Original Article

Factors associated with mortality in acute respiratory failure patients without acute respiratory distress syndrome

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Background: Excess tidal volume and driving pressure were associated with increased mortality in patients with acute respiratory distress syndrome (ARDS). Still, the appropriate mechanical ventilation strategy for patients who do not have ARDS needs to be understood. This study aimed to identify risk factors for mortality in acute respiratory failure patients without ARDS.

Methods: We included all mechanically ventilated patients who did not meet the criteria for ARDS and were admitted to the medical intensive care unit (ICU) from October 2017 to September 2018. Patients who had tracheostomy before admission, were intubated for more than 24 hours before transfer to ICU, or underwent extracorporeal membrane oxygenation within 24 hours of ICU admission were excluded. Clinical and physiologic data were recorded and compared between survived and non-survived patients.

Results: Of 289 patients with acute respiratory failure, 134 patients without ARDS were included; 69 (51%) died within 28 days. Demographics, principal diagnosis, and lung injury score on the first day of admission were not significantly different between survived and non-survived patients. In multivariate analysis, higher peak inspiratory pressure (PIP) during the first 3 days of admission [odds ratio (OR) 1.11, 95% confidence interval (CI): 1.01–1.22, P=0.04], higher sequential organ failure assessment score (OR 1.15, 95% CI: 1.04–1.28, P=0.008) and underlying cerebrovascular diseases (OR 7.09, 95% CI: 1.78–28.28, P=0.006) were independently associated with mortality in these patients, whereas dynamic lung compliance (C_{dyn}) and respiratory rate were not associated with mortality in the multivariate model.

Conclusions: Mortality was high in mechanically ventilated patients without ARDS. Higher PIP is a potentially modifiable risk factor for mortality in these patients, independent of the baseline C_{dyn}. Underlying cerebrovascular diseases and increased disease severity are also independent factors associated with 28-day mortality.

Keywords: Peak inspiratory pressure (PIP); acute respiratory failure; mechanical ventilation (MV); risk factor; mortality

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Introduction

Mechanical ventilation (MV) is an indispensable treatment for acute respiratory failure patients, although its pulmonary and hemodynamic complications are well-known (1). Standard recommendations for MV strategy are available for patients with acute respiratory distress syndrome (ARDS) (2). Lung-protective ventilation strategies using low tidal volume, 4–8 mL/kg predicted body weight (PBW), and limited plateau pressure have reduced mortality among ARDS patients (2,3). For those with moderate to severe ARDS, prone positioning, referring patients who meet the criteria for extracorporeal membrane oxygenation (ECMO) to ECMO centers, and avoiding high-pressure recruitment maneuvers are recommended to reduce mortality (2-5). Recent studies also revealed associations between high driving pressure and mechanical power and increased mortality in ARDS patients (6-8). However, only 6–8% of patients requiring MV had ARDS at the start of MV, and ARDS accounts for only 23% of mechanically ventilated patients in the intensive care unit (ICU) (2,9). Most patients receiving invasive MV do not have ARDS; therefore, data on appropriate ventilation strategies in these patients are essential. This cohort study aimed to determine factors associated with increased mortality among acute respiratory failure patients without ARDS. We focused on the MV parameters that can be adjusted to improve patient outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-58/rc).

Highlight box

Key findings

- Higher peak inspiratory pressure (PIP) during the first 3 days of admission is associated with 28-day mortality in acute respiratory failure patients without acute respiratory distress syndrome (ARDS) independent of baseline dynamic lung compliance. Higher baseline sequential organ failure assessment scores and underlying cerebrovascular diseases are also independent factors associated with increased mortality in these patients.

What is known and what is new?

- Only 6–8% of mechanically ventilated patients had ARDS at the start of mechanical ventilation (MV), but data on appropriate ventilation strategies in these patients is limited.
- This study provided information on factors associated with increased mortality among acute respiratory failure patients without ARDS. We focused on the MV parameters that can be adjusted to improve patient outcomes.

What is the implication, and what should change now?

- In acute respiratory failure patients without ARDS, carefully ventilating with the lowest possible PIP to achieve an acceptable gas exchange and patient-ventilator synchrony might be a suitable MV strategy to improve patient outcomes. Further randomized controlled studies should be performed to confirm this hypothesis.

Methods

Study population

We prospectively collected the data of all consecutive patients aged ≥18 years who did not meet the diagnostic criteria for ARDS according to the Berlin definition (10) and were admitted to the medical ICU and received MV at Siriraj Hospital, Bangkok, Thailand, from October 2017 to September 2018. Patients intubated more than 24 hours before transfer to the ICU or those who had tracheostomy before admission were excluded.

This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Human Research Protection Unit of the Faculty of Medicine Siriraj Hospital, Mahidol University (Certificate of Approval No. Si 546/2017). Written informed consent was obtained from all patients or their legal guardians if the participants could not provide the consent.

Data collection

The collected data included patient demographics, principal diagnosis of acute respiratory failure, comorbid diseases including diabetes mellitus, hypertension, chronic obstructive pulmonary diseases and chronic lung diseases, asthma, chronic kidney disease, cirrhosis, malignancy, coronary artery disease, cerebrovascular disease, immunosuppression, and smoking, sequential organ failure assessment (SOFA) score (11), baseline dynamic lung compliance (C_{dyn}) and lung injury score (LIS) (12), arterial blood gas and initial MV parameters at ICU admission, arterial blood gas and the ratio of partial pressure of oxygen in arterial blood to the fraction of inspiratory oxygen concentration (PaO_2/FiO_2) during invasive MV on the first day of ICU admission, ICU treatments during the first 3 days of ICU admission including MV parameters, renal replacement therapy and the use of fentanyl, midazolam, propofol, and neuromuscular blocking agent. The collected MV parameters during the first three days of ICU admission included ventilator mode, tidal volume (TV) in mL/kg PBW, peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), dynamic driving pressure (ΔP)

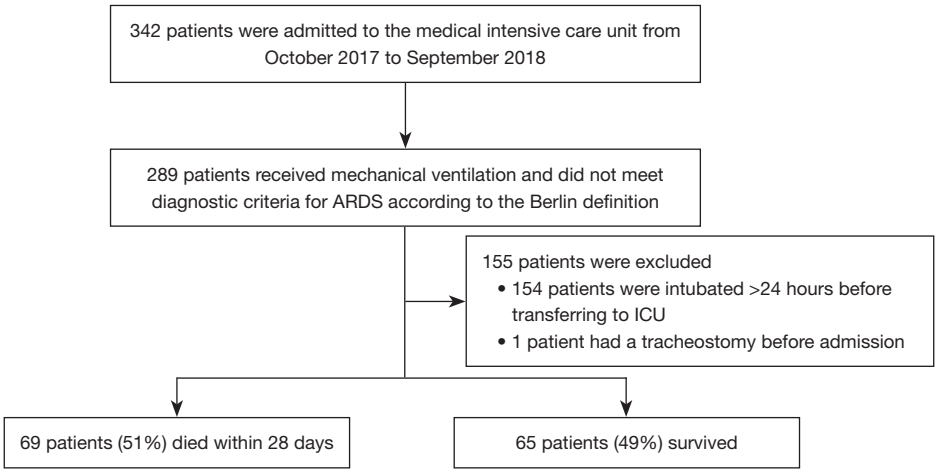

Figure 1 Patient population. ARDS, acute respiratory distress syndrome; ICU, intensive care unit.

defined as inspiratory pressure set in pressure-controlled ventilation mode or the difference between PIP and PEEP in volume-controlled ventilation mode, the set and actual respiratory rates, minute ventilation, and fraction of inspired oxygen (FiO_2). Dynamic respiratory system compliance (C_{dyn}) is a ratio of tidal volume and the difference between PIP and PEEP. We recorded the parameters for the most prolonged duration of each day for all MV variables. We averaged variables during the first three days of ICU admission to represent ventilator strategies provided to the patients.

Outcomes

The primary outcome was all-cause 28-day mortality. Secondary outcomes were respiratory complications, including arterial pH, PaO_2/FiO_2, $PaCO_2$, and HCO_3, and C_{dyn} on day 3 of ICU admission, LIS on day 7, worsening lung injury defined as an increase in LIS of ≥0.25 points from baseline LIS at day 7 of ICU admission, newly developed pneumothorax, ventilator-associated pneumonia or ARDS, and use of rescue therapy for refractory hypoxemia, including prone positioning, recruitment maneuvers, or ECMO.

Statistical analysis

To identify factors associated with increased mortality in acute respiratory failure patients without ARDS, we compared data between survived and deceased patients at 28 days of admission. Continuous data were presented as mean ± standard deviation, median [interquartile range (IQR)] as appropriate, while categorical data were described as counts and column percentages. Univariate two-group comparisons were performed using independent two-group *t*-tests for normally distributed continuous variables, Mann-Whitney *U* tests for non-normally distributed continuous variables, and Chi-square or Fisher exact tests for categorical variables. Multivariable logistic regression modeling was performed to identify independent risk factors for 28-day mortality, and adjusted odds ratios (ORs) with 95% confidence intervals (CI) were reported. We planned to include all baseline characteristics and treatment variables reaching statistical significance in univariate analysis in the multivariable model. Statistical significance is set at $P<0.05$. All analyses were performed with SPSS version 18 (13).

Results

Study population

From October 2017 to September 2018, 342 patients were admitted to the medical ICU at Siriraj Hospital; 289 patients required MV and did not meet the diagnostic criteria for ARDS according to the Berlin definition. One hundred fifty-five patients were excluded, 154 patients were intubated ≥24 hours before transferring to ICU, and one had a tracheostomy placed before admission. One hundred and thirty-four patients were included in the final analysis; 69 patients (51%) died within 28 days, and 65 (49%) survived (*Figure 1*).

Baseline characteristics

The median age of patients was 64 years, and 57% were

male. Septic shock (59%) is the most common principal diagnosis, followed by pneumonia (37%) and heart failure (5%), with no significant difference in the principal diagnosis between survived and dead patients (*Table 1*). Compared with patients who survived, patients who died were more likely to have underlying cerebrovascular diseases (20% *vs.* 5%, P=0.006) and had higher baseline SOFA scores [11 (IQR, 8–14) *vs.* 8 (IQR, 6–12), P<0.001]. Other patient demographics were not significantly different between the two groups (*Table 1*).

For the baseline respiratory variables, 115 patients (86%) received pressure-controlled ventilation, and 19 patients (14%) received volume-controlled ventilation at ICU admission with a median TV and PIP of 8.2 (IQR, 6.8–10) mL/kg PBW and 23 (IQR, 19–26) cmH_2O, respectively. Deceased patients had lower baseline C_{dyn} [26 (IQR, 20–32) *vs.* 30 (IQR, 23–40) mL/cmH_2O, P=0.02] and were ventilated with higher ΔP [18 (IQR, 14–20) *vs.* 16 (IQR, 14–20), P=0.03] compared with survived patients. Other respiratory variables, arterial blood gas results, and LIS on admission were not significantly different between alive and dead patients; the median PaO_2/FiO_2 ratio was 258 (IQR, 161–413). The MV settings and outputs and other respiratory variables on the first day of ICU admission are shown in *Table 1*.

Treatments during the first three days of ICU admission

Patients who died within 28 days were ventilated with higher average PIP [24 (IQR, 21–27) *vs.* 21 (IQR, 19–25), P=0.001], ΔP [17 (IQR, 15–21) *vs.* 15 (IQR, 13–18), P<0.001], and actual respiratory rate [22 (IQR, 19–25) *vs.* 19 (IQR, 17–23), P=0.008] during the first 3 days of ICU admission, compared with those who were alive. Other MV parameters during the first three days were not different between the two groups, with a median TV of 8.1 mL/kg PBW, PEEP 5 cmH_2O, and FiO_2 0.4. There were no significant differences in the administration of sedative and neuromuscular blocking drugs and receipt of renal replacement therapy in both groups (*Table 2*).

Respiratory parameters and complications

Compared with survived patients, deceased patients had higher LIS [1.5 (IQR, 1–2.25) *vs.* 0.67 (IQR, 0–1.25), P<0.001] and were more likely to have worsening LIS (43% *vs.* 17%, P=0.009) on day 7. There were no significant differences in the incidence of pneumothorax, ventilator-associated pneumonia, new-onset ARDS, and rescue therapy for refractory hypoxemia (*Table 3*).

Factors associated with hospital mortality in multivariable analysis

In multivariable analysis, underlying cerebrovascular diseases (OR 7.09, 95% CI: 1.78–28.28, P=0.006), higher SOFA score (OR 1.15, 95% CI: 1.04–1.28, P=0.008), and higher average PIP used during the first three days of admission (OR 1.11, 95% CI: 1.01–1.22, P=0.04) were factors independently associated with hospital mortality in acute respiratory failure patients without ARDS (*Table 4*), whereas baseline C_{dyn} (OR 1.01, 95% CI: 0.98–1.03, P=0.56) and actual respiratory rate (OR 0.98, 95% CI: 0.88–1.08, P=0.67) were not associated with mortality in the multivariable model.

Discussion

This study demonstrated high mortality (51%) among acute respiratory failure patients without ARDS, especially in patients who had severe organ dysfunction [median SOFA score was 10 (IQR, 7–13)]. The majority of patients in our cohort had mild hypoxemia on day 1 because most of them were intubated due to septic shock from extrapulmonary infections, and only 37% had pneumonia. There were differences in some parameters in baseline characteristics, treatment, respiratory variables, and complications between the surviving group and the deceased group. However, the multivariable analysis disclosed only higher PIP during the first three days of ICU admission, the presence of cerebrovascular disease, and the higher SOFA score at admission were associated with 28-day mortality.

The mortality of non-ARDS patients in our study was 51%, which was higher than that reported in the other non-ARDS cohorts (21–35%) (14-18). This could be explained by the finding that more organ dysfunction was found in our study. As noted in *Table 1*, the median SOFA score for overall patients was 10 (IQR, 7–13), 8 (IQR, 6–12) for alive, and 11 (IQR, 8–14) for dead patients, while median total SOFA score for patients in the prior non-ARDS cohorts was 6 (IQR, 4–9) (14,15). Moreover, multivariate analysis showed an association between higher admission SOFA scores and 28-day mortality. The predicted mortality rate by SOFA score was correlated with the mortality rate of non-ARDS patients in our population and the previous studies (14,15); the SOFA score of 10 was related to an approximate

Table 1 Baseline characteristics

Baseline characteristics	Survived (N=65)	Deceased (N=69)	P value
Age, years	63 [45–74]	70 [56–78]	0.07
Male	37 [57]	39 [57]	0.96
Principal diagnosis			
Septic shock	39 [60]	40 [58]	0.81
Pneumonia	27 [42]	22 [32]	0.25
Congestive heart failure	4 [6]	3 [4]	0.71
Other diagnosis[a]	12 [18]	20 [29]	0.15
Comorbid diseases			
Diabetes mellitus	28 [43]	32 [46]	0.70
Hypertension	32 [49]	43 [62]	0.13
Chronic lung diseases	7 [11]	3 [4]	0.20
Asthma	1 [2]	4 [6]	0.37
Chronic kidney disease	20 [31]	26 [38]	0.40
Cirrhosis	3 [5]	5 [7]	0.72
Malignancy	10 [15]	17 [25]	0.18
Coronary artery disease	10 [15]	16 [23]	0.25
Cerebrovascular diseases	3 [5]	14 [20]	0.006
Immunosuppression	16 [25]	9 [13]	0.09
Smoking	1 [2]	1 [1]	>0.99
SOFA score at ICU admission	8 [6–12]	11 [8–14]	<0.001
LIS[b] at ICU admission	1.5 [0.9–2.3]	1.25 [1–1.9]	0.98
Arterial blood gas at ICU admission			
pH	7.36±0.10	7.34±0.13	0.25
PaO_2/FiO_2 ratio	242 [147–416]	280 [187–416]	0.32
$PaCO_2$, mmHg	30 [25–35]	28 [22–37]	0.43
HCO_3, mEq/L	18 [13–22]	16 [12–20]	0.15
Respiratory variables at ICU admission			
Mode of mechanical ventilation			0.92
Pressure controlled ventilation	56 [86]	59 [86]	
Volume controlled ventilation	9 [14]	10 [14]	
Tidal volume, mL/kg predicted body weight	8.5 [6.7–10.1]	8.1 [7.0–9.9]	0.81
Peak inspiratory pressure, cmH_2O	21 [19–25]	23 [19–27]	0.11
Dynamic driving pressure (ΔP)[c], cmH_2O	16 [14–20]	18 [14–20]	0.03
Positive end-expiratory pressure, cmH_2O	5 [5–7]	5 [5–6]	0.99
Respiratory rate set, breath/min	18 [16–24]	20 [16–24]	0.33

Table 1 (*continued*)

Table 1 (*continued*)

Baseline characteristics	Survived (N=65)	Deceased (N=69)	P value
Actual respiratory rate, breath/min	20 [18–25]	24 [20–26]	0.12
Minute ventilation, L/min	10.1 [7.2–13.6]	9.6 [8.2–12.6]	0.99
FiO_2	0.4 [0.4–0.6]	0.4 [0.4–0.6]	0.65
Dynamic respiratory system compliance (C_{dyn}), mL/cmH_2O	30 [23–40]	26 [20–32]	0.02

Data are n [%], mean ± standard deviation, or median [interquartile range]. [a], other diagnoses included diabetic ketoacidosis, acute liver failure, postcardiac arrest, hemorrhagic shock, cardiogenic shock, dengue shock syndrome, massive hemoptysis, acute pulmonary embolism, neurological diseases including hypertensive encephalopathy, intracerebral hemorrhage, cryptococcal meningitis, status epilepticus and myasthenia gravis, solid and hematologic malignancies, ethanol intoxication, and systemic lupus erythematosus. [b], LIS consists of four components: pulmonary infiltration on chest radiograph, degree of hypoxemia assessed by PaO_2/FiO_2, positive end-expiratory pressure level, and respiratory system compliance. The LIS scores range from 0–4; the higher scores indicate more severe lung injury. [c], dynamic driving pressure (ΔP) = inspiratory pressure in pressure-controlled ventilation mode, or the difference between peak inspiratory pressure and positive end-expiratory pressure in volume-controlled ventilation mode. ICU, intensive care unit; SOFA, sequential organ failure assessment; LIS, lung injury score; PaO_2/FiO_2 ratio, the ratio of partial pressure of oxygen in arterial blood to the fraction of inspiratory oxygen concentration; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; HCO_3, bicarbonate.

Table 2 Treatments during the first 3 days of intensive care unit admission

Treatments	Survived (N=65)	Deceased (N=69)	P value
Average respiratory variables between days 1–3			
Tidal volume, mL/kg predicted body weight	8.1 [6.8–9.6]	8.1 [6.9–9.5]	0.89
Peak inspiratory pressure, cmH_2O	21 [19–25]	24 [21–27]	0.001
Dynamic driving pressure (ΔP)[a], cmH_2O	15 [13–18]	17 [15–21]	<0.001
Positive end-expiratory pressure, cmH_2O	5 [5–6]	5 [5–7]	0.14
Respiratory rate set, breath/min	18 [15–21]	19 [17–23]	0.09
Actual respiratory rate, breath/min	19 [17–23]	22 [19–25]	0.008
Minute ventilation, L/min	9.2 [7.6–11.6]	9.2 [8.2–12]	0.56
FiO_2	0.4 [0.4–0.5]	0.4 [0.4–0.6]	0.13
Sedation used[b]	45 [69]	44 [64]	0.50
Fentanyl	44 [68]	43 [62]	0.52
Midazolam	17 [26]	21 [30]	0.58
Propofol	0	1 [1]	>0.99
Neuromuscular blocking agents used[c]	9 [14]	14 [20]	0.32
Renal replacement therapy	26 [40]	36 [52]	0.16

Data are n [%] or median [interquartile range]. [a], dynamic driving pressure (ΔP) = inspiratory pressure in pressure-controlled ventilation mode, or the difference between peak inspiratory pressure and positive end-expiratory pressure in volume-controlled ventilation mode. [b], sedation use is defined as fentanyl, midazolam, or propofol administered at any time during the first three days of intensive care unit admission. [c], neuromuscular blocking agent use is defined as cisatracurium used at any time during the first 3 days of intensive care unit admission. FiO_2, fraction of inspiratory oxygen concentration.

50% mortality rate in critically ill patients, while the SOFA score of 6 predicted a 20–30% mortality rate (11); The other two non-ARDS cohorts did not report SOFA scores; one used acute physiology scores (17), and one used SAPS scores (18), which did not directly reflect the severity of organ dysfunction. Since most patients in this study had

Table 3 Respiratory complications

Variables	Survived (N=65)	Deceased (N=69)	P value
LIS on day 7[a]	0.67 (0–1.25)	1.5 (1–2.25)	<0.001
Worsening lung injury on day 7[b] (≥+0.25)	11 [17]	16 [43]	0.009
Pneumothorax	1 [2]	3 [4]	0.62
Ventilator-associated pneumonia	22 [34]	27 [39]	0.53
New-onset acute respiratory distress syndrome	9 [14]	14 [20]	0.34
Rescue therapy for refractory hypoxemia[c]	8 [12]	14 [20]	0.21

Data are n [%] or median (interquartile range). [a], data on LIS on day 7 are available in 96 patients, 59 survived and 37 deceased patients. [b], worsening lung injury on day 7 is defined as an increase in the LIS of ≥0.25 points from baseline LIS on day 7 of ICU admission. [c], rescue therapy for refractory hypoxemia included prone positioning, recruitment maneuvers, or extracorporeal membrane oxygenation. LIS, lung injury score; ICU, intensive care unit.

Table 4 Factors associated with 28-day mortality in multivariable analysis

Variables	OR (95% CI)	P value
Comorbid cerebrovascular diseases	7.09 (1.78–28.28)	0.006
SOFA score on admission	1.15 (1.04–1.28)	0.008
Average peak inspiratory pressure during the first three days	1.11 (1.01–1.22)	0.04
Baseline dynamic respiratory system compliance	1.01 (0.98–1.03)	0.56
Average actual respiratory rate during the first three days	0.98 (0.88–1.08)	0.67

OR, odds ratio; CI, confidence interval; SOFA, sequential organ failure assessment.

mild hypoxemia (*Table 1*), high SOFA scores should mainly result from non-respiratory organ dysfunctions. Achieving early definitive treatment for the primary disease and providing comprehensive organ support therapy is crucial, in addition to ventilator adjustment, for managing acute respiratory failure patients without ARDS.

Concerning MV strategy, we found that higher average PIP during the first 3 days of ICU admission was the only factor associated with increased mortality. Two prior cohort studies on non-ARDS patients reported similar results. In the PRoVENT trial, maximum airway pressure (P_{max}) was the only ventilatory variable independently associated with hospital mortality (14). Another study by Sahetya *et al.* demonstrated that plateau (P_{plat}) and driving pressure, the difference between P_{plat} and PEEP, were associated with higher mortality in these patients (15). On the contrary, some studies found no relationship between the plateau and driving pressure and mortality in non-ARDS patients, but in these studies, only a minority of patients (4–7%) were intubated due to pulmonary conditions (17,18). The discrepancy in patient characteristics may be attributable to different results, as 37% of patients in our cohort had pneumonia, and 28–50% of patients in the PRoVENT trial and Sahetya *et al.* were intubated for respiratory conditions (14,15).

The definition of PIP in our study differs from the P_{max} in the PRoVENT study and P_{plat} in Sahetya *et al.* The PIP in this study was the maximum airway pressure of both pressure-controlled and volume-controlled ventilation, not plateau pressure measured by end-inspiratory hold maneuver. Most patients (86%) in our cohort received pressure-controlled ventilation. The P_{max} in the PRoVENT study was defined as PIP in pressure-controlled ventilation and plateau pressure in volume-controlled ventilation (14). The definition of P_{plat} in the Sahetya *et al.* study was similar to that of P_{max} in the PRoVENT trial (14,15). We used the average values of respiratory variables over the first three days of ICU admission rather than a single data point to represent the actual ventilator parameters. The PIP in our study was attributed to the ΔP used to ventilate the patients because the PEEP levels were similar in both groups, so we omitted the ΔP in the multivariate analysis. We hypothesized that the baseline C_{dyn} might influence the PIP

level; thus, we included the baseline C_{dyn} in the multivariable model, and the result confirmed that ventilating with higher PIP increased the risk of 28-day mortality independent of the baseline C_{dyn} value. Notably, deceased patients were more likely to experience worsening lung injury on day 7. This may be due to ventilator-induced lung injury caused by high PIP levels. Thus, carefully ventilating patients with the lowest possible PIP to achieve an acceptable gas exchange and patient-ventilator synchrony might be an appropriate MV strategy to improve outcomes of patients without ARDS who require MV.

We found an association between a prior history of cerebrovascular diseases and 28-day mortality in non-ARDS patients requiring MV (*Table 4*). We hypothesized that patients with a previous history of cerebrovascular diseases may have poor functional status, which leads to limited therapeutic effort; the findings in the PRoVENT trial support this hypothesis. The partially dependent functional status of the patients before admission was independently associated with in-hospital mortality in the multivariate analysis of the PRoVENT study (14).

This study had some limitations. First, our study collected data from a tertiary care and academic hospital in Bangkok, Thailand. Due to a shortage of ICU beds, only the most severely ill patients in our hospital were transferred to the ICU. As a result, most of the patients in our study had severe organ dysfunction. This might limit the generalizability of our study results to other hospitals with different circumstances. Second, we obtained hourly MV parameters from the nurse records. Variations in respiratory parameters within each hour were not taken into account. Third, we could not obtain plateau pressure and static driving pressure, the difference between plateau pressure and PEEP, since they are not regularly monitored for non-ARDS patients in our unit. Nonetheless, we believe that PIP is a more practical measure, as it is constantly displayed on the ventilator screen and does not require any special maneuvers. Fourth, despite most patients in our cohort having septic shock as a principal diagnosis, the data on vasoactive drug use was not available in our record. However, the use of vasoactive drugs is a part of the SOFA scores used to assess the disease severity, and we also found an association between higher SOFA scores and 28-day mortality in the multivariate analysis results. Finally, only 13% of patients (n=17) in this study had a history of strokes before admission. And we did not have data on their baseline functional status. Hence, further research is required to confirm an association between prior history of cerebrovascular diseases and mortality in non-ARDS patients.

Conclusions

Mortality was high in acute respiratory failure patients without ARDS. Factors associated with 28-day mortality included higher average PIP during the first three days of ICU admission, higher baseline SOFA scores, and underlying cerebrovascular diseases. Thus, carefully ventilating with the lowest possible PIP to achieve an acceptable gas exchange and patient-ventilator synchrony might be a suitable MV strategy to improve the outcomes of these patients. Further randomized controlled studies should be performed to confirm this hypothesis.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-58/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Human Research Protection Unit of the Faculty of Medicine Siriraj Hospital, Mahidol University (certificate of approval No. Si 546/2017). Written informed consent was obtained from all patients or their legal guardians if the participants could not

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