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Research article

Adherence to lung protective mechanical ventilation in patients admitted to a surgical intensive care unit and the associated increased mortality

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ABSTRACT

Background: The adherence rate to the lung protective ventilation (LPV) strategy, which is generally accepted as a standard practice in mechanically ventilated patients, reported in the literature is approximately 40%. This study aimed to determine the adherence rate to the LPV strategy, factors associated with this adherence, and related clinical outcomes in mechanically ventilated patients admitted to the surgical intensive care unit (SICU).

Methods: This prospective observational study was conducted in the SICU of a tertiary university-based hospital between April 2018 and February 2019. Three hundred and six adult patients admitted to the SICU who required mechanical ventilation support for more than 12 h were included. Ventilator parameters at the initiation of mechanical ventilation support in the SICU were recorded. The LPV strategy was defined as ventilation with a tidal volume of equal or less than 8 ml/kg of predicted body weight plus positive end-expiratory pressure of at least 5 cm H_2O. Demographic and clinical data were recorded and analyzed.

Results: There were 306 patients included in this study. The adherence rate to the LPV strategy was 36.9%. Height was the only factor associated with adherence to the LPV strategy (odds ratio for each cm, 1.10; 95% confidence interval (CI), 1.06–1.15). Cox regression analysis showed that the LPV strategy was associated with increased 90-day mortality (hazard ratio, 1.73; 95% CI, 1.02–2.94).

Conclusion: The adherence rate to the LPV strategy among patients admitted to the SICU was modest. Further studies are warranted to explore whether the application of the LPV strategy is simply a marker of disease severity or a causative factor for increased mortality.

1. Introduction

Most patients admitted to the intensive care unit (ICU) usually require mechanical ventilation (MV) as organ support due to either respiratory failure or hemodynamic instability or both. Although MV can provide respiratory support and is considered a life-saving intervention, it, on the other hand, can cause ventilator-induced lung injury (VILI) including volutrauma, barotrauma, atelectrauma,

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and biotrauma, which potentially increases morbidity and mortality [1]. To lessen VILI and possibly reduce morbidity and mortality in patients receiving MV support, the lung protective mechanical ventilation (LPV) strategy has been described [1,2]. The strategy includes ventilating with low tidal volume of 6–8 ml/kg of predicted body weight (PBW) and applying sufficient positive end-expiratory pressure (PEEP) to prevent atelectasis [1,2]. The beneficial effects of the LPV strategy including minimized acute lung injury and acute respiratory distress syndrome (ARDS), reduced pulmonary complications such as atelectasis and pneumonia, and decreased MV duration, length of stay (LOS), and mortality have been proved in patients with ARDS [3], patients without lung pathology [4–7] and surgical patients receiving general anesthesia [8–10]. However, current studies demonstrated that only around 40% of both patients with normal lungs [11–13] and those with ARDS [14–19] received MV support according to the LPV strategy.

A recent survey of respiratory support in ICU in Thailand found that more than two-thirds of patients admitted to the surgical ICU (SICU) required MV support either following surgery or during ICU stay [20]. However, data regarding MV management in these patients are rather limited. We hypothesized that the LPV strategy has been applied to patients admitted to the SICU at a similar rate to other populations [11–19]. Therefore, the primary objective of this study was to find out the adherence rate to the LPV strategy in patients admitted to a SICU and receiving MV support. The secondary objectives were to reveal variables associated with the application of the LPV strategy in these patients and to determine the clinical outcomes related to the application of the LPV strategy.

2. Materials and methods

2.1. Ethics

This study was approved by the Institutional Review Board of Siriraj Hospital, Bangkok, Thailand (Chairperson Prof. Chairat Shayakul, M.D.; COA No. Si 184/2018; approval date March 23, 2018) prior to patient enrollment and was registered at ClinicalTrials.gov (NCT03698799). Written informed consent was obtained from all patients or their relatives before inclusion or as soon as possible, and the study was conducted in accordance with the guidelines and regulations of our faculty and university.

2.2. Study design and patient population

This prospective observational study was conducted at the SICU of a tertiary university-based hospital in Bangkok, Thailand. Patients undergoing vascular, abdominal, urological, head and neck, orthopedic, plastic, otorhinolaryngologic, gynecological, obstetric, and ophthalmologic surgeries who require intensive perioperative care are admitted to this SICU. The unit is a closed ICU model with a 14-bed capacity covered 24/7 by anesthesia-based intensivists, critical care fellows, and anesthesiology residents. Patients undergoing cardiothoracic, neurological, pediatric, and trauma surgeries were admitted to other specific ICUs. All patients admitted to the SICU between April 9, 2018, and February 26, 2019, were screened for inclusion. Patients aged ≥18 years who required MV support ≥12 h during SICU stay were included. Patients who did not receive MV support or received MV support <12 h during SICU stay, patients who received MV support for more than 24 h prior to SICU admission, patients who re-admitted to the SICU, patients who received non-invasive MV support, and moribund or terminal cases were excluded from this study.

2.3. Study procedure

Inclusion started on the day of initiation of MV support in the SICU. All included patients received medical care on the basis of general standard practices of the primary care team including resuscitation, medication, and MV management. During the study period, there was no standard protocol for the initiation and liberation of MV implemented in our SICU. Pulmonary and other complications were evaluated daily for seven consecutive days following inclusion or until patients were discharged from the SICU or pronounced deceased, whichever came first. Hospital discharge status and status at 90 days following inclusion were also recorded.

2.4. Data collection

The investigators responsible for the data collection were not involved in patient care and management. Demographic records obtained on the inclusion day included age, gender, weight, height, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, lung injury prediction score (LIPS) [21], laboratory values, and chest radiographs. The ventilator parameters recorded at the initiation of MV support on the inclusion day included exhaled tidal volume, airway pressure, PEEP level, measured respiratory rate, fraction of inspired oxygen (FiO_2), and minute ventilation. Pulmonary complications [22,23] including new pulmonary infiltration, ARDS, pneumonia, pleural effusion, atelectasis, cardiogenic pulmonary edema, pneumothorax, restoration of MV support, and tracheostomy, and other complications including stroke, myocardial ischemia/infarction, arrhythmias, AKI, and sepsis, were monitored for seven consecutive days following inclusion or until patients were discharged from the SICU or pronounced deceased, whichever came first. Outcomes including re-admission to the SICU, duration of MV support, LOS in the SICU and hospital, SICU and hospital discharge status, and status at 90 days either alive or dead were also collected.

2.5. Study endpoints and sample size calculation

The primary endpoint of this study was to determine the adherence rate to the LPV strategy at the initiation of MV support in mechanically ventilated patients in the SICU. In this study, the LPV strategy was defined as ventilation with a tidal volume equal to or less than 8 ml/kg of PBW plus the application of PEEP of at least 5 cm H_2O. PBW was calculated according to the equation; 50 + 0.91 x (height in cm – 152.4) for male and 45.5 + 0.91 x (height in cm – 152.4) for female [24]. Based on the previously reported adherence rate to the LPV strategy in mechanically ventilated patients of approximately 40% [11–19] with a margin of error of 5% and 95% confidence interval (CI), a sample size of 270 patients was required. After a 10% inflation for possible missing data, we planned to include 300 patients in the study. The secondary endpoint was to identify potential factors associated with adherence to the LPV strategy, incidence of pulmonary and other complications, duration of MV support, LOS in the SICU and hospital, SICU and hospital discharge status, and status at 90 days following the initiation of MV support in patients receiving and not receiving the LPV strategy.

2.6. Statistical analysis

Data were expressed as means with standard deviations, medians with interquartile ranges, or numbers with percentages as appropriate. The Student's t-test or Mann-Whitney *U* test was used to compare continuous variables, and the chi-squared test or Fisher's exact test was used for categorical variables as appropriate. A multivariate logistic regression analysis was used to identify the independent factors associated with adherence to the LPV strategy by entering variables that had a *P* value lower than 0.05 from the univariate analysis into the model. To determine the hazard ratio of 90-day mortality, a multivariate Cox proportional hazard model was obtained by entering the LPV strategy as a dependent variable and other predefined covariates associated with 90-day mortality including age, gender, comorbidities, sites of surgery, severity scores, and reasons for SICU admission. All statistical analyses were 2-tailed and *P* values lower than 0.05 were considered statistically significant. Data were prepared and analyzed using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA).

3. Results

During the study period, 587 eligible patients were screened, and 281 patients were excluded mainly because they did not receive MV support or received MV support for less than 12 h during the SICU stay (74.7%) (Fig. 1). Consequently, there were 306 patients included in this study, and all were followed-up. A total of 113 (36.9%) patients received the LPV strategy at the initiation of MV support. When compared with patients not receiving the LPV strategy, those receiving the LPV strategy showed a significantly higher proportion of male, higher height, higher PBW, more comorbidity of vascular disease, and more frequent smoking (Table 1). There was no difference between the groups regarding the APACHE II score, SOFA score, LIPS, and other clinical parameters as well as laboratory values, except patients receiving the LPV strategy had significantly higher serum HCO_3^- and serum albumin (Table 2). Patients receiving the LPV strategy received a significantly lower tidal volume (410.0 ± 73.9 ml vs. 509.0 ± 109.2 ml, $P < 0.001$), lower tidal volume per kg of PBW (7.1 ± 0.8 ml/kg vs. 9.8 ± 1.8 ml/kg, $P < 0.001$), and higher PEEP (5.4 ± 1.2 cm H_2O vs. 5.1 ± 0.9 cm H_2O, $P = 0.04$) than those not receiving the LPV strategy (Table 2). Consequently, they had significantly lower minute ventilation and higher $PaCO_2$. However, there was no significant difference in the acid-base status between the groups (Table 2).

Various factors associated with adherence to the LPV strategy were identified in the univariate analysis (Table 3), however, height was the only independent factor associated with adherence to the LPV strategy identified in the multivariate analysis (odds ratio for each cm, 1.10; 95% CI 1.06–1.15; $P < 0.001$).

Regarding clinical outcomes, the duration of MV support did not differ between the groups, and there were no significant

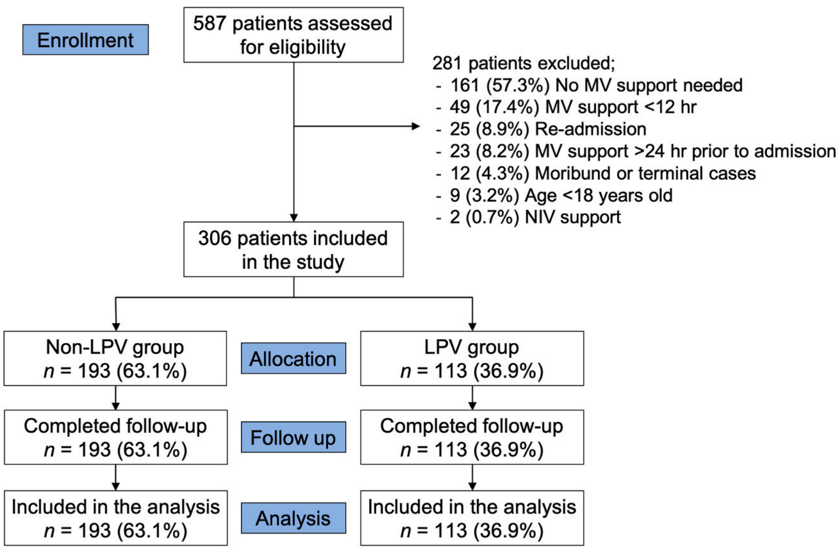

Fig. 1. Study flow diagram.

Table 1
Demographic data of all patients categorized into those received and did not receive lung protective mechanical ventilation.

Patient characteristics	Non-LPV (N = 193)	LPV (N = 113)	*P*
Age (year)	66.5 ± 15.8	64.2 ± 15.5	0.21
Male gender	96 (49.7)	76 (67.3)	0.003
Weight (kg)	58.5 ± 15.1	59.9 ± 19.0	0.48
Height (cm)	157.4 ± 8.1	162.9 ± 7.8	<0.001
Body mass index (kg/m^2)	23.6 ± 5.7	22.4 ± 6.0	0.08
Predicted body weight (kg)	52.3 ± 9.0	58.1 ± 8.6	<0.001
Charlson Comorbidity Index	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.81
Comorbidity			
- Hypertension	115 (59.6)	56 (49.6)	0.09
- Vascular diseases	21 (10.9)	22 (19.5)	0.04
- Coronary artery disease	21 (10.9)	15 (13.3)	0.53
- COPD	6 (3.1)	2 (1.8)	0.72
- Chronic kidney disease	47 (24.4)	33 (29.2)	0.35
- Diabetes	46 (23.8)	25 (22.1)	0.73
- Cancer	92 (47.7)	52 (46.0)	0.78
Smoking	56 (29.0)	48 (42.5)	0.02
Surgical sites[a]			
- Upper and lower abdomen	78 (42.4)	37 (34.3)	0.62
- Major and peripheral vascular	28 (15.2)	25 (23.1)	
- Head and neck	24 (13.0)	14 (13.0)	
- Urology	18 (9.8)	8 (7.4)	
- Spine	12 (6.5)	5 (4.6)	
- Obstetrics and gynaecology	7 (3.8)	5 (4.6)	
- Joint and musculoskeletal	7 (3.8)	6 (5.6)	
- Others	10 (5.4)	8 (7.4)	
Duration of surgery (hour)[a]	340 (177.5, 522.5)	350 (207.5, 487.5)	0.72
Intraoperative fluid balance (ml)[a]	1938 (783.5, 3156)	1743 (851.5, 2985)	0.42
Reasons for SICU admission			
- After elective surgery	92 (47.7)	46 (40.7)	0.52
- After emergency surgery	62 (32.1)	38 (33.6)	
- Unplanned admission	13 (6.7)	12 (10.6)	
- Medical condition	26 (13.5)	17 (15.0)	

Data are presented as mean ± standard deviation, median (interquartile range), or N (%) as appropriate.
COPD, chronic obstructive pulmonary disease; LPV, lung protective mechanical ventilation; SICU, surgical intensive care unit.
[a] Data from 292 patients undergoing either elective or emergency surgery; 184 in non-LPV group and 108 in LPV group.

differences between the groups in terms of pulmonary and non-pulmonary complications, LOS in the SICU and in the hospital, and SICU, hospital and 90-day mortality (Table 4). However, Cox regression analysis for 90-day mortality adjusted for age, gender, Charlson Comorbidity index, APACHE II score, SOFA score, intraabdominal or vascular surgery as sites of surgery, and reasons for SICU admission other than after elective surgery found that the application of the LPV strategy was associated with an increased 90-day mortality (hazard ratio 1.73, 95% CI 1.02–2.94, $P = 0.04$) (Fig. 2).

4. Discussion

The main finding of this prospective observational study was that the adherence rate to the LPV strategy defined as MV with tidal volume equal to or less than 8 ml/kg of PBW plus applying PEEP of at least 5 cm H_2O at the initiation of MV in patients admitted to the SICU and requiring MV support for more than 12 h, was 36.9%, which was in concordance with those reported in previous studies [11–19]. The only independent factor associated with the adherence to LPV strategy was the patient's height. Contrary to other studies [3,4], we demonstrated that the application of the LPV strategy increased the hazard ratio of 90-day mortality.

The LPV strategy has been proposed for decades and has been accepted as the standard practice, not only in mechanically ventilated patients with ARDS but also in those without ARDS, either in the operating room or ICU [1,2]. Nevertheless, adherence to this strategy is modest in practice [11–19]. A difficult task in clinical research may be how to define adherence to the LPV strategy. Some studies defined the LPV strategy as a low tidal volume ventilation strategy, in which using different cut-off values of tidal volume per kg of PBW yielded different adherence rates [11,14]. Another study used an algorithmic definition consisting of the tidal volume per kg of PBW, plateau pressure, and pH to define the LPV strategy [17]. Moreover, it seemed unclear whether the determination of adherence should be at a specific time point, such as 24–48 h after initiation of MV support [13–17], or the total time of MV support [11,12,18, 25]. In this study, we determined the adherence to LPV strategy at the initiation of MV in a similar manner to the recent large cohorts of patients with and without ARDS [26–28], focusing on ventilator management on the first day. Sjoding et al. [25] found that an initial tidal volume >8 ml/kg of PBW predicted exposure to MV support with a tidal volume >8 ml/kg of PBW for more than 24 h, which was associated with increased mortality. We considered the initiation of MV support as the critical timeframe for patients, and if an inappropriate setting of MV is delivered, it can subsequently potentiate VILI.

Various factors associated with adherence to the LPV strategy have been proposed in the literature, such as being male [11], high

Table 2
Clinical data at the initiation of mechanical ventilation and ventilatory support parameters of all patients categorized into those received and did not receive lung protective mechanical ventilation.

Patient characteristics	Non-LPV (N = 193)	LPV (N = 113)	*P*
APACHE II score	12.5 ± 5.7	11.9 ± 5.2	0.34
SOFA score	3.0 (1.0, 6.0)	4.0 (1.0, 6.0)	0.80
Lung injury prediction score	5.0 (3.0, 7.0)	4.5 (3.0, 6.75)	0.91
Sepsis at SICU admission	59 (30.6)	32 (28.3)	0.68
Acute kidney injury at SICU admission	41 (21.2)	24 (21.2)	>0.99
Reasons for mechanical ventilation			
-After general anesthesia	148 (76.7)	85 (75.2)	0.30
- Respiratory failure	25 (13.0)	20 (17.7)	
- Hemodynamic instability	12 (6.2)	5 (4.4)	
- Post-cardiac arrest	5 (2.6)	0 (0.0)	
- Depressed level of consciousness	3 (1.6)	3 (2.7)	
Laboratory values			
- Hemoglobin (g/dl)	10.6 ± 2.3	11.0 ± 2.2	0.22
- Na (mmol/l)	138.8 ± 5.4	138.7 ± 5.1	0.86
- K (mmol/l)	4.2 ± 0.7	4.1 ± 0.8	0.11
- HCO_3^- (mmol/l)	19.0 ± 4.3	20.1 ± 5.2	0.05
- Creatinine (mg/dl)	1.3 ± 1.3	1.5 ± 1.9	0.43
- Albumin (g/dl)	2.6 ± 0.6	2.7 ± 0.6	0.04
- pH	7.36 ± 0.09	7.36 ± 0.09	0.67
- PaO_2 (mmHg)	169.2 ± 76.5	171.4 ± 72.2	0.81
- $PaCO_2$ (mmHg)	35.2 ± 6.6	37.1 ± 7.5	0.02
- PaO_2/FiO_2 ratio	385.7 ± 177.7	375.6 ± 161.9	0.62
Abnormal chest X-ray	48 (24.9)	29 (25.7)	0.88
Ventilator support parameters			
- Tidal volume (ml)	509.0 ± 109.2	410.0 ± 73.9	<0.001
- TV per kg of PBW (ml/kg)	9.8 ± 1.8	7.1 ± 0.8	<0.001
- Peak inspiratory pressure (cmH_2O)	14.5 ± 4.5	14.4 ± 5.1	0.89
- PEEP (cmH_2O)	5.1 ± 0.9	5.4 ± 1.2	0.04
- FiO_2	0.5 ± 0.1	0.5 ± 0.1	0.12
- Respiratory rate (/min)	17.1 ± 4.8	17.1 ± 4.2	0.90
- Minute ventilation (L/min)	8.6 ± 3.1	7.0 ± 2.2	<0.001

Data are presented as mean ± standard deviation, median (interquartile range), or N (%) as propriate.
APACHE II, Acute Physiology and Chronic Health Evaluation II score; LPV, lung protective mechanical ventilation; PBW, predicted body weight; PEEP, positive end-expiratory pressure; SOFA, Sequential Organ Failure Assessment score; TV, tidal volume.

Table 3
Factors associated with the adherence to the lung protective mechanical ventilation strategy.

Factors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Male gender	2.08 (1.28–3.37)	0.003	1.33 (0.63–2.79)	0.46
Height, each cm	1.09 (1.06–1.12)	<0.001	1.10 (1.06–1.15)	<0.001
Vascular disease	1.98 (1.03–3.79)	0.04	1.79 (0.87–3.66)	0.11
Smoking	1.81 (1.11–2.94)	0.02	0.99 (0.52–1.87)	0.97
HCO_3^-, each mmol/l	1.05 (1.00–1.11)	0.05	1.03 (0.97–1.10)	0.33
Albumin, each g/dl	1.51 (1.02–2.23)	0.04	1.50 (0.97–2.34)	0.07
$PaCO_2$, each mmHg	1.04 (1.01–1.08)	0.03	1.02 (0.98–1.07)	0.28

APACHE II, Acute Physiology and Chronic Health Evaluation II score; CI, confidence interval; OR, odds ratio.

peak inspiratory pressure [11], high PEEP [11], low partial pressure of oxygen (PaO_2) to FiO_2 ratio in arterial blood [11,15], low static compliance of the respiratory system [15], high lung injury severity [16] and use of neuromuscular blocking agents [16]. The only factor associated with adherence to the LPV strategy identified in our study was height, which was similarly reported in other studies [12,17,19,25]. This might reflect our practice of omitting the calculation of PBW and setting tidal volume with a preset value. In two large international, multicenter, observational studies on MV management in patients admitted to ICUs [27,28], patients without ARDS seemed to receive a preset tidal volume of 450–500 ml regardless of the risk of acute lung injury or the patient's PBW. In our study, patients received an absolute tidal volume of 472.4 ± 108.7 ml. When expressed as tidal volume per kg of PBW, patients who were taller and subsequently had higher PBW received lower tidal volume per kg of PBW, and apparently more of them adhered to the LPV strategy than those who were shorter. At the time of conducting this study, no protocol for MV management was implemented in our SICU. To improve adherence to the LPV strategy, providing knowledge and education [12] and implementing a written protocol [12,14] or structural checklist [13] for MV management are necessary.

To the best of our knowledge, this study is the first to demonstrate that application of the LPV strategy is associated with increased mortality. A meta-analysis of patients with ARDS demonstrated that the application of the LPV strategy with low tidal volume

Table 4
Clinical outcomes and mortality.

Outcomes	Non-LPV (N = 193)	LPV (N = 113)	*P*
Duration of mechanical ventilation (hour)	43.0 (20.0, 88.0)	42 (18.0, 95.0)	0.71
Pulmonary complications	52 (26.9)	33 (29.2)	0.67
- Restoration of MV support	25 (13.0)	13 (11.5)	0.71
- Pulmonary edema	15 (7.8)	5 (4.4)	0.25
- Tracheostomy	9 (4.7)	7 (6.2)	0.56
- Pleural effusion	8 (4.1)	7 (6.2)	0.42
- Pneumonia	8 (4.1)	4 (3.5)	>0.99
- Pulmonary infiltration	5 (2.6)	1 (0.9)	0.42
- ARDS	2 (1.0)	3 (2.7)	0.36
- Atelectasis	3 (1.6)	1 (0.9)	>0.99
- Pneumothorax	1 (0.5)	2 (1.8)	0.56
Non-pulmonary complications	54 (28.0)	28 (24.8)	0.54
- Acute kidney injury	29 (15.0)	16 (14.2)	0.84
- Arrhythmias	16 (8.3)	6 (5.3)	0.33
- Sepsis	9 (4.7)	8 (7.1)	0.37
- Myocardial ischemia/infarction	2 (1.0)	3 (2.7)	0.36
- Cerebrovascular diseases	1 (0.5)	1 (0.9)	>0.99
Length of stay in SICU (day)	4.0 (3.0, 8.0)	4.0 (3.0, 7.0)	0.64
Length of stay in hospital (day)	20.0 (12.0, 34.5)	18.0 (11.0, 30.5)	0.20
SICU mortality	10 (5.2)	11 (9.7)	0.13
Hospital mortality	29 (15.0)	18 (15.9)	0.83
90-day mortality	33 (17.1)	26 (23.0)	0.21

Data are presented as median (interquartile range) or N (%) as appropriate.
ARDS, acute respiratory distress syndrome; LPV, lung protective mechanical ventilation; MV, mechanical ventilation; SICU, surgical intensive care unit.

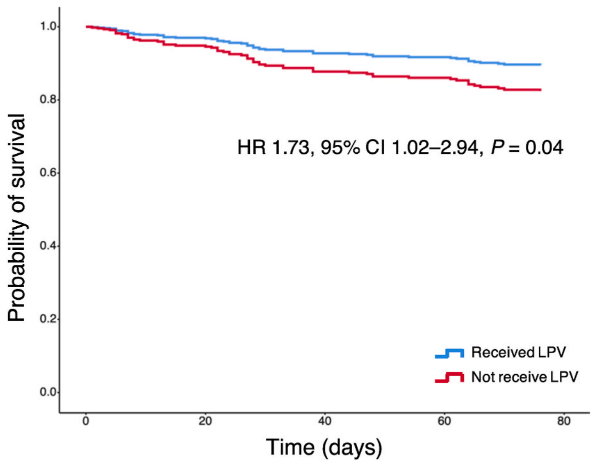

Fig. 2. Cox regression analysis for 90-day mortality and the application of the lung protective ventilation strategy adjusting for age, gender, Charlson Comorbidity index, Acute Physiology and Chronic Health Evaluation II score, Sequential Organ Failure Assessment score, intraabdominal or vascular sites of surgery, and reasons for SICU admission other than after elective surgery.

ventilation significantly reduced hospital and 28-day mortality [3]. Nevertheless, the data from patients without ARDS are controversial. One meta-analysis showed an association between the LPV strategy with low tidal volume ventilation and a decrease in mortality [4], but others did not [5,6]. In addition, the intraoperative LPV strategy had no apparent effect on mortality in patients undergoing surgery under general anesthesia [8,9]. Our findings may indicate a causative effect of LPV strategy on mortality. Alternatively, it may be a marker of severity in mechanically ventilated patients.

The work of breathing increased inversely to the amount of tidal volume delivered; for example, the lower the tidal volume delivered, the higher the work of breathing [29]. Moreover, ventilator dyssynchrony occurred more often when patients were ventilated with a lower tidal volume [30]. Both increased work of breathing and subsequent ventilator dyssynchrony associated with lower tidal ventilation could potentially lead to prolonged duration of MV, prolonged hospitalization, and possibly increased mortality [31]. Unfortunately, we did not record patient-ventilator dyssynchrony in our study. Therefore, we cannot draw any conclusions regarding this hypothesis. On the other hand, applying the LPV strategy might simply be a marker of severity in mechanically ventilated patients. Several studies found that patients adhered more to the LPV strategy if they had a higher acuity [12,17,19] or a higher degree of lung injury [15,16,19]. This might contribute to the higher mortality, rather than the application of the LPV strategy per se. Nevertheless, we did not observe such an association in the present study. Another postulated explanation is the association between gender and mortality in critically ill patients. Recent studies demonstrated that critically ill male patients had higher mortality rates than females [32,33]. In this study, a higher proportion of male patients adhered to the LPV strategy. The higher mortality observed in this study was probably associated with gender difference rather than the LPV strategy per se.

The strength of our study was that it focused on the surgical patient population requiring MV support in the ICU, whereas most other studies were conducted in the medical patient population [16] or combined medical, surgical, and trauma patient populations [11–14,17,18]. Therefore, our results provide more insight into this patient population, in which the clinical course, such as acuity of illness or MV management, is generally different from other populations. Moreover, our study is likely the only to report an association between the application of the LPV strategy in mechanically ventilated patients without ARDS and increased mortality. A question may arise regarding the benefits to these patients. Interestingly, a recent large randomized controlled trial in mechanically ventilated patients without ARDS demonstrated that there were no differences in terms of ventilator-free days and mortality when comparing ventilating patients with a low tidal volume (e.g., 6 ml/kg of PBW) and an intermediate tidal volume (e.g., 10 ml/kg of PBW) [34]. Nevertheless, as this was an observational study, we could not prove the causation between LPV strategy and increased mortality.

Our study had some limitations. First, as a single-center study in the SICU of a tertiary university-based hospital, the data may not be generalized to other settings with different organizational structures, such as the number of hospital beds or nurse-to-patient ratio, which may show different adherence rates to the LPV strategy and outcomes [13]. Second, as an observational study, it might not permit the acquisition of information regarding why physicians did or did not apply the LPV strategy to their mechanically ventilated patients. In a survey study of critical care nurses and respiratory therapists, the authors found that the perception of the LPV strategy being contraindicated in their patients was an important barrier to apply LPV strategy in patients on MV support [35]. Providing knowledge and education in this circumstance would help physicians to apply the LPV strategy more confidently [12]. Third, data regarding respiratory mechanics, such as compliance, plateau pressure, and driving pressure, as well as patient-ventilator dyssynchrony were not collected in this study. These parameters are important in determining the clinical outcomes of patients [1,2]. In the recent large randomized controlled trial in mechanically ventilated patients without ARDS comparing ventilation with a tidal volume of 10 ml/kg of PBW to 6 ml/kg of PBW, there was no difference in clinical outcomes in terms of ventilator-free day or mortality if plateau pressure or maximal airway pressure did not exceed 25 cm H_2O [34]. Forth, data regarding the hospital course including before SICU admission and after SICU discharge were not taken into consideration. These could be potential confounding factors for the patient outcomes. Lastly, as the study aimed to investigate the adherence to LPV in all mechanically ventilated patients in SICU, not specific to any population. Therefore, our study included very small proportion of obesity patients (11.4%) or ARDS patients (2.0%). We had very limited data regarding ventilator management and our finding might not represent the clinical practice and outcomes in these groups of patients.

5. Conclusions

The adherence rate to the LPV strategy in mechanically ventilated patients admitted to the SICU was 36.9%, which was comparable to that reported in the literature. Height was the only independent factor associated with adherence to LPV strategy. We demonstrated that the application of the LPV strategy was associated with an increased 90-day mortality. Unfortunately, we could not conclude whether the application of the LPV strategy was the truly causative factor for the increased mortality in these patients or whether it was a marker of disease severity in mechanically ventilated patients. Further studies are required to address this question. Until then, we still recommend applying the LPV to all mechanically ventilated patients. In addition, closed monitoring of respiratory mechanics as well as ventilator synchrony and respiratory drive to avoid excess stress and strain and subsequent VILI as well as patient-self inflicted lung injury are mandatory in patients receiving MV support.

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Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Annop Piriyapatsom: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ajana Trisukhonth:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Ornin Chintabanyat:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Onuma Chaiwat:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Suneerat Kongsayreepong:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Chayanan Thanakiattiwibun:** Writing – review & editing, Visualization, Investigation, Formal analysis, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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