intra-operative ventilation on physiological variables but not clinical pulmonary outcomes [16, 17].

We assessed whether the rate of pulmonary complications after pressure-controlled ventilation during surgery was higher than that after volume-controlled ventilation.

Methods

The Institutional Review Board at the Massachusetts General Hospital approved the study. We analysed data for adults whose lungs were mechanically ventilated via a tracheal tube during surgery at one of three hospitals in Massachusetts, USA between January 2007 and December 2015. We did not study patients with pulmonary complications in the seven days before surgery, those who were not extubated immediately after surgery, those with ASA physical status 6 and those with missing data.

We categorised patients by the mode of ventilation (pressure or volume control) that was used most during an operation. The primary outcome was major pulmonary complications within seven postoperative days, a composite of re-intubation, pulmonary oedema, pulmonary failure or pneumonia, as defined by the ninth and tenth revisions of the International Classification of Diseases codes and by Current Procedural Terminology codes (see also Supporting Information, Table S1) [2, 17–19]. We regressed mode of ventilation

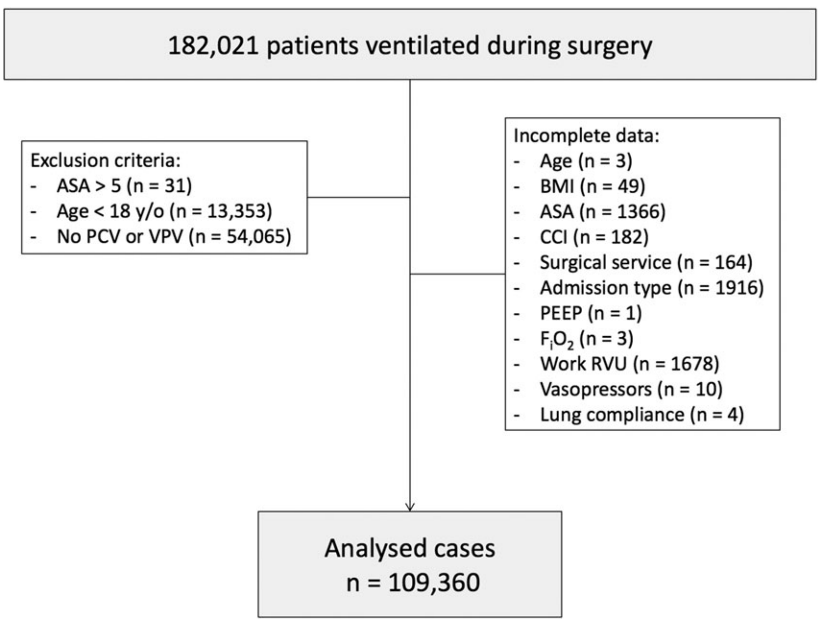

Figure 1 Flow of patients through study. ASA, ASA physical status; BMI, body mass index, CCI, Charlson Comorbidity Index; F_IO_2, inspired oxygen fraction; PEEP, positive end-expiratory pressure; PCV, pressure-controlled ventilation; RVU, relative value units; VCV, volume-controlled ventilation.

Table 1 Baseline characteristics of 109,360 surgical patients for whom ventilation was pressure-controlled or volume-controlled. Values are mean (SD), number (proportion) or median (IQR [range]).

	Original cohort		Propensity score-matched cohort	
	Pressure n = 18,268	Volume n = 91,092	Pressure n = 18,085	Volume n = 18,085
Age; years	55.3 (15.9)	54.5 (16.4)	55.3 (15.5)	54.9 (16.1)
Sex; female	9770 (53.5%)	50,599 (55.5%)	9673 (53.5%)	9770 (54.0%)
BMI	29.7 (8.1)	28.3 (6.8)	29.7 (8.1)	29.4 (7.6)
ASA				
< 3	11,721 (64.1%)	63,409 (69.6%)	11,624 (64.3%)	11,696 (64.7%)
≥ 3	6559 (35.9%)	27,731 (30.4%)	6461 (35.7%)	6389 (35.3%)
CCI	2 (0–4 [0–24])	2 (0–3 [0–26])	2 (0–4 [0–24])	2 (0–4 [0–25])
COPD	4384 (24.0%)	14,622 (16.0%)	4318 (23.9%)	4060 (22.5%)
Heart failure	1561 (8.5%)	7057 (7.8%)	1538 (8.5%)	1530 (8.5%)
High-risk surgery	9363 (51.2%)	36,890 (40.5%)	9178 (50.8%)	8767 (48.5%)
Admission type (%)				
Ambulatory	4318 (23.6%)	19,788 (21.7%)	4280 (23.7%)	4654 (25.7%)
Inpatient	3290 (18.0%)	17,993 (19.7%)	3251 (18.0%)	3320 (18.4%)
Same day admission	10,672 (58.4%)	53,359 (58.6%)	10,554 (58.4%)	10,111 (55.9%)
PRBC units (%)				
0	17,665 (96.6%)	87,855 (96.4%)	17,476 (96.6%)	17,451 (96.5%)
1	287 (1.6%)	1433 (1.6%)	282 (1.6%)	294 (1.6%)
2	217 (1.2%)	1210 (1.3%)	216 (1.2%)	220 (1.2%)
> 2	111 (0.6%)	642 (0.7%)	111 (0.6%)	120 (0.7%)
Neostigmine; mg	3 (0–4 [0–10])	2 (0–3.5 [0–15])	3 (0–4 [0–10])	2 (0–4 [0–10])
Duration of surgery; min	155 (98–233 [17–4626])	157 (100–238 [8–6529])	155 (98–234 [17–4626])	148 (92–232 [15–6212])
NDNMBA ED95	3 (2–4 [0–29])	2 (2–4 [0–44])	3 (2–4 [0–29])	2 (1–4 [0–42])
Hypotension; min	0 (0–2 [0–369])	0 (0–2 [0–659])	0 (0–2 [0–369])	0 (0–2 [0–590])
Median PEEP	4.07 (2.22)	4.28 (2.04)	4.08 (2.22)	4.17 (2.17)
Compliance ml.cmH_2O	34.2 (12.2)	36.8 (10.5)	34.15 (12.14)	34.80 (10.76)
MAC age adjusted	0.82 (0.33)	0.85 (0.30)	0.82 (0.33)	0.82 (0.34)
Work RVU	16.97 (10.45)	17.43 (10.81)	16.97 (10.44)	16.39 (10.83)
Fluids; ml	1579 (2242)	1550 (2316)	1581 (2242)	1572 (2264)
Morphine equivalent; mg	3 (0–8 [0–200])	4 (0–8 [0–200])	3.3 (0–8 [0–200])	3.3 (0–8 [0–180])
Noradrenaline equivalent; mg	0.05 (0–0.29 [0–50.00])	0.04 (0–0.27 [0–50.00])	0.05 (0–0.28 [0–50.00])	0.04 (0–0.26 [0–50.00])
S/F ratio	62.6 (16.3)	58.2 (13.1)	62.5 (16.1)	61.4 (14.9)
Surgical service				
Anaesthesiology	276 (1.5%)	2563 (2.8%)	276 (1.5%)	263 (1.5%)
Burn	150 (0.8%)	1183 (1.3%)	150 (0.8%)	166 (0.9%)
Cardiac	25 (0.1%)	395 (0.4%)	25 (0.1%)	35 (0.2%)
Emergent-urgent	587 (3.2%)	4039 (4.4%)	587 (3.3%)	579 (3.2%)
General surgery	2816 (15.4%)	17,121 (18.8%)	2816 (15.6%)	2901 (16.0%)
Gynaecology	1372 (7.5%)	7803 (8.6%)	1372 (7.6%)	1452 (8.0%)

(continued)

Table 1 (*continued*)

	Original cohort		Propensity score-matched cohort	
	Pressure n = 18,268	Volume n = 91,092	Pressure n = 18,085	Volume n = 18,085
Neurosurgery	1265 (6.9%)	10,009 (11.0%)	1265 (7.0%)	1219 (6.7%)
Oral/Maxillofacial	329 (1.8%)	2141(2.4%)	329 (1.8%)	361 (2.0%)
Orthopaedic	2764 (15.1%)	16,247 (17.8%)	2764 (15.3%)	2841 (15.7%)
Otolaryngology	337 (1.8%)	410 (0.5%)	332 (1.8%)	375 (2.1%)
Paediatric surgery	62 (0.3%)	293 (0.3%)	62 (0.3%)	60 (0.3%)
Plastic surgery	632 (3.5%)	4927 (5.4%)	632 (3.5%)	649 (3.6%)
Radiology	101 (0.6%)	964 (1.0%)	101 (0.6%)	111 (0.6%)
Surgical oncology	986 (5.4%)	5893 (6.5%)	986 (5.5%)	1058 (5.9%)
Thoracic	4280 (23.4%)	3693 (4.0%)	4102 (22.7%)	3591 (19.9%)
Transplant	225 (1.2%)	1691 (1.9%)	225 (1.2%)	231 (1.3%)
Urology	1168 (6.4%)	7798 (8.6%)	1168 (6.4%)	1186 (6.6%)
Vascular	620 (3.4%)	3172 (3.5%)	620 (3.4%)	659 (3.6%)
Other	273 (1.5%)	755 (0.8%)	272 (1.5%)	348 (1.9%)
Year of surgery	2011 (2)	2012 (2)	2011 (2)	2011 (2)
SPOSA	21 (16–26 [2–47])	19 (15–25 [1–48])	21 (16–26 [2–47])	21 (16–26 [2–48])

BMI, body mass index; ASA, ASA physical status; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; MAC, minimum alveolar concentration (of volatile anaesthetic); NDNMBA ED95, non-depolarising neuromuscular blocking agent dose, multiples of 95% effective dose; Hypotension, minutes of mean arterial pressure < 55 mmHg; PEEP, positive end-expiratory pressure; PRBC, packed red blood cell; RVU, relative value units; S/F, mean S_PO_2/F_IO_2 ratio; SPOSA, Score for Pre-operative Prediction of Obstructive Sleep Apnoea [20].

Table 2 Intra-operative characteristics for 103,960 adults with ventilation controlled by pressure or volume. Values are median (IQR [range]) or mean (SD).

	Pressure control	Volume control	p value
Tidal volume; $ml.kg^{-1}$	8.0 (6.7–9.2 [1.5–27.3])	8.2 (7.2–9.2 [0.2–29.4])	< 0.001
Tidal volume variance	1.61 (1.36)	1.23 (1.11)	< 0.001
Driving pressure; cmH_2O	15.7 (5.2)	14.8 (4.3)	< 0.001
Driving pressure variance	3.9 (3.5)	3.4 (2.7)	< 0.001
PEEP	5 (3–5 [0–15])	5 (4–5 [0–17])	< 0.001
Inspiratory pressure			
Median plateau; cmH_2O	19 (16–23 [5–60])	18 (16–22 [5–62])	< 0.001
Median peak; cmH_2O	19 (16–23 [6–60])	20 (17–24 [6–66])	< 0.001
Compliance; $ml.cmH_2O^{-1}$	33 ([25–42 [5–99])	36 (29–43 [1–138])	< 0.001

PEEP, positive end-expiratory pressure.

and the following covariates against the primary outcome: sex; age; body mass index; ASA physical status; chronic pulmonary disease; heart failure; the Charlson Comorbidity Index [18]; emergency surgery; high-risk surgery (neurosurgery, general, transplant, thoracic, vascular or burns) [19]; Score for Pre-operative Prediction of Obstructive Sleep Apnoea (SPOSA) [20]; surgical service; duration of surgery; surgical complexity; age-adjusted minimum alveolar concentration of inhalational anaesthetics; opioid dose in morphine equivalents; neuromuscular blocking drug dose; neostigmine dose; volumes of intra-operative intravenous fluids and blood products; PEEP; mean S_PO_2/F_IO_2 ratio; pulmonary compliance.

We used these covariates to calculate a propensity score to minimise the effects of observed confounding by matching patients ventilated with each mode. We performed nearest-neighbour matching with a caliper of 0.1 times the standard deviation of the logit of the estimated propensity score in a 1:1 fashion using a greedy algorithm. We performed a subgroup analysis of patients who had abdominal surgery. We further analysed the risk of high tidal volume ventilation and high driving pressure ventilation.

We performed subgroup analyses of the association of postoperative pulmonary complications with mode of ventilation classified by: ASA physical status (< 3 vs. ≥ 3); SPORC (Score for Prediction of Postoperative Respiratory Complications) (< 7 vs. ≥ 7); and PEEP (< 5 cmH_2O vs. ≥ 5 cmH_2O). We explored whether any association of ventilatory mode and postoperative pulmonary complications interacted with high tidal volumes, high inspiratory plateau pressures and PEEP. We included these interaction terms one by one in the full regression model. We performed several sensitivity analyses, which are described in the online Supporting Information.

We used a mixed-effects logistic regression model with ventilatory mode as the exposure variable, the primary anaesthesia provider as a random effect and other covariates as fixed effect. We used complete cases for the primary analysis. We evaluated the potential for bias arising from missing data by repeating this analysis using multiple imputations by chained equations [20]. We used Stata version 13 or 14 (StataCorp LLC, TX, USA) for all analyses. We considered two-tailed $p < 0.05$ statistically significant.

Results

Pressure control was used to ventilate the lungs of 18,268 of 109,360 (17%) patients, of whom 18,085 were matched with 18,085 of 91,092 patients ventilated with volume control, within the caliper limit of the propensity score (Fig. 1 and Table 1). The pressures and volumes delivered by the two ventilatory modes were different: pressure-controlled ventilation delivered more varied, as well as higher, driving pressures and tidal volumes than volume-controlled ventilation (Table 2 and Fig. 2).

Pulmonary complications were more common after pressure-controlled ventilation in both the unmatched cohort and that matched for propensity score (Table 3). The odds ratio (OR) (95%CI) for pulmonary complications, 1.29 (1.21–1.37), was unaffected by adjustment for anaesthesia provider, 1.28 (1.20–1.37), $p = 0.87$, or by imputation for missing data, 1.28 (1.21–1.36), $p = 0.86$.

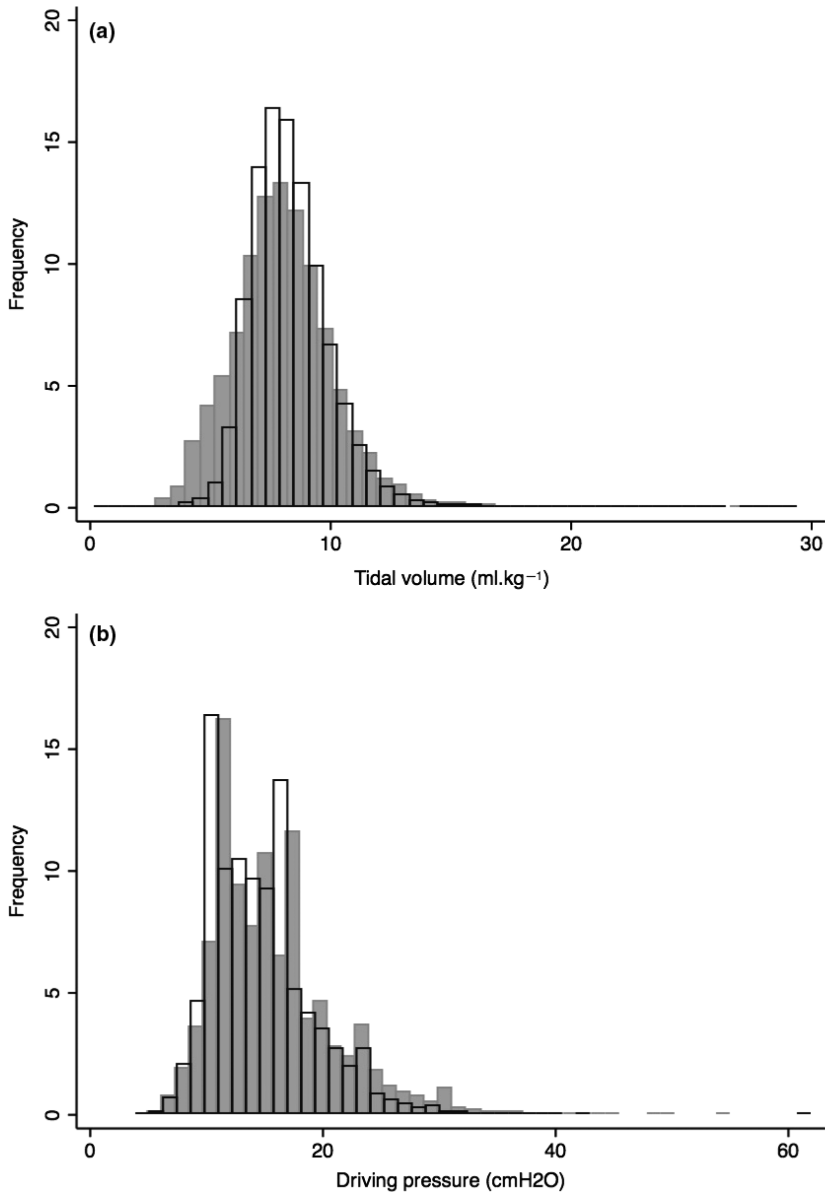

Figure 2 (a) The tidal volumes and (b) the driving pressures delivered by pressure-controlled ventilation (■) and volume-controlled ventilation (□) during surgery in 18,268 patients and 91,092 patients, respectively.

Postoperative pulmonary complications were more frequent after pressure-controlled ventilation than volume-controlled ventilation when we categorised patients by PEEP, ASA physical status, predicted rate of pulmonary complications (SPORC) and ventilatory driving pressures (Table 4). The rates of pulmonary complications were not associated with ventilatory mode when tidal volumes exceeded 12 $ml.kg^{-1}$.

The association of ventilatory mode and rates of postoperative pulmonary complications was modified by three variables, OR (95%CI): tidal volume (within two standard deviations of the mean vs. < 5 $ml.kg^{-1}$ or > 12 $ml.kg^{-1}$), 0.65 (0.52–0.81), $p < 0.001$; driving pressure (within one standard deviation of the mean vs. < 10 cmH_2O or > 19 cmH_2O), 0.87 (0.77–0.99), $p = 0.025$; and PEEP (≥ 5 cmH_2O vs. < 5 cmH_2O), 0.82 (0.73–0.92), $p = 0.001$ (see also Supporting Information, Table S4 and Fig. S2).

There were 23,222 patients (21.2%) ventilated for abdominal surgery: 3426 (14.8%) with pressure control

Table 3 The odds ratio (OR) for study outcomes in patients receiving pressure-controlled ventilation compared with volume-controlled ventilation. Values are number (proportion).

Unmatched study cohort				
	Pressure n = 18,268	Volume n = 91,092	OR 95%CI	p value
Pulmonary complications				
Any	3235 (17.7%)	7080 (7.8%)	1.29 (1.21–1.37)	< 0.001
Re-intubation	126 (0.69%)	532 (0.58%)	0.96 (0.77–1.20)	0.7
Pulmonary oedema	1971 (10.8%)	4637 (5.1%)	1.21 (1.12–1.30)	< 0.001
Respiratory failure	1645 (9.0%)	2492 (2.7%)	1.23 (1.13–1.35)	< 0.001
Pneumonia	724 (4.0%)	1638 (1.8%)	1.17 (1.05–1.30)	0.005
Tidal volume > 12 $ml.kg^{-1}$	638 (3.5%)	2168 (2.4%)	1.37 (1.24–1.51)	< 0.001
Driving pressure > 19 cmH_2O	3749 (21%)	12,589 (14%)	1.26 (1.20–1.32)	< 0.001
Propensity score-matched cohort				
	n = 18,085	n = 18,085		
Any pulmonary complication	3145 (17.4%)	2148 (11.9%)	1.56 (1.47–1.66)	< 0.001

Table 4 The odds ratio (OR) for postoperative respiratory complications in patients receiving pressure-controlled ventilation compared with volume-controlled ventilation, according to pre-defined sub-groups of ventilatory pressures and susceptibility to complications. Values are number (proportion).

	Pressure vs. Volume		Sub-group vs. Sub-group	
Variable and sub-group	OR (95%CI)	p value	RRR (95%CI)	p value
PEEP				
< 5 (n = 39,015)	1.40 (1.26–1.55)	< 0.001	1.17 (1.02–1.33)	0.023
≥ 5 (n = 70,344)	1.20 (1.11–1.31)	< 0.001		
ASA				
< 3 (n = 75,098)	1.29 (1.16–1.43)	< 0.001	1.06 (0.89–1.16)	0.82
≥ 3 (n = 34,261)	1.27 (1.17–1.37)	< 0.001		
SPORC				
< 7 (n = 106,407)	1.28 (1.20–1.37)	< 0.001	1.00 (0.79–1.27)	1
≥ 7 (n = 2952)	1.28 (1.03–1.62)	0.029		
Tidal volume				
< 12 $ml.kg^{-1}$ (n = 105,012)	1.32 (1.23–1.41)	< 0.001	1.22 (0.95–1.57)	0.11
≥ 12 $ml.kg^{-1}$ (n = 4348)	1.08 (0.85–1.37)	0.536		
Driving pressure				
< 19 cmH_2O (n = 77,424)	1.37 (1.27–1.48)	< 0.001	1.18 (1.07–1.30)	0.016
≥ 19 cmH_2O (n = 31,936)	1.16 (1.04–1.30)	0.011		

ASA, ASA physical status; RRR, relative risk ratio; PEEP, positive end-expiratory pressure; SPORC, Score for Prediction of Postoperative Respiratory Complications [21].

and 19,796 (85.2%) with volume control (see also Supporting Information, Table S2). The rate of postoperative pulmonary complications was higher after pressure-controlled ventilation than volume-controlled ventilation, 1.56 (1.36–1.80), $p < 0.001$ (see also Supporting Information, Table S3). Pressure-controlled ventilation was more frequently associated with driving pressures > 19 cmH_2O, 1.21 (1.10–1.34), $p < 0.001$, but not with tidal volumes > 12 $ml.kg^{-1}$, 1.16 (0.96–1.40), $p = 0.12$ (Table S3).

Discussion

We found that the rate of postoperative pulmonary complications was higher when intra-operative ventilation was controlled by pressure than when it was controlled by volume. Pressure-controlled ventilation resulted in more variable tidal volumes and driving pressures and more frequent delivery of extreme values (> 12 $ml.kg^{-1}$ predicted body weight and > 19 cmH_2O, respectively). The association of pressure-controlled ventilation with pulmonary complications was most marked with low PEEP.

Postoperative pulmonary complications are associated with mortality and morbidity, which contribute to surgical harm and costs [22–24]. Pulmonary postoperative complications are more frequent than any other, even in academic centres that use 'lung-protective' strategies [23, 25]. Some trials and systematic reviews have reported no differences in physiological measurements with ventilatory mode while others have [16, 17, 26–31]. Pulmonary system compliance changes during surgery, for instance, with patient positioning, pneumoperitoneum, abdominal content retraction or packing, and fluid infusion or loss. The tidal volumes delivered by pressure-controlled ventilation will therefore vary and may become large after a sudden increase in compliance, while volume-controlled ventilation should deliver more consistent tidal volumes. Driving pressure, which is the inspiratory plateau pressure minus the end-expiratory pressure, may be a more important determinant of lung damage than tidal volume [2, 32, 33]. Pressure-controlled ventilation delivered driving pressures > 19 cmH_2O more often than volume-controlled ventilation, either because higher inspiratory pressures were set or lower expiratory pressures were set.

Values of PEEP > 5 cmH_2O were associated with fewer postoperative pulmonary complications, which agree with other studies [2, 11, 12, 34]. A plausible mechanism is a reduction in cyclical collapse and opening of lung segments and subsequent inflammation, which would be accompanied by variable tidal volumes with pressure-controlled ventilation [35]. Pulmonary complications were consistently less with volume-controlled ventilation when we categorised patients by ASA physical status and patient susceptibility to postoperative pulmonary complications [19, 36].

Like any observational study, our results might be biased by unmeasured confounding factors and the misclassification of outcomes. In addition, we used a composite outcome to define 'pulmonary failure'. However, our administrative dataset has been validated, as has the use of this outcome [19, 37], and we have no reason to think that its classification should differ with ventilatory mode [38].

We believe that appropriate PEEP and the minimisation of driving pressure are key to reducing pulmonary damage [2]. We think that damage associated with pressure-controlled ventilation is mediated through increased strain caused by erratic driving pressures and tidal volumes [1, 32, 33, 39, 40].

In summary, we showed that rates of postoperative pulmonary complications are higher after pressure-controlled ventilation than after volume-controlled ventilation, in part due to more variable and higher driving pressures and tidal volumes, exacerbated by low or no PEEP. Our data support volume-controlled ventilation during surgery, particularly for patients more likely to suffer postoperative pulmonary complications.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. In order to ensure the stability of our findings, several additional statistical analyses were performed in addition to those reported in the primary manuscript.

Table S1. CPT, ICD-9 and ICD-10 codes to generate the primary composite outcome.

Table S2. Baseline characteristics of 23,222 patients whose lungs were ventilated for an abdominal operation. Values are mean (SD), median (IQR [range]) or number (proportion).

Table S3. The odds ratio (OR) for outcomes in abdominal surgical patients receiving pressure-controlled ventilation compared with volume-controlled ventilation. Values are number (proportion).

Table S4. Odds ratio (OR) and relative excess risk due to interaction (RERI) for interaction analyses of mode of ventilation (Ventmode) with intra-operative ventilation settings.

Figure S1. a) Percentage use of pressure control ventilation () and volume control ventilation () and b) Predicted postoperative respiratory complication rate by ventilator mode (PCV & VCV) over time in years.

Figure S2. Graphs of a) ASA physical status b) SPORC and c) PEEP and postoperative respiratory complications using component plots.

