A randomized comparison of different ventilator strategies during thoracotomy for pulmonary resection

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Objective: Protective lung ventilation is reported to benefit patients with acute respiratory distress syndrome. It is not known whether protective lung ventilation is also beneficial to patients undergoing single-lung ventilation for elective pulmonary resection.

Methods: In an institutional review board–approved prospective randomized trial, 34 patients undergoing elective pulmonary resection requiring single-lung ventilation were enrolled. Informed consent was obtained. Patients were randomized to 1 of 2 groups: (1) high tidal volume (Hi-TV) of 10 mL/kg, rate of 7 breaths/min, and zero positive end-expiratory pressure or (2) low tidal volume (Lo-TV) of 5 mL/kg, rate of 14 breaths/min, and 5 cmH₂O positive end-expiratory pressure. Ventilator settings were continued during both double- and single-lung ventilation. Pulmonary functions, hemodynamics, and postoperative outcomes were recorded.

Results: Patient demographics, operative characteristics, intraoperative hemodynamics, and postoperative pain and sedation scores were similar between the 2 groups. During most time periods, airway pressures (peak and plateau) were significantly higher in the Hi-TV group; however, plateau pressures remained less than 30 cmH₂O at all times for all patients. The Hi-TV group had significantly lower arterial carbon dioxide tension, less arterial carbon dioxide tension–end-tidal carbon dioxide gradient, lower alveolar dead space ratio, and higher dynamic pulmonary compliance. There were no differences in postoperative morbidity and hospital days between the 2 groups, but atelectasis scores on postoperative days 1 and 2 were lower in the Hi-TV group.

Conclusions: The use of Hi-TV during single-lung ventilation for pulmonary resection resulted in no increase in morbidity and was associated with less hypercarbia, less dead space ventilation, better dynamic compliance, and less postoperative atelectasis. (*J Thorac Cardiovasc Surg* 2013;146:38-44)

In critically ill patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) requiring mechanical ventilation, protective lung ventilation is thought to reduce volu-trauma, baro-trauma, and endothelial injury with the use of low tidal volumes (TVs) and by maintaining low airway pressures.^{1,2} Although the critical care community has adopted these practices, it is unclear whether protective lung ventilation is of benefit to patients without ALI or ARDS undergoing elective surgical procedures.^{3,4} Limitations of low TV ventilation have included hypoventilation, leading to side effects of hypercarbia (arrhythmia, pulmonary hypertension, intracranial hypertension, and depressed renal blood flow), atelectasis, and higher oxygen requirement.⁵

The purpose of this study was to compare the intraoperative pulmonary functions and clinical outcomes of high TV (Hi-TV) single-lung ventilation versus low TV (Lo-TV)

single-lung ventilation in patients undergoing elective thoracotomy for pulmonary resection. We hypothesized that Hi-TV (10 mL/kg) ventilation provides better intraoperative pulmonary function (ventilation, oxygenation, and pulmonary compliance) compared with Lo-TV (5 mL/kg) ventilation, but without an increase in postoperative morbidity.

MATERIALS AND METHODS

A prospective randomized clinical trial was performed at an academic tertiary care center, enrolling patients scheduled for elective thoracotomy and pulmonary resection for clinical stage I or II non–small cell lung cancer as assessed by computed tomography (CT) scan and integrated positron emission tomography/CT scan. Eligible patients were aged between 18 and 90 years with postoperative predicted forced expiratory volume in 1 second and diffusion capacity of the lung for carbon monoxide of 40% or more predicted. Exclusion criteria included a preoperative history of arrhythmia, history or radiographic evidence of interstitial lung disease, need for supplemental oxygen before surgery, and prior receipt of chemotherapy or radiation or positive mediastinoscopy. Randomization was performed in groups of 4 (2 for Hi-TV and 2 for Lo-TV) to ensure equal distribution into 2 study groups. The anesthesiologist implemented the randomization sequence and assigned patients to the intervention groups. Although the anesthesiologist was aware of the study group assignment, the surgery team and nursing staff were blinded. All patients received a thoracic epidural (thoracic level 5/6 or 6/7), placed before induction of general anesthesia.

Patients were monitored using the standard noninvasive monitors and radial arterial catheter. The latter was transduced with the Flo-Trac System and Vigileo Monitor (Edwards Lifesciences, Irvine, Calif) to assess the cardiac output. Induction of general anesthesia included propofol and

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Abbreviations and Acronyms

ALI	= acute lung injury
ARDS	= acute respiratory distress syndrome
CT	= computed tomography
ETCO ₂	= end-tidal carbon dioxide
F _{IO₂}	= inspired oxygen fraction
Hi-TV	= high tidal volume (group)
ICU	= intensive care unit
Lo-TV	= low tidal volume (group)
Paco ₂	= arterial carbon dioxide tension
Pao ₂	= arterial oxygen tension
PEEP	= positive end-expiratory pressure
Sao ₂	= arterial oxygen saturation
TV	= tidal volume

rocuronium. All patients were intubated with a left-sided, double-lumen endotracheal tube sized according to the height and sex of the patient. Confirmation of precise positioning of the double lumen tube was accomplished by bronchoscopy. Anesthesia was maintained with an inhalation agent (sevoflurane) and intermittent doses of rocuronium. Analgesia was provided with medications (preservative-free morphine and bupivacaine) administered via the epidural catheter. During the surgical procedure, 2 to 4 mg of morphine and 8 to 10 mL of 0.125% bupivacaine were administered via the epidural catheter. Patients were then managed with an infusion of morphine (or hydromorphone) mixed with bupivacaine (0.1%) infused at 6 to 10 mL/h. Exact dosing of all medications was at the discretion of the attending anesthesiologist.

Oxygen was administered in a 50:50 mixture with air during 2-lung ventilation. During single-lung ventilation, the inspired oxygen fraction (F_{IO₂}) was at the discretion of the attending anesthesiologist to maintain arterial oxygen saturation (Sao₂) at 95% or greater per institutional practice. If the Sao₂ decreased to less than 95%, the following maneuvers were performed until the Sao₂ was 95% or greater: (1) increase F_{IO₂} to 100%, (2) apply continuous positive airway pressure (5 cmH₂O) to the nondependent or surgical lung, or (3) intermittent 2-lung ventilation. Need for the latter practice would result in removal of the patient from the study.

A Dräger Apollo anesthesia machine (Dräger Medical Inc, Telford, Pa) was used. Volume-controlled ventilation was the mode of ventilation chosen to allow a definitive TV to be administered. The inspiratory flow was set at 3 L/min, and the inspiratory time was set to maintain an inspiratory to expiratory ratio of 1:1.7. Patients were randomized to receive a TV of 5 mL/kg (Lo-TV group) or 10 mL/kg (Hi-TV group) on the basis of ideal body weight.⁶ Ideal body weight was 51.6 + 1.9 kg (height in inches – 60) for men and 48.7 + 1.7 kg (height in inches – 60) for women. The respiratory rates for the Lo-TV and Hi-TV groups were set to 14 and 7 breaths/min, respectively, thus maintaining a minute ventilation of 70 mL/kg/min for all patients studied. The Lo-TV group received 5 cmH₂O of positive end-expiratory pressure (PEEP), and the Hi-TV group had zero PEEP. These ventilator settings were kept while changing from 2-lung ventilation to single-lung ventilation and then back to 2-lung ventilation. For the Hi-TV group, the delivered TV was decreased if peak inspiratory pressure reached more than 40 cmH₂O or plateau airway pressure reached more than 30 cmH₂O.

Intraoperative baseline hemodynamic and pulmonary function data were obtained after induction of general anesthesia and during 2-lung ventilation in the lateral decubitus position. These data were repeated during single-lung ventilation at 5-minute intervals. A final set of data were obtained after reinstitution of 2-lung ventilation in the lateral decubitus position. Dynamic and static pulmonary compliances were calculated on

the basis of the peak inspiratory pressures and plateau airway pressures, respectively, and TV was delivered as assessed by the ventilator. Dynamic pulmonary compliance = TV/(peak inspiratory pressure – PEEP) and static pulmonary compliance = TV/(plateau airway pressure – PEEP). Arterial blood gas analyses (pH, arterial oxygen tension [Pao₂], arterial carbon dioxide tension [Paco₂]) were obtained at 2 time points: at baseline during 2-lung ventilation in the lateral decubitus position and after 20 minutes of single-lung ventilation. From the blood gas data, the CO₂ gradient (Paco₂ – end-tidal carbon dioxide [ETCO₂]) and alveolar dead space ratio (Vd [dead space volume]/Vt [tidal volume] = [Paco₂ – ETCO₂]/Paco₂) were calculated to assess the relative amounts of dead space ventilation. The ratio between the Pao₂ and the F_{IO₂} (Pao₂/F_{IO₂}) was calculated as a measure of oxygenation.

For the surgical procedure, all patients underwent mediastinoscopy to rule out metastatic involvement of mediastinal lymph nodes, followed by lateral muscle-sparing thoracotomy for pulmonary resection. At the conclusion of the procedure, bronchoscopy was performed to evacuate secretions and positive pressure of 25 cmH₂O was applied to the nondependent or surgical lung for 5 seconds to assess for bronchial stump air leak and to ensure lung expansion before closure of the thoracotomy. All surgical procedures were performed by a single surgeon (T.N.). Intraoperative fluid was restricted to 15 mL/kg of crystalloid for the entire case unless hemodynamic instability occurred because of blood loss. In the postoperative period, patients received intravenous fluid at a rate below maintenance with fluid bolus of 250 mL given only if urine output decreased to less than 10 mL/h. Vasopressors were used to maintain mean arterial pressure at more than 60 mm Hg. An atelectasis score, as described by Wilcox and colleagues,⁷ was assigned on the basis of daily chest radiographs. A score of 0 = no atelectasis, 1 = subsegmental atelectasis, 2 = mild lobar atelectasis, 3 = moderate lobar atelectasis, and 4 = complete lobar atelectasis. The physician reading the chest radiographs (T.N.) was blinded to the patient group assignment.

Postoperative pain and sedation scores were recorded in the post-anesthesia care unit and at 7 AM on each of the first 2 postoperative days. A 10-point pain (0 = no pain, 100 = unbearable severe pain) and sedation (0 = unresponsive, 100 = severe agitation and uncooperative) scale was used. The nursing staff recording these data was blinded with regard to the patient group assignment. Postoperative outcome data, complications within 30 days of surgery, and death within 90 days of surgery were recorded by the surgery team, who was also blinded to the patient group assignment.

The institutional review board at Rhode Island Hospital approved this randomized study (#023306). Informed consent was obtained from all patients. As stated earlier, we hypothesized that the Hi-TV group would have better intraoperative pulmonary functions, specifically ventilation, but without an increase in postoperative morbidity. Therefore, hypercarbia (Pco₂ > 45) was selected as the end point for sample size calculation. With a greater than 40% incidence of hypercarbia seen in ARDS trials during low TV ventilation,^{1,8-10} we calculated a sample size of 34 patients needed to detect a 20% difference, with a statistical power of 80% and an alpha error of 5%. Continuous variables are presented as mean with standard deviation and compared using the Student *t* or Mann-Whitney *U* test where appropriate. Categorical variables are presented as number with percentage and compared using the chi-square or Fisher exact test where appropriate. All tests were 2-tailed. Analyses were performed using StatView 4.5 (Abacus, Berkeley, Calif).

RESULTS

A study flow diagram is shown in Figure 1. After 7 months, enrollment of patients into the trial was stopped because the accrual goal was met. Thirty-five patients were enrolled with 1 patient excluded from randomization because of positive node biopsy at mediastinoscopy as

FIGURE 1. Study flow diagram.

assessed by intraoperative frozen-section. Thirty-four patients were randomized with 2 patients (1 from each group) excluded from intervention because of difficulties in maintaining lung isolation with the double-lumen endotracheal tube. Thirty-two patients were therefore analyzed: 16 in the Hi-TV group and 16 in the Lo-TV group. No patients required continuous positive airway pressure applied to the nondependent/surgical lung or intermittent 2 ventilation for Sao_2 less than 95% despite Fio_2 of 100%. No patients received intraoperative blood transfusion, and all patients were extubated at the end of the surgical procedure. Demographic and surgical data were similar between the 2 study groups (Table 1). Intraoperative hemodynamic functions were also similar between the 2 groups (Table 2).

In terms of intraoperative pulmonary functions, peak inspiratory pressures and plateau pressures tended to be higher in the Hi-TV group at most time periods (Table 3). However, at no time did any patient in the Hi-TV group experience plateau airway pressures greater than 30 cmH_2O or peak inspiratory pressures greater than 40 cmH_2O , which would mandate a decrease in delivered TV. For both groups, airway pressures increased and pulmonary compliance decreased with the initiation of single-lung ventilation (Table 3). However, dynamic pulmonary compliance was significantly greater for the Hi-TV group (Table 3). The Lo-TV group also had significantly higher Paco_2 and greater dead space ventilation (larger $\text{Paco}_2 - \text{ETCO}_2$ gradient and greater Vd/Vt) during single-lung ventilation (Table 4). The number of patients with hypercarbia (arterial carbon dioxide tension > 45 mm Hg) was significantly

greater in the Lo-TV group (12/16; 75%) than in the Hi-TV group (1/16; 6%) ($P < .001$). For the parameters assessing oxygenation, there was no difference between the 2 groups with regard to Fio_2 or $\text{PaO}_2/\text{Fio}_2$ (Tables 3 and 4, respectively). The number of patients with $\text{PaO}_2/\text{Fio}_2$ less than 300 was not different between the 2 groups during

TABLE 1. Demographic and surgical data

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
Age (y)	61.2 (14.4)	69.6 (12.9)	.71
Male gender	7 (44%)	6 (38%)	.72
Weight (kg)	71.4 (16.8)	73.9 (13.6)	.53
% predicted DLCO	78.1 (23.3)	67.0 (12.6)	.11
FEV1 (L)	2.02 (0.61)	1.85 (0.47)	.38
% predicted FEV1	85.8 (21.7)	75.4 (16.4)	.14
ASA classification	2.6 (0.5)	2.7 (0.4)	.46
Procedure			.84
Wedge resection	1 (6.3%)	2 (12.5%)	
Lobectomy	13 (81.2%)	11 (68.7%)	
Bilobectomy	1 (6.3%)	1 (6.3%)	
Pneumonectomy	1 (6.3%)	2 (12.5%)	
Right side surgery	9 (56%)	7 (44%)	.48
Single-lung ventilation time (min)	42 (8.3)	46 (9.5)	.56
Estimated blood loss (mL)	262.5 (269.3)	140.4 (82.6)	.13
Surgical time (min)	104.7 (50.1)	122.5 (49.1)	.34
Intraoperative crystalloid (mL)	436.7 (156.4)	380.0 (111.5)	.26
Intraoperative urine output (mL)	216.2 (117.5)	208.7 (133.0)	.88

Lo-TV, Low tidal volume (5 mL/kg); Hi-TV, high tidal volume (10 mL/kg); DLCO, diffusion capacity of lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; ASA, American Society of Anesthesiologists.

TABLE 2. Intraoperative hemodynamic data

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
Lateral 2 lung			
mBP (mm Hg)	88.3 (20.7)	86.0 (10.3)	.69
HR (beats/min)	68.6 (10.1)	69.9 (13.8)	.76
CO (L/min)	4.76 (1.4)	4.57 (0.57)	.64
SV (L/beat)	70.0 (19.0)	68.1 (14.0)	.74
ETCO ₂ (mm Hg)	34.8 (2.9)	33.7 (3.6)	.34
Lateral 1 lung 5 min			
mBP (mm Hg)	83.2 (16.2)	90.8 (15.8)	.18
HR (beats/min)	66.3 (8.0)	69.0 (13.5)	.50
CO (L/min)	4.37 (0.89)	4.72 (0.62)	.22
SV (L/beat)	67.0 (16.0)	70.0 (13.0)	.61
ETCO ₂ (mm Hg)	33.1 (3.5)	33.0 (3.3)	.92
Lateral 1 lung 10 min			
mBP (mm Hg)	79.2 (17.0)	84.3 (12.7)	.34
HR (beats/min)	66.4 (8.1)	67.6 (13.3)	.76
CO (L/min)	4.42 (1.11)	4.67 (0.72)	.47
SV (L/beat)	68.0 (20.0)	70.0 (11.0)	.73
ETCO ₂ (mm Hg)	34.2 (4.0)	32.9 (1.7)	.22
Lateral 1 lung 15 min			
mBP (mm Hg)	80.6 (13.7)	84.6 (14.0)	.43
HR (beats/min)	67.4 (8.7)	67.1 (13.5)	.95
CO (L/min)	4.36 (0.67)	4.73 (0.67)	.12
SV (L/beat)	66.0 (12.0)	73.0 (15.4)	.73
ETCO ₂ (mm Hg)	33.7 (2.9)	33.1 (2.3)	.55
Lateral 1 lung 20 min			
mBP (mm Hg)	77.7 (23.1)	84.0 (14.9)	.37
HR (beats/min)	65.6 (8.3)	66.4 (14.7)	.84
CO (L/min)	4.17 (0.82)	4.64 (0.52)	.05
SV (L/beat)	66.2 (12.6)	73.5 (15.0)	.16
ETCO ₂ (mm Hg)	33.7 (3.5)	32.7 (1.8)	.35
Lateral 1 lung 30 min			
mBP (mm Hg)	77.2 (21.1)	83.2 (14.5)	.36
HR (beats/min)	65.3 (8.2)	67.1 (15.5)	.68
CO (L/min)	4.16 (0.95)	4.59 (0.41)	.11
SV (L/beat)	66.4 (15.2)	71.7 (16.9)	.31
ETCO ₂ (mm Hg)	33.6 (3.0)	33.1 (2.5)	.61
Lateral 2 lung 10 min			
mBP (mm Hg)	79.3 (19.2)	81.5 (16.0)	.68
HR (beats/min)	66.2 (8.0)	68.3 (12.5)	.50
CO (L/min)	4.5 (0.62)	4.56 (0.60)	.90
SV (L/beat)	68.0 (14.5)	67.6 (15.4)	.82
ETCO ₂ (mm Hg)	35.8 (3.1)	33.7 (3.5)	.44

Lo-TV, Low tidal volume (5 mL/kg); Hi-TV, high tidal volume (10 mL/kg); mBP, mean systemic blood pressure; HR, heart rate; CO, cardiac output; SV, stroke volume; ETCO₂, end-tidal carbon dioxide.

single-lung ventilation (Lo-TV 11/16 [67%] vs Hi-TV 8/16 [50%]; $P = .473$).

Postoperative outcomes included no deaths within 90 days of surgery and no cases of ALI or ARDS. Atrial fibrillation and bronchoscopy (for symptomatic moderate to complete lobar atelectasis) were the only complications seen, with no difference found in the incidence of these complications between the 2 groups (Table 5). Pain and

TABLE 3. Intraoperative pulmonary function data

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
TV (mL)	363.1 (87.7)	738.7 (135.6)	<.001
Respiratory rate (breaths/min)	14	7	<.001
Lateral 2-lung baseline			
PIP (cmH ₂ O)	19.7 (5.8)	24.4 (4.2)	.014
P _{PLAT} (cmH ₂ O)	16.2 (3.9)	20.2 (3.9)	.007
Dynamic compliance (mL/cmH ₂ O)	26.5 (8.6)	31.9 (7.4)	.07
Static compliance (mL/cmH ₂ O)	34.6 (12.4)	38.2 (12.1)	.41
SaO ₂ (%)	99.1 (1.2)	99.5 (0.63)	.28
FiO ₂	0.70 (0.26)	0.83 (0.23)	.14
Lateral 1 lung 5 min			
PIP (cmH ₂ O)	24.3 (7.3)	27.2 (3.7)	.16
P _{PLAT} (cmH ₂ O)	18.8 (4.6)	23.1 (4.1)	.01
Dynamic compliance (mL/cmH ₂ O)	18.7 (6.2)	27.7 (6.0)	<.001
Static compliance (mL/cmH ₂ O)	28.5 (13.1)	32.8 (7.8)	.26
SaO ₂ (%)	97.9 (2.5)	99.0 (1.3)	.15
FiO ₂	0.70 (0.25)	0.66 (0.24)	.65
Lateral 1 lung 10 min			
PIP (cmH ₂ O)	23.7 (7.1)	27.9 (4.3)	.054
P _{PLAT} (cmH ₂ O)	19.0 (4.3)	23.4 (4.4)	.008
Dynamic compliance (mL/cmH ₂ O)	19.2 (5.6)	27.1 (6.7)	<.001
Static compliance (mL/cmH ₂ O)	27.7 (12.6)	32.5 (7.8)	.21
SaO ₂ (%)	98.2 (1.9)	98.2 (2.0)	.93
FiO ₂	0.71 (0.25)	0.64 (0.25)	.41
Lateral 1 lung 15 min			
PIP (cmH ₂ O)	23.9 (7.0)	27.8 (4.3)	.066
P _{PLAT} (cmH ₂ O)	18.8 (4.3)	23.2 (4.3)	.007
Dynamic compliance (mL/cmH ₂ O)	18.8 (5.2)	27.1 (6.7)	<.001
Static compliance (mL/cmH ₂ O)	28.2 (12.9)	32.6 (7.8)	.25
SaO ₂ (%)	97.5 (2.7)	98.4 (1.8)	.25
FiO ₂	0.72 (0.25)	0.64 (0.25)	.40
Lateral 1 lung 20 min			
PIP (cmH ₂ O)	24.3 (6.9)	27.1 (4.4)	.18
P _{PLAT} (cmH ₂ O)	18.7 (4.0)	22.5 (4.2)	.013
Dynamic compliance (mL/cmH ₂ O)	18.6 (5.4)	27.8 (6.6)	<.001
Static compliance (mL/cmH ₂ O)	27.6 (10.6)	33.4 (7.4)	.082
SaO ₂ (%)	97.4 (3.1)	98.3 (1.9)	.32
FiO ₂	0.71 (0.25)	0.64 (0.25)	.44
Lateral 1 lung 30 min			
PIP (cmH ₂ O)	24.1 (7.0)	27.4 (4.6)	.13
P _{PLAT} (cmH ₂ O)	18.6 (4.0)	22.8 (4.5)	.008
Dynamic compliance (mL/cmH ₂ O)	18.6 (4.9)	27.6 (6.8)	<.001
Static compliance (mL/cmH ₂ O)	28.0 (10.4)	33.3 (7.9)	.11
SaO ₂ (%)	97.8 (2.1)	97.9 (2.0)	.31
FiO ₂	0.72 (0.23)	0.64 (0.25)	.41
Lateral 2 lung 10 min			
PIP (cmH ₂ O)	20.0 (4.2)	23.9 (4.3)	.06
P _{PLAT} (cmH ₂ O)	16.4 (4.0)	19.0 (4.3)	.08

(Continued)

TABLE 3. Continued

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
Dynamic compliance (mL/cmH ₂ O)	25.8 (7.5)	30.0 (7.5)	.08
Static compliance (mL/cmH ₂ O)	35.0 (12.1)	41.5 (25.6)	.10
Sao ₂ (%)	98.4 (1.5)	99.0 (0.9)	.30
Fio ₂	0.60 (0.28)	0.50 (0.22)	.35

Lo-TV, Low tidal volume (5 mL/kg); Hi-TV, high tidal volume (10 mL/kg); TV, tidal volume; PIP, peak inspiratory pressure; P_{PLAT}, plateau airway pressure; Sao₂, arterial oxygen saturation; Fio₂, fraction of inspired oxygen.

sedation scores also were similar between the 2 groups (Table 5). However, the atelectasis score was significantly higher for the Lo-TV group on both postoperative days 1 and 2 (Table 5).

DISCUSSION

The ARDS Network² randomized 861 patients to receive 6 mL/kg versus 12 mL/kg of TV during mechanical ventilation. This trial was stopped early after interim analysis found mortality to be lower in the Lo-TV group (31.0% vs 39.8%). However, randomized trials published earlier have resulted in conflicting conclusions. Trials by Stewart and colleagues,⁸ Brochard and colleagues,⁹ and Brower and colleagues¹⁰ found no difference in mortality (in-hospital mortality or survival to discharge) between low and high TV ventilation in patients with ARDS, whereas a trial by Amato and colleagues¹ found a lower 28-day mortality favoring low TV ventilation, but survival to discharge was not different. Despite conflicting data, the strength of the ARDS Network trial² has led the critical care community to adopt the use of low TV ventilation for patients with

TABLE 4. Data derived from arterial blood gas

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
Baseline 2-lung ventilation			
pH	7.39 (0.37)	7.41 (0.36)	.18
Paco ₂ (mm Hg)	42.8 (4.1)	40.9 (3.8)	.18
Paco ₂ – ETCO ₂ gradient	11.1 (4.2)	10.1 (5.6)	.57
Vd/Vt (%)	26.9 (10.2)	25.0 (9.0)	.59
Pao ₂ (mm Hg)	271.7 (125.3)	261.2 (126.4)	.81
Pao ₂ /Fio ₂ ratio (mm Hg/%)	410.7 (152.0)	328.8 (176.8)	.17
20 min 1-lung ventilation			
pH	7.37 (0.04)	7.41 (0.05)	.013
Paco ₂ (mm Hg)	47.1 (7.5)	41.9 (5.8)	.037
Paco ₂ -ETCO ₂ gradient	13.4 (7.0)	8.8 (4.5)	.034
Vd/Vt (%)	27.1 (11.3)	20.2 (7.2)	.04
Pao ₂ (mm Hg)	132.2 (49.5)	167.4 (94.6)	.37
Pao ₂ /Fio ₂ ratio (mm Hg/%)	255.7 (148.8)	240.2 (140.1)	.76

Lo-TV, Low tidal volume (5 mL/kg); Hi-TV, high tidal volume (10 mL/kg); Paco₂, arterial carbon dioxide tension; ETCO₂, end-tidal carbon dioxide; Vd, dead space volume; Vt, tidal volume; Vd/Vt (alveolar dead space ratio), [Paco₂ – ETCO₂]/Paco₂; Pao₂, arterial oxygen tension; Fio₂, fraction of inspired oxygen.

TABLE 5. Postoperative outcomes

	Lo-TV group (n = 16)	Hi-TV group (n = 16)	P value
Pain score			
PACU	1.80 (0.48)	1.72 (0.44)	.63
POD 1	1.84 (0.47)	1.80 (0.43)	.77
POD 2	1.94 (0.35)	2.03 (0.26)	.39
Sedation score			
PACU	4.78 (0.75)	4.87 (0.55)	.69
POD 1	5.11 (0.34)	5.08 (0.22)	.76
POD 2	5.23 (0.25)	5.14 (0.18)	.23
Atelectasis score			
PACU	0.81 (0.65)	0.69 (0.51)	.54
POD 1	1.25 (0.77)	0.81 (0.40)	.05
POD 2	1.37 (0.88)	0.87 (0.34)	.04
Postoperative outcomes			
Atrial fibrillation	3 (19%)	3 (19%)	1.0
Bronchoscopy for atelectasis	1 (6.2%)	0	1.0
Chest tube d	3.4 (1.2)	4.1 (3.8)	.46
Hospital d	5.6 (1.4)	7.1 (5.0)	.26

Lo-TV, Low tidal volume (5 mL/kg); Hi-TV, high tidal volume (10 mL/kg); PACU, postanesthesia care unit; POD, postoperative day.

ARDS or ALI; however, it remains unclear whether this strategy would benefit patients with relatively healthy lungs undergoing single-lung ventilation for pulmonary resection or other procedures.

Retrospective and randomized studies have been published to evaluate the clinical outcomes of low versus high TV during single-lung ventilation. A retrospective study by Licker and colleagues¹¹ evaluated 2 cohorts of patients undergoing pulmonary resection during 2 different time periods: Lo-TV group (mean 5.3 mL/kg, later time period) versus Hi-TV group (mean 7.1 mL/kg, earlier time period). In this study, the Lo-TV group was found to have a lower incidence of ALI and atelectasis, along with less intensive care unit (ICU) and hospital days. However, the in-hospital mortality was not different, and there was a significant bias in this trial because the Hi-TV group was treated during an earlier time period than the Lo-TV group. In another retrospective study, Fernández-Pérez and colleagues¹² evaluated patients undergoing pneumonectomy, finding high TV ventilation (high TV mean 8.3 mL/kg vs low TV mean 6.7 mL/kg) and large volume fluid administration to be risk factors for developing respiratory failure. The authors included a variety of causes of respiratory failure, many of which seemed unrelated to ventilation strategy, such as cardiac failure and pulmonary embolism. In addition, the direct effect of TV on morbidity and mortality was not assessed in this study. A retrospective study by van der Werff and colleagues,¹³ also evaluating patients undergoing pneumonectomy, found risk factors for developing pulmonary edema to include transfusion of fresh-frozen plasma and high ventilation pressures (>40 cmH₂O). However, TV itself was not analyzed as a variable,

and ventilating airway pressures greater than 40 cmH₂O described in this study would be unacceptable by today's standard.

Two randomized trials have been published evaluating the clinical outcomes of low versus high TV during single-lung ventilation. Michelet and colleagues¹⁴ randomized 52 patients to receive 5 mL/kg versus 9 mL/kg TV during single-lung ventilation for esophagectomy and found a greater Pao₂/Fio₂ ratio at 1 hour postoperatively and a shorter duration of postoperative mechanical ventilation (mean of 56 minutes shorter) in favor of low TV. However, there was no difference in ICU days and postoperative morbidity and mortality at 30 days. Yang and colleagues¹⁵ randomized 100 patients to receive TV of 6 mL/kg versus 10 mL/kg during single-lung ventilation for pulmonary resection and found a greater Pao₂/Fio₂ ratio and less radiographic infiltrates at 7 hours, favoring the Lo-TV group. However, there was no difference between the Hi-TV and Lo-TV groups in terms of ICU days, hospital days, or postoperative morbidity and mortality after a short clinical follow-up of only 1 week. For these 2 randomized trials, the greater Pao₂/Fio₂ ratio observed in the Lo-TV group during the early postoperative period is of doubtful clinical significance because ICU days, morbidity, and mortality were ultimately not different.

Our current randomized study, with a follow-up time of 90 days, found high TV of 10 mL/kg during single-lung ventilation for pulmonary resection to result in less hypercarbia, less dead space ventilation, and higher dynamic compliance compared with low TV of 5 mL/kg. The improved intraoperative pulmonary functions observed in the Hi-TV group are likely a reflection of less atelectasis in the dependent or nonsurgical lung. This is supported by a randomized trial by Kozian and colleagues,¹⁶ who also demonstrated less atelectasis with the use of higher TV (10 vs 5 mL/kg) during single-lung ventilation as assessed by CT imaging of the dependent pig lung. Our study did not evaluate the postoperative Pao₂/Fio₂ ratio because arterial blood gases were not routinely obtained unless clinically indicated. However, our study does show that TV of 10 mL/kg can be safely delivered during single-lung ventilation without an increase in postoperative morbidity or mortality. Unlike patients with ARDS, the lungs of a patient undergoing elective pulmonary resection are more compliant and higher TV can be delivered with relatively small increases in airway pressures, even during single-lung ventilation. For patients with ARDS, it seems that ventilation with high airway pressure is the major factor associated with adverse outcomes rather than the TV delivered.^{5,17} In a meta-analysis of the 5 randomized ARDS trials discussed earlier, Petrucci and Iacovelli⁵ found that the clinical outcome of high TV ventilation was not different than that of low TV ventilation when plateau pressure was maintained at 31 cmH₂O or less. Our study observed no plateau

pressure measured more than 30 cmH₂O with the use of 10 mL/kg TV during single-lung ventilation in patients with relatively healthy compliant lungs. Furthermore, in the lateral position, the ventilator-measured peak and plateau airway pressures of the dependent lung during single-lung ventilation are likely an overestimate of the true transalveolar pressure because the extra-alveolar pressure is unlikely to be zero because of the weight exerted by the patient's torso.

Although our data do not demonstrate improved clinical outcomes with high TV ventilation, quality data are also lacking to support the routine use of low TV ventilation for all patients undergoing elective pulmonary resection because hypercarbia has potential adverse effects on the cardiopulmonary, renal, and neurologic systems.⁵ The optimal ventilation strategy during single-lung ventilation is currently not known. The selection of TV should be individualized to achieve desired airway pressure, oxygenation, CO₂ elimination, and surgical conditions. It may be appropriate to avoid low TV ventilation in patients with a history of arrhythmia, pulmonary hypertension, intracranial hypertension, or renal insufficiency because these conditions may be aggravated by hypercarbia. Higher TV can be safely delivered as long as plateau airway pressure is closely monitored and maintained at less than 30 cmH₂O.

Study Limitations

Our study has several limitations. First, the number of patients is small. However, because this and other randomized trials have demonstrated no difference in clinical outcomes, it may be that a larger randomized trial also will fail to show clinical significant differences between low and high TV ventilation for this patient population. Second, the choice of hypercarbia as the end point of our trial can be criticized. Before this trial, our group routinely used higher TVs during single-lung ventilation for pulmonary resection and observed no increase in postoperative morbidity or mortality.^{18,19} On the basis of this experience, we hypothesized that clinical outcomes would not be different between low and high TV ventilation (as stated in the "Materials and Methods" section); therefore, intraoperative parameters remained as end points to evaluate. Because of the potential adverse effects of hypercarbia, we thought it appropriate to use this intraoperative parameter as our primary end point. Third, because of the short operative times observed in both groups (Table 1), the results of our study may not apply to procedures that require longer duration of single-lung ventilation. Finally, our study did not evaluate the role of PEEP or recruitment maneuvers. Recruitment maneuvers, aimed to prevent atelectasis, may be undesirable after pulmonary resection because of the stress exerted on the parenchymal and bronchial stump staple/suture line, which may lead to prolonged air leak.

Further studies are needed to evaluate PEEP and recruitment maneuvers for this patient population.

CONCLUSIONS

The use of high TV during single-lung ventilation is associated with less hypercarbia, less dead space ventilation, better dynamic compliance, and less postoperative radiographic atelectasis compared with low TV. High TV can be safely delivered during single-lung ventilation if plateau pressure is maintained at less than 30 cmH₂O. Current data do not support the routine use of low TV ventilation during single-lung ventilation as practiced in the ICU for patients with ARDS. An individualized approach to single-lung ventilation based on patient characteristics seems appropriate.

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