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Intraoperative High Tidal Volume Ventilation and Postoperative Acute Respiratory Distress Syndrome in Liver Transplant

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ABSTRACT

Background. Mechanical ventilation plays an important role in perioperative management and patient outcomes. Although mechanical ventilation with high tidal volume (HTV) is injurious in patients in the intensive care unit, the effects of HTV ventilation in patients undergoing liver transplant (LT) has not been reported. The aim of this study was to determine if intraoperative HTV ventilation was associated with the development of acute respiratory distress syndrome (ARDS).

Methods. Patients undergoing LT between 2013 and 2018 at a tertiary medical center were reviewed. The tidal volume was recorded at 3 time points: after anesthesia induction, before liver reperfusion, and at the end of surgery. Patients were divided into 2 groups: HTV (>10 mL/kg predicted body weight [pBW]) and non-HTV (≤ 10 mL/kg pBW). The 2 groups were compared. Independent risk factors were identified by multivariable logistic models.

Results. Of 780 LT patients, 85 (10.9%) received HTV ventilation. Female sex and greater difference between actual body weight and pBW were independent risk factors for HTV ventilation. Patients who received HTV ventilation had a significantly higher incidence of ARDS (10.3% vs 3.9%; P = .01) than those who received non-HTV ventilation.

Conclusions. In this retrospective study, we showed that HTV ventilation during LT was common and was associated with a higher incidence of ARDS. Therefore, tidal volume should be carefully selected during LT surgery. More studies using a prospective randomized controlled design are needed.

M ECHANICAL ventilation is essential to many patients in the operating room and intensive care unit (ICU) and plays an important role in perioperative management and patient outcomes [1]. Historically, mechanical ventilation with high tidal volume (HTV) was used to prevent the development of atelectasis and hypoxemia [2]. In the past 2 decades, HTV ventilation has been linked to pulmonary injury, extrapulmonary complications, and high mortality in numerous studies [1,3]. Patients who are critically ill and are in the ICU setting are particularly vulnerable to the adverse effects of HTV ventilation [3]. Today, the use of HTV is generally avoided, and lung-protective strategies with low tidal volume (LTV) are widely used in patients in the ICU.

Although LTV ventilation has been increasingly used in the operating room in the past 2 decades and has been recommended by international experts, the ideal intraoperative tidal volume

© 2022 Elsevier Inc. All rights reserved. 230 Park Avenue, New York, NY 10169 (TV) for patients undergoing surgery is still actively debated [1,4-8]. Clinical trials on intraoperative ventilation have generated conflicting results. Some studies demonstrate that HTV ventilation is harmful, whereas others show no difference in outcomes or even opposing results. Healthy lungs and a shorter duration of mechanical ventilation are thought to render surgical patients

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more resistant to potential adverse effects of HTV ventilation. LT patients, unlike the majority of patients undergoing non-LT surgery, are severely ill and have underlying multiorgan dysfunction [9,10]. LT surgery is complex and lasts significantly longer than non-LT surgeries. It is assumed that LT patients are sensitive to the detrimental effects of intraoperative HTV ventilation and are at risk for postoperative pulmonary complications. Understanding the effects of intraoperative ventilation and risk factors of potentially detrimental ventilation use in patients undergoing LT is important because it may help us to develop an optimal intraoperative ventilation strategy, which may further decrease postoperative complications and improve patient outcomes. However, there is very little published information regarding intraoperative ventilation management in LT patients. Clinical trials on ventilation effects have excluded LT patients. To date, the relationship between intraoperative ventilation and postoperative outcome in LT populations has never been reported.

The goals of this retrospective study were to describe the patterns of intraoperative ventilation with a focus on determining the prevalence of HTV use during LT surgery and identifying its risk factors. Furthermore, we aimed to investigate a potential relationship between intraoperative HTV ventilation and postoperative acute respiratory distress syndrome (ARDS). We hypothesized that patients who received intraoperative HTV ventilation would experience a higher incidence of postoperative ARDS.

MATERIALS AND METHODS

After receiving approval from the institutional review board of the University of California, Los Angeles (UCLA) and a waiver of the informed consent, we reviewed medical records of consecutive adult (≥18 years) patients who underwent primary LT at the UCLA Medical Center between April 2013 and December 2018. Preoperative, intraoperative, and postoperative variables were retrieved from the UCLA transplant database. Intraoperative ventilation data were extracted from the UCLA perioperative data warehouse. ARDS diagnoses were confirmed by reviewing electronic medical records, laboratory values, and radiographic reports.

All LT patients underwent general anesthesia with endotracheal intubation. A standardized institution-based anesthetic management technique was used in all patients during the study period [11]. In addition to the American Society of Anesthesiologists standard monitors, intraarterial catheters, central venous catheters, and pulmonary artery catheters were routinely placed. A transesophageal echocardiogram was used if there were no contraindications. Intraoperative ventilation was largely performed by an anesthesia machine in a designated room for LT (Perseus A500 and Apollo; Dräger Inc., Houston, Tex, United States). Intraoperative ventilation management was at the discretion of anesthesiologists. Volume-controlled ventilation was most commonly used during LT surgery. Positive end-expiratory pressure (PEEP) and recruitment maneuvers were applied at the anesthesiologist's discretion. Ventilation data were collected at 3 time points: 30 minutes after anesthesia induction, 30 minutes before reperfusion of the liver graft, and at the end of surgery. Postoperatively, all patients were transferred to the ICU and managed by a multidisciplinary team. Lung-protective ventilation, including LTV, was universally applied in all LT patients in the ICU.

Patients were divided into HTV and non-HTV groups. HTV was defined as maximum TV >10 mL/kg predicted body weight (pBW) at any of the 3 time points. Patients with TV of 10 mL/kg pBW or less at all 3 points were included in the non-HTV group. pBW for each patient

was calculated on the basis of the following equations: $50 + 0.91 \times (\text{height [cm]} - 152.4)$ for men and $45.5 + 0.91 \times (\text{height [cm]} - 152.4)$ for women [3]. Actual body weight (aBW) was the weight measured and recorded immediately before transplant surgery.

The diagnosis of ARDS was established using the Berlin ARDS definition [12]. These criteria include new-onset respiratory symptoms within 1 week after LT, new bilateral infiltrates on chest radiography or computed tomography that cannot be fully explained by effusions, lobar/lung collapse, nodules, cardiac failure or fluid overload, and ratio of partial pressure of oxygen to fraction of inspired oxygen (FiO₂) \leq 300 mm Hg with PEEP \geq 5 cm H₂O.

All statistical analyses were performed using IBM SPSS version 26.0 for Windows software (IBM, Armonk, NY, United States). Continuous data were presented as mean \pm SD or median (interquartile range [IQR]) and compared by using the Student *t* test. Binary data were summarized via frequency and percentage and analyzed with Pearson's χ^2 test. Preoperative and intraoperative factors and ventilation settings were compared between the non-HTV and HTV groups. Independent risk factors for HTV were identified by using multivariable logistic regression analysis. Univariate and multivariable analyses were performed to identify risk factors for postoperative ARDS. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported. A *P* value <.05 denoted statistical significance.

RESULTS

A total of 780 adult patients underwent LT in 6 years between 2013 and 2018. The mean age of the study population was 54.8 \pm 11.9 years. Male patients were 62.9% of the study sample. The mean calculated model for end-stage liver disease-sodium (MELD-Na) score at the time of LT surgery was 28.7 (\pm 11.6).

Volume control ventilation was used in the vast majority of patients (98%). Mean TV was 470.5 (\pm 82.6 mL), 479.9 (\pm 77.2 mL), and 483.3 (\pm 80.6 mL) at post-induction, before reperfusion, and at the end of surgery, respectively. Among 780 patients, 85 (10.9%) patients received HTV ventilation and 695 patients received non-HTV ventilation during LT surgery

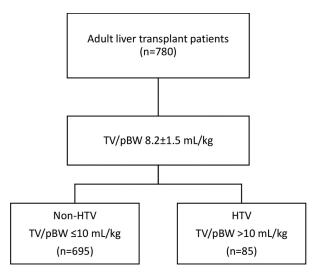


Fig 1. Flowchart of patients in two groups divided by tidal volume (mL)/predicted body weight (kg). HTV, high tidal volume.

	in v aroups		
Variables	Non-HTV (n = 695)	HTV (n = 85)	P Value
Age (in years)	54.5 ± 12.0	57.0 ± 10.9	.07
Sex (Female)	33.4 (232)	67.1 (57)	<.001
Height (cm)	170.1 ± 10.2	156.9 ± 8.7	<.001
Actual body weight (kg)	$\textbf{79.8} \pm \textbf{21.3}$	$\textbf{82.5} \pm \textbf{21.3}$.27
Body mass index, kg/m ²	27.3 ± 6.2	33.3 ± 7.4	<.001
Predicted body weight (kg)	64.6 ± 10.7	51.1 ± 9.0	<.001
Actual predicted body weight MELD Na	15.2 ± 18.3	31.4 ± 18.5	<.001
MELDINA	$\textbf{28.9} \pm \textbf{11.4}$	$\textbf{26.9} \pm \textbf{12.8}$.15
History of hypertension (%)	29.4 (187)	36.3 (29)	.21
Diabetes mellitus (%)	27.0 (172)	36.7 (29)	.07
Gastroesophageal bleeding (%)	40.4 (256)	27.8 (22)	.03
Encephalopathy (%)	55.1 (351)	50.0 (40)	.39
Intubation (%)	24.3 (155)	23.8 (19)	.92
Preoperative pressors (%)	27.4 (175)	25.3 (20)	.70
Preoperative dialysis (%)	50.0 (320)	48.8 (39)	.83
Ascites (>1 L) (%)	43.5 (270)	41.8 (33)	.76
Hepatocellular carcinoma (%) Nonalcoholic steatohepatitis (%)	26.0 (166) 16.4 (94)	30.0 (24) 28.9 (22)	.44 .01
Alcoholic cirrhosis (%)	37.7 (216)	20.9 (22) 22.4 (17)	.01
Acute liver failure (%)	6.8 (39)	5.3 (4)	.61
Hepatitis C (%)	23.7 (136)	27.6 (21)	.46
Hepatitis B (%) Laboratory values	4.9 (28)	2.6 (2)	.38
Hematocrit (%)	$\textbf{26.3} \pm \textbf{10.5}$	$\textbf{26.3} \pm \textbf{8.5}$.95
Platelet (× 10 ³ /mL)	68.6 ± 56.1	69.3 ± 49.5	.91
International normalized ratio	2.0 ± 0.7	2.0 ± 0.7	.48
Fibrinogen (mg/dL)	144.4 ± 82.0	146.8 ± 79.1	.81
Bilirubin (mg/dL)	17.3 ± 15.3	16.8 ± 16.3	.78

Table 1. Comparison of Preoperative Variables Between the Non-HTV and HTV Groups

HTV, high tidal volume; MELD Na, model for end-stage liver disease-sodium.

(Fig 1). Of 85 patients, 44 patients (51.8%) received HTV at 1 time point, 26 (30.6%) received HTV at 2 time points, and 15 patients (17.6%) received HTV at all 3 time points.

Preoperative variables in the non-HTV and HTV groups are displayed in Table 1. HTV was used significantly more frequently in women. The mean height was significantly shorter in the HTV group than in the non-HTV group. In addition, patients with nonalcoholic steatohepatitis were more significantly represented in the HTV group, and patients with gastroesophageal bleeding and alcoholic cirrhosis were more common in the non-HTV group. Body mass index (BMI) was significantly higher in the HTV group than in the non-HTV group. Patient aBW was not significantly different between the 2 groups. However, pBW was significantly lower in the HTV group than in the non-

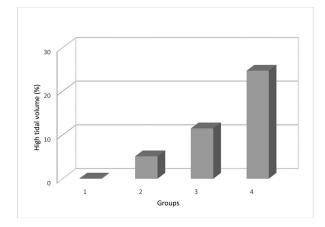


Fig 2. Relationships between high tidal volume (HTV) and 4 different weight groups. Patients were divided into 4 groups according to difference between actual body weight and predicted body weight (aBW-pBW in kg): group 1, \leq 0 kg; group 2, 1-9 kg; group 3, 10-29 kg; group 4, \geq 30 kg.

HTV group, and the difference between aBW and pBW was significantly higher in the HTV group than in the non-HTV group. We divided patients into 4 quartile groups by differences between aBW and pBW. In patients whose aBW was equal to or less than pBW (group 1 in Fig 2), no patient received HTV ventilation. As the difference between aBW and pBW increased, so did the percentage of patients who received HTV. Among patients whose aBW was 30 kg or greater than pBW (group 4 in Fig 2), 24.9% received HTV.

Intraoperative variables, including blood transfusion and vasopressor use, were not significantly different between patients in the non-HTV and HTV groups (Table 2). Intraoperative ventilation settings between the non-HTV and HTV groups are displayed in Table 3. In addition to TV and TV/kg, the peak airway pressures were significantly higher at

Table 2. Comparison of Intraoperative Variables Between the Non-HTV and HTV Groups

Variables	Non-HTV (n = 695)	HTV (n = 85)	P Value
Red blood cell transfused (unit)	23.7 ± 20.8	23.9 ± 20.0	.95
Fresh frozen plasma transfused (unit)	25.7 ± 21.8	26.1 ± 23.1	.88
Platelets transfused (U)	1.4 ± 1.2	1.5 ± 1.2	.72
Cryoprecipitate transfused (unit)	$\textbf{2.3} \pm \textbf{2.2}$	1.8 ± 1.7	.06
Cold ischemia time (min)	461.2 ± 149.6	464.6 ± 185.6	.85
Warm ischemia time (min)	$\textbf{52.3} \pm \textbf{14.5}$	52.6 ± 10.9	.84
Surgical time (min)	401.0 ± 91.0	420.6 ± 110.8	.29
Intraoperative dialysis (%)	25.4	22.5	.58
Vasopressor: infusion (%)	93.1	88.6	.15
Vasopressor: bolus (%)	46.1	55.0	.13
Venovenous bypass (%)	51.1	49.3	.78
Antifibrinolytics (%)	14.7	16.7	.64

HTV, high tidal volume.

Time Points	Variables	Non-HTV(n = 695)	HTV(n = 85)	P Value
After anesthesia induction	FiO ₂	73.4 ± 19.0	$\textbf{77.9} \pm \textbf{18.7}$.06
	Tidal volume (mL)	464.1 ± 83.4	497.0 ± 109.9	.01
	TV/kg (mL/kg)	7.3 ± 1.2	9.8 ± 1.5	<.001
	Ventilation rate (time/min)	13.1 ± 2.8	13.0 ± 3.5	.72
	Peak airway pressure (cmH ₂ O)	$\textbf{21.4} \pm \textbf{5.6}$	24.9 ± 6.0	<.001
	PEEP (cmH ₂ O)	$\textbf{4.3} \pm \textbf{2.2}$	4.4 ± 2.1	.63
Before liver reperfusion	FiO ₂	64.9 ± 15.7	67.9 ± 16.9	.13
	Tidal volume (mL)	474.6 ± 74.0	516.2 ± 100.0	<.001
	TV/kg (mL/kg)	7.4 ± 1.0	10.2 ± 1.3	<.001
	Ventilation rate (time/min)	14.9 ± 3.5	14.0 ± 3.5	.02
	Peak airway pressure (cmH ₂ O)	$\textbf{20.1} \pm \textbf{4.5}$	23.5 ± 4.2	<.001
	PEEP (cmH ₂ O)	$\textbf{4.9} \pm \textbf{1.8}$	4.7 ± 2.0	.49
End of surgery	FiO ₂	$\textbf{60.3} \pm \textbf{14.2}$	66.7 ± 17.2	.003
	Tidal volume (mL)	477.6 ± 76.1	519.9 ± 116.1	.002
	TV/kg (mL/kg)	7.5 ± 1.1	10.2 ± 1.4	<.001
	Ventilation rate (time/min)	$\textbf{16.9} \pm \textbf{3.4}$	15.9 ± 3.8	.01
	Peak airway pressure (cmH ₂ O)	$\textbf{19.8} \pm \textbf{4.4}$	$\textbf{23.5} \pm \textbf{4.2}$	<.001
	PEEP (cmH ₂ O)	$\textbf{4.9} \pm \textbf{1.8}$	5.1 ± 1.8	.31
Entire surgery (maximum values)	FiO ₂	$\textbf{77.5} \pm \textbf{18.2}$	82.8 ± 16.9	.01
	Tidal volume (mL)	498.6 ± 77.3	564.4 ± 110.5	<.001
	TV/kg (mL/kg)	$\textbf{7.8} \pm \textbf{1.0}$	11.1 ± 1.1	<.001
	Ventilation rate (time/min)	17.3 ± 3.6	16.5 ± 4.1	.07
	Peak airway pressure (cmH ₂ O)	$\textbf{23.4} \pm \textbf{5.3}$	27.6 ± 5.0	<.001
	PEEP (cmH ₂ O)	5.2 ± 1.8	5.3 ± 1.7	.43

Table 3. Intraoperative Ventilation Setting Between the Non-HTV and HTV Groups

FiO₂, fraction of inspired oxygen; HTV, high tidal volume; PEEP, positive end-expiratory pressure; TV, tidal volume.

all 3 time points in the HTV group than in the non-HTV group. Ventilation rates were significantly lower at prereperfusion and at the end of surgery in the HTV group as well. FiO₂ was significantly higher only at the end of surgery in the HTV group. PEEP was not significantly different at all 3 time points between the 2 groups.

Multivariable logistic analysis showed that preoperative variables, including female sex (OR, 4.006; 95% CI, 2.35-6.82; P < .001), no history of gastroesophageal bleeding (OR, 1.92; 95% CI, 1.10-3.35; P = .02), higher BMI (OR, 1.07; 95% CI, 1.01-1.14; P = .03), and aBW greater than pBW (OR, 1.78; 95% CI, 1.02-3.08; P < .04) were independent risk factors for the use of HTV during LT surgery. Low respiratory rate (OR, 1.10; 95% CI, 1.02-1.19; P = .01) and high positive airway pressure (OR, 1.11; 95% CI, 1.05-1.17; P < .001) were 2 ventilator parameters that were associated with HTV ventilation.

Patients who received HTV during LT experienced a significantly higher incidence of ARDS (10.3%) than those in the non-HTV group (3.9%; P = .01) (Fig 3). Patients who received HTV at 2 or 3 time points had a higher incidence of ARDS (12.8%) than those who received HTV at 1 time point (7.7%). Multivariable logistic regression showed that patients who received HTV had a fourfold increased risk of developing posttransplant ARDS compared with those who did not receive HTV. Other risk factors for postoperative ARDS included preoperative intubation, low preoperative platelet counts, and high PEEP (Table 4).

DISCUSSION

Patients with the most severe liver disease are prioritized by the current donor allocation system in the United States and many other countries [11]. This is reflected in our study cohort that had high MELD-Na scores and a large percentage of patients with multiorgan dysfunction. In addition, patients with end-stage liver disease may have various underlying respiratory disorders before transplant [13,14]. Ascites, hepatic hydrothorax, and pulmonary infections are prevalent in patients with for transplants. Pulmonary edema may occur in patients with

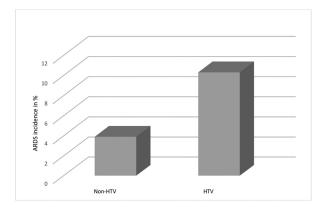


Fig 3. The incidences of ARDS in the non-HTV and HTV groups. ARDS, acute respiratory distress syndrome; HTV, high tidal volume.

	Univariate Analysis OR (95% CI)	P Value	Multivariable Analysis OR (95% Cl)	P Value
Female sex	2.02 (1.01-4.03)	.05		
Body mass index	1.04 (0.99-1.09)	.10		
MELD-Na	1.09 (1.05-1.14)	<.001		
Encephalopathy	2.88 (1.28-6.45)	.01		
Intubation before transplant	8.79 (4.11-18.81)	<.001	8.22 (3.45-19.57)	<.001
Dialysis before transplant	4.21 (1.81-9.82)	.001		
The use of vasopressor before transplant	8.6327 (3.95-48.86)	<.001		
History of gastroesophageal bleeding	2.66 (1.31-5.40)	.007		
Platelet counts	0.95 (0.95-0.99)	<.001	0.97 (0.95-0.99)	.005
Preoperative bilirubin	1.05 (1.03-1.07)	<.001		
Intraoperative Dialysis	3.27 (1.63-6.57)	.001		
Venovenous bypass	6.40 (2.19-18.72)	.001		
Red blood cell transfusion (U)	1.01 (1.001-1.03)	.03		
Fresh frozen plasma transfusion (U)	1.10 (1.00-1.02)	.11		
Platelet transfusion	1.568 (1.238-1.986)	<.001		
Entire surgery (maximum values)				
FiO ₂	1.01 (0.99-1.03)	.27		
Tidal volume	0.99 (0.94-1.00)	.42		
TV/kg	1.03 (0.97-1.4599)	.09		
HTV	2.85 (1.24-5.53)	.01	4.08 (1.57-10.63)	.004
Ventilation rate	1.16 (1.07-1.27)	.001	· · ·	
Peak airway pressure	1.15 (1.08-1.22)	<.001		
PEEP	1.55 (1.25-1.92)	<.001	1.49 (1.15-1.93)	.002

Table 4. Univariate and Multivariate Analysis for Acute Respiratory Distress Syndrome

CI, confidence interval; FiO₂, fraction of inspired oxygen; MELD Na, model for end-stage liver disease-sodium; OR, odds ratio; PEEP, positive end-expiratory pressure; TV, tidal volume.

volume overload, hepatorenal syndrome, and cirrhotic cardiomyopathy. Deconditioning, immobility, and malnutrition are additional pulmonary risk factors in patients undergoing LT. Severe encephalopathy is a risk factor for aspiration and pneumonia. Portopulmonary hypertension and hepatopulmonary syndrome may contribute to respiratory failure in LT patients.

Mechanisms that cause lung injury in critically ill patients due to HTV have been extensively studied [15]. HTV ventilation is associated with high airway pressure and overdistension of lung tissue; the former causes barotrauma, and the latter leads to volutrauma. HTV ventilation creates cyclic opening and collapse of the atelectatic but recruitable lung units, which causes atelectrauma [16]. Biotrauma is defined as a biological response to HTV ventilation that results in the production of systemic proinflammatory and proinjurious cytokines. This response promotes extrapulmonary organ injury, predisposing to multiorgan failure and mortality [16-19]. HTV ventilation may have additional adverse effects for patients undergoing LT surgery. During LT surgery, a "low central venous pressure" technique has been shown to promote venous blood return from the portal system and to decrease intraoperative blood loss [20,21]. HTV ventilation has been associated with elevated central venous pressure, which may contribute to increased blood loss and higher transfusion requirements [22].

Implementing a lung-protective strategy and avoiding HTV during LT surgery has many obstacles and challenges. Consistent with previous studies [23], we confirmed that female patients were at high risk for receiving HTV ventilation. This is because female patients often have

overestimated pBW. Accurate pBW requires calculation, which is cumbersome and time-consuming. LT patients have many conditions that may lead to overestimated pBW. Ascites, liver mass, obesity, fluid overload, or edema are common in LT patients and can contribute to an overestimation of pBW. Patients with higher BMI may have similar overestimated pBW, resulting in the use of HTV. Even in patients with accurate body weight estimates, there are additional challenges in LT patients. Hemodynamic instability and metabolic disorders are common, particularly during critical surgical events such as hepatectomy and reperfusion. Ventilatory parameters may receive less attention from the anesthesiologist during these episodes.

During LT surgery, ventilator adjustments are constantly required, based on clinical conditions. Removal of the inferior vena cava clamps and organ reperfusion are often associated with acidosis, hyperkalemia, and a transient increase in end-tidal CO₂. Hyperventilation is often employed during this phase of the surgery. An intentional increase in minute ventilation by using HTV, increased respiratory rate, or both may be necessary during this phase of the operation. Other acute cardiovascular and metabolic events during LT, such as allograft dysfunction, pulmonary embolism/intracardiac thrombi, pleural effusion, and pneumothorax may require major ventilatory adjustments that may result in prolonged HTV.

Other ventilatory parameters in addition to TV are important, too, in the management of mechanically ventilated patients. Many lung-protective ventilation proposals include the use of a low to moderate PEEP [1]. In LT surgery, high levels of PEEP may impede venous blood return, reduce hepatic perfusion pressure, and compromise liver graft function. In addition, patients exposed to high levels of PEEP may experience intraoperative hypotension and require vasopressor support [24]. Recruitment maneuvers may be employed during LT to expand lungs or to test surgical vascular anastomosis periodically. However, the benefits of recruitment maneuvers have been questioned [4]. In addition, recruitment maneuvers have been shown to be associated with oxygen desaturation and arrhythmia [25].

To implement intraoperative lung-protective ventilation strategies in LT patients, several actions can be taken. Education on the detrimental effects of HTV on postoperative lung injury has been shown to reduce TV size during surgery [7]. Because the default TV of the anesthesia machine is commonly used at the beginning of anesthesia, redesigning a default low TV may reduce the chance of exposing patients to potentially harmful HTV ventilation. In addition, our study found that patients in the HTV group had lower respiratory rates, suggesting that the same amount of minute ventilation can be achieved by using an increased respiratory rate, thus avoiding HTV.

Our study has limitations. This was a retrospective study with inherent shortcomings. Patients in the 2 groups were different in various aspects. Although we used multivariable analysis to minimize selection bias, some unmeasured confounders may have been present. The intraoperative ventilation settings are dynamic and may change continuously according to clinical conditions. This dynamic variable presents challenges for data analysis. We decided in this study to collect ventilation data at 3 key time points during LT surgery. Although our method does not completely reflect the intraoperative ventilatory settings that may have occurred in each patient, we believe that our data represent the best overall survey of intraoperative ventilation in our study population and have advantages over other methods using the initial ventilator setting or median value for the entire surgery. In this study, we only studied the potentially harmful effect of HTV (defined as >10 mL/kg pBW), not the protective effect of LTV (usually defined as $\leq 6 \text{ mL/kg pBW}$), due to the sample size and other constraints. Because this is a retrospective study, the association between intraoperative HTV and postoperative ARDS found in this study cannot be interpreted as a causal relationship.

In this retrospective study, we found that the use of HTV ventilation is common during LT, especially in female patients and patients with a greater difference between aBW and pBW. Intraoperative mechanical ventilation with HTV was associated with a higher incidence of ARDS. Due to its potentially harmful effects, the tidal volume should be carefully selected during LT. More studies using a prospective randomized controlled design are needed.

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INTRAOPERATIVE HIGH TIDAL VOLUME VENTILATION AND P

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