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Brief communication (original) **Open access**

Clinical outcomes of acute respiratory distress syndrome in a university hospital

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Abstract

Background: Mortality rates of acute respiratory distress syndrome (ARDS) are different, depending on severity, etiology, and management.

Objective: To determine 7-day and 28-day mortalities, hospital length of stay (LOS), duration of mechanical ventilation (MV) of ARDS patients, and factors associated with poor outcomes.

Methods: A retrospective study was conducted to review the database of ARDS patients admitted in medical intensive care units (ICUs) at a university hospital between 2010 and 2014. The cases were identified by using International Classification of Diseases, 10th Revision (ICD-10) code-J80 ARDS.

Results: Of 266 patients, 11.7%, 44.4%, and 44% fulfilled mild, moderate, and severe ARDS criteria, respectively. The main cause of ARDS was pneumonia. The 7-day and 28-day mortalities, median LOS, and median MV duration were 31.1%, 69.3%, 18, and 11 days, respectively. Pressure control was the most favorite mode, used with average tidal volume (TV) of 8.63 (2.16) mL/kg ideal body weight (IBW). Recruitment maneuver was most frequently used as adjunctive intervention, whereas prone position was applied to 3.75% of the patients. One-third of the patients received neuromuscular blockades. The median 7-day fluid balance was +6,600 mL. The mean PaO_2/FiO_2 ratio during the first 3 days, cumulative fluid balance on day 3, and average daily calories during the first week were independent predictors for adjusted 7-day mortality, whereas Acute Physiology and Chronic Health Evaluation (APACHE II) score, fluid balance on day 1, cumulative fluid balance, and average daily calories during the first week were independent predictors for adjusted 28-day mortality.

Conclusions: The 28-day mortality of ARDS was high. In addition, TV and fluid balance were greater than protective limits. These findings indicated the potential improvement of ARDS outcomes in our hospital.

Keywords: acute respiratory distress syndrome; intensive care units; positive pressure respiration

Acute respiratory distress syndrome (ARDS) is characterized by severe hypoxemia and non-cardiogenic pulmonary edema. In 1967, Ashbaugh et al. [1] reported a case series of 12 critically ill patients with tachypnea and hypoxemia accompanied by decreased lung compliance and pulmonary infiltrates on chest X-rays from different etiologies. This was the first established ARDS. Thenceforth, there was no common definition of ARDS [2], resulting in various published prevalences in intensive care units (ICUs). Until 2012, Berlin definition of ARDS was created by a consensus panel of experts (an initiative of the European Society of Intensive Care Medicine endorsed by the American Thoracic Society and the Society of Critical Care Medicine) to simplify the diagnosis and prognosticate outcomes [3]. ARDS was defined as a clinical entity, which consisted of an acute onset (less than 1 week), bilateral opacities on computed tomography or chest radiograph, a ratio

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of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2/FiO_2 ratio) ≤300 mmHg with a minimum of 5 cm H_2O positive end-expiratory pressure (PEEP), and no cardiac failure or fluid overload.

ARDS is associated with high mortality. For over 20 years, many therapeutic strategies have been provided to improve patients' outcomes. In 2000, the ARDS network established an important study "Ventilation with lower tidal volumes as compared with traditional tidal volumes for ALI and ARDS." The study demonstrated that the use of low tidal volume (TV; 6 mL/kg predicted weight) significantly reduced mortality from 40% to 30% and increased ventilator-free days, compared with traditional TV (12 mL/kg predicted weight) [4]. In 2010, the ACURASYS study investigators reported that the use of neuromuscular blockade (cisatracurium) in patients with early ARDS with PaO_2/FiO_2 ratio <150 for 48 h significantly reduced both 28-day and 90-day mortalities and increased ventilator-free days without increased incidence of ICU-acquired weakness [5]. In addition, PROSEVA study showed that prone position with lung-protective strategy reduced 28-day and 90-day mortalities and this strategy should be considered in patients with early ARDS and severe hypoxemia who have the PaO_2/FiO_2 ratio of <150 despite FiO_2 of ≥0.6 and PEEP of ≥5 cm H_2O [6].

On the contrary, some strategies did not improve survival and might be harmful to ARDS patients. There were 2 landmark studies of high-frequency oscillation ventilation (HFOV), including OSCAR and OSCILATE trials [7, 8]. The former study showed that HFOV did not reduce mortality and increased the need of sedatives and muscle relaxants. The latter study showed that HFOV increased hospital mortality (47% in the HFOV group vs 35% in the low TV with the high PEEP group) and the need of sedatives, muscle relaxants, and vasopressors. Furthermore, a recent study showed that lung recruitment with PEEP set by respiratory system compliance significantly increased 28-day and 6-month mortalities with higher incidences of barotrauma and hypotension in moderate to severe ARDS patients [9].

Besides the ventilator management, several trials demonstrated benefits of conservative fluid management in patients with ARDS [10–13]. The Fluid and Catheter Treatment Trial (FACTT) demonstrated that a conservative fluid management strategy improved oxygenation, shortened duration of mechanical ventilation (MV), and ICU stay without a risk of nonpulmonary organ failure in ARDS patients [10]. However, it did not show a mortality benefit and potentially increased a risk of long-term cognitive impairment [14].

Epidemiological studies of the practice and outcomes of ARDS were mostly conducted in high-income countries, and the data in low- to middle-income countries were still limited. Moreover, some studies such as LUNG SAFE study were not focused on ARDS patients [15]. We hypothesized that routine clinical practice and outcomes of ARDS in our hospital might be different from the previous reported data from developed countries due to limited ICU resource and shortage of health care personnel. This study aimed to evaluate the clinical outcomes of ARDS patients, associated factors predicting outcomes, and current physicians' practice in our medical ICUs.

Materials and methods

Study design

We conducted a retrospective cross-sectional study of clinical outcomes of ARDS patients and physicians' practice in the medical ICUs at tertiary referral university teaching hospital. We included all ARDS patients admitted in the medical ICUs from September 2010 to September 2014. The patients were identified using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code: J80 (ARDS) and Diagnosis and Procedure Codes (ICD-9-CM) codes: 997x, 96.7. The data were collected from inpatient medical records. Only patients with fulfilled ARDS criteria (Berlin definition) were reviewed and analyzed. This study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University, for authorization for medical record review (approval certificate no. 457/59). The clinical trial registration number is TCTR20180212002.

Eligibility criteria

ARDS patients admitted in medical ICUs at tertiary referral university teaching hospital with 14 beds in ICU between September 2010 and September 2014, using the raw data that made up the various components of the Berlin ARDS definition [3].

Statistical analyses

Acute Physiology and Chronic Health Evaluation (APACHE II) was determined at the onset of ARDS. Other recorded variables included age, sex, etiology, blood gas analysis, ventilator management, and clinical outcomes of ARDS. The primary outcome was 28-day mortality. The secondary outcomes

were 7-day mortality, and other clinical outcomes were hospital length of stay (LOS) and duration of MV, and ventilator management.

SPSS (versions 22) was used to analyze the data, using odds ratio (OR), *P*-value, and 95% confidence intervals (CIs). Univariate and multivariate analyses (using variables with $P < 0.2$ in univariate analysis) for 7- and 28-day mortalities were performed using a binary logistic regression model.

Results

Between 2010 and 2014, 266 of 4,090 (6.5%) patients admitted in our medical ICUs met the Berlin criteria for ARDS diagnosis. Approximately 11.7%, 44.4%, and 44.0% of the patients fulfilled mild, moderate, and severe ARDS criteria, respectively. The severity of ARDS correlated with APACHE II score ($r^2 = 0.235$, $P < 0.001$). Demographic data of the patients are summarized in **Table 1**.

The majority of the ARDS patients had pneumonia and were assisted with pressure-controlled ventilation with the mean peak inspiratory pressure (PIP) and PEEP on the first day of MV of 31 ± 6 and 10 ± 4 cm H_2O, respectively. The plateau pressure (Pplat) was recorded in only 4.1% of the patients. The mean TV on the first day was 8.56 ± 2.48 mL/kg ideal body weight (IBW), and the average TV during the first 3 days of MV was 8.81 ± 2.39 mL/kg IBW. Approximately 55.4% of the patients had TV on the first day of MV of >8 mL/kg IBW and 60.9% of the patients had average TV during the first 3 days of MV of >8 mL/kg IBW.

Table 1. Characteristics of enrolled patients

	Overall	Mild ARDS	Moderate ARDS	Severe ARDS
N (%)	266 (100.0%)	31 (11.7%)	118 (44.4%)	117 (44.0%)
Age (years), mean ± SD	54.81 ± 18.66	48.84 ± 21.40	53.67 ± 18.64	57.54 ± 17.56
Gender, n (%)				
Male	153 (57.5%)	16 (51.6%)	66 (55.9%)	71 (60.7%)
Female	113 (42.5%)	15 (48.4%)	52 (44.1%)	46 (39.3%)
BMI (kg/m^2), mean ± SD	22.21 ± 4.44	21.91 ± 3.59	21.96 ± 3.97	22.56 ± 5.11
Etiology of ARDS (%)				
Pneumonia	217 (81.6%)	26 (83.9%)	100 (84.7%)	91 (77.8%)
Sepsis	25 (9.4%)	4 (12.9%)	6 (5.1%)	15 (12.8%)
HLH	3 (1.1%)	0 (0%)	2 (1.7%)	1 (0.9%)
Pneumonitis	10 (3.8%)	1 (3.2%)	4 (3.4%)	5 (4.3%)
Multiple factors	6 (2.3%)	0 (0%)	5 (4.2%)	1 (0.9%)
Unspecified cause	2 (0.8%)	0 (0%)	1 (0.8%)	1 (0.9%)
Diffuse alveolar hemorrhage	3 (1.1%)	0 (0%)	0 (0%)	3 (1.1%)
APACHE II median (25%, 75% quartile)	26 (22, 31)	23.16 (19, 27)	25.09 (21, 29)	27.69 (23, 32)
PaO_2/FiO_2, day 1, mean ± SD	122.40 ± 58.64	237.88 ± 53.81	138.96 ± 28.08	75.29 ± 18.04
Initial mode (%)				
PCV	233 (87.6%)	22 (71%)	105 (89%)	106 (90.6%)
VCV	5 (1.9%)	1 (3.2%)	2 (1.7%)	2 (1.7%)
PSV	14 (5.3%)	4 (12.9%)	5 (4.2%)	5 (4.3%)
SIMV	2 (0.8%)	1 (3.2%)	1 (0.8%)	0 (0%)
NIV	7 (2.6%)	2 (6.5%)	1 (0.8%)	4 (3.4%)
Bird mark 7	4 (1.5%)	0 (0%)	4 (3.4%)	0 (0%)
Nasal high flow	1 (0.4%)	1 (3.2%)	0 (0%)	0 (0%)
Adjunctive interventions (%)				
APRV	15 (5.6%)	1 (3.2%)	4 (3.4%)	10 (8.5%)
HFOV	4 (1.5%)	0 (0%)	3 (2.5%)	1 (0.9%)

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Table 1. Continued

	Overall	Mild ARDS	Moderate ARDS	Severe ARDS
Prone	10 (3.8%)	0 (0%)	5 (4.2%)	5 (4.3%)
Recruitment maneuver	128 (48.1%)	10 (32.3%)	58 (49.1%)	60 (51.3%)
PIP in PCV, day 1, mean ± SD (cm H_2O)	31 ± 6	27 ± 5	31 ± 6	32 ± 6
TV/kg IBW day 1, mean ± SD (mL/kg IBW)	8.56 ± 2.48	8.71 ± 2.22	8.45 ± 2.56	8.64 ± 2.47
PEEP, day 1, mean ± SD (cm H_2O)	10 ± 4	7 ± 3	10 ± 4	12 ± 5
Neuromuscular blockade use (%)	94 (35.3%)	7 (22.6%)	46 (39%)	41 (35%)
Sedative drugs (%)	229 (86.1%)	25 (80.6%)	102 (86.4%)	102 (87.2%)
Morphine	30 (11.3%)	1 (3.2%)	11 (9.3%)	18 (15.4%)
Fentanyl	194 (72.9%)	22 (71.0%)	86 (72.9%)	86 (73.5%)
Midazolam	197 (74.0%)	20 (64.5%)	87 (73.7%)	90 (76.9%)
Propofol	45 (16.9%)	7 (22.3%)	19 (16.1%)	19 (16.2%)
I/O balance, day 1, mean ± SD (mL/day)	2,484.94 ± 2,406.92	2,221.45 ± 2,202.28	2,161.26 ± 2,145.60	2,881.19 ± 2,694.55
Total I/O balance in 3 days, mean ± SD (mL/day)	5,029.31 ± 4,550	3,760 ± 3,370	4,370 ± 4,306	6,037 ± 4,892
Total I/O balance in 7 days, mean ± SD (mL/day)	6,634.97 ± 6,718.06	4,615.92 ± 6,327.18	5,771.69 ± 6,947.38	8,052.71 ± 6,337.84
Enteral calories (kcal/day), AVG in 7 days, mean ± SD	673.75 ± 546.29	651.57 ± 590.71	724.63 ± 533.06	628.30 ± 547.78
Ventilator day (days), mean ± SD	16.46 ± 20.11	24.77 ± 30.88	16.61 ± 17.38	14.11 ± 20.11
Hospital LOS (days), mean ± SD	27.1 ± 26.47	34.26 ± 33.60	29.63 ± 25.01	22.65 ± 25.26
7-day mortality, n (%)	83 (31.1)	4 (12.9)	30 (25.4)	49 (41.9)
28-day mortality, n (%)	184 (69.2)	16 (51.6)	82 (69.5)	86 (73.5)

APACHE II, Acute Physiology and Chronic Health Evaluation; APRV, airway pressure release ventilation; ARDS, acute respiratory distress syndrome; AVG, average; BMI, body mass index; HFOV, high-frequency oscillation ventilation; HLH, hemophagocytic lymphohistiocytosis; IBW, ideal body weight; I/O, intake/output; LOS, length of stay; NIV, noninvasive ventilation; PaO_2/FiO_2, the ratio of partial pressure arterial oxygen and fraction of inspired oxygen; PCV, pressure-controlled ventilation; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; PSV, pressure support ventilation; SIMV, simultaneous invasive mechanical ventilation; VCV, volume-controlled ventilation; TV, tidal volume

Neuromuscular blockades and sedative drugs were prescribed to 35.3% and 86.09% of the patients, respectively. Adjunctive interventions including prone position, recruitment maneuver, and rescued modes such as airway pressure release ventilation (APRV) and HFOV were applied to patients with moderate and severe ARDS (**Table 1**). Noticeably, recruitment maneuver was performed in a half of the patients, especially in the patients with moderate to severe ARDS. However, the incidence of pneumothorax was not different between the patients who received recruitment maneuver (79.7%) and who did not receive recruitment maneuver (82%).

Overall, the crude 7-day mortality was 31.1%, associated with age, ARDS severity, APACHE II score, PaO_2/FiO_2 ratio on day 1, mean PaO_2/FiO_2 ratio during the first 3 days, fluid balance on day 1 and cumulative fluid balance during the first 3 and 7 days, and average daily calories during the first week (**Table 2**). The crude 28-day mortality was 68.9%, associated with age, ARDS severity, APACHE II score, PaO_2/FiO_2 ratio on day 1, mean PaO_2/FiO_2 ratio during the first 3 days, TV/kg IBW on day 1, PIP on day 1, neuromuscular blockade use, fluid balance on day 1 and cumulative fluid balance during the first 3 and 7 days, and average daily calories during the first week (**Table 2**). After adjusting for confounding factors, the mean PaO_2/FiO_2 ratio during the first 3 days, cumulative fluid balance on day 3, and average daily calories during the first week were independent predictors for 7-day mortality, whereas APACHE II score, fluid balance on day 1, cumulative fluid balance during the first

Table 2. Univariate analysis for 7- and 28-day mortalities

Univariate analysis	7-day mortality			28-day mortality		
	Crude HR	95% CI	*P*	Crude HR	95% CI	*P*
Age (years)	1.015	1.001–1.030	0.04	1.023	1.009–1.038	<0.01*
Gender						
Male (%)	1			1		
Female (%)	0.742	0.436–1.262	0.27	0.789	0.468–1.333	0.38
BMI	0.994	0.930–1.063	0.87	0.967	0.906–1.031	0.31
ARDS severity						
Mild	1			1		
Moderate	2.301	0.744–7.115	0.15	2.135	0.954–4.781	0.07
Severe	4.684	1.599–14.795	<0.01*	2.601	1.151–5.878	0.02*
APACHE II	1.108	1.060–1.159	<0.01*	1.101	1.055–1.150	<0.01*
PaO_2/FiO_2 ratio, day 1	0.992	0.987–0.997	<0.01*	0.997	0.993–1.001	0.18
Mean PaO_2/FiO_2 ratio	0.99	0.980–0.992	<0.01*	0.994	0.990–0.998	<0.01*
TV/kg IBW, day 1	0.996	0.883–1.124	0.95	0.914	0.810–1.031	0.14
Mean TV/kg IBW	0.924	0.801–1.067	0.28	0.917	0.802–1.048	0.20
PEEP, day 1	1.006	0.948–1.067	0.85	0.966	0.911–1.024	0.25
Mean PEEP	1.030	0.965–1.100	0.37	0.994	0.931–1.062	0.86
PIP, day 1	1.061	1.004–1.121	0.04	1.040	0.983–1.101	0.17
Recruitment maneuver	0.910	0.542–1.529	0.77	1.312	0.778–2.211	0.31
Pneumothorax	0.478	0.226–1.008	0.05	1.079	0.553–2.104	0.82
Neuromuscular blockade	0.718	0.412–1.252	0.22	1.471	0.840–2.578	0.18
I/O balance, day 1 (L/day)	1.325	1.175–1.495	<0.01*	1.200	1.063–1.354	<0.01*
Total I/O balance in 3 days (L/day)	1.229	1.142–1.324	<0.01*	1.137	1.066–1.212	<0.01*
Total I/O balance in 7 days (L/day)	1.112	1.071–1.176	<0.01*	1.128	1.077–1.181	<0.01*
7-day AVG enteral calories (kcal/day)	0.998	0.997–0.999	<0.01*	0.999	0.998–0.999	<0.01*

APACHE II, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; AVG, average; BMI, body mass index; CI, confidence interval; HR, hazard ratio; IBW, ideal body weight; I/O, intake/output; mean PaO_2/FiO_2 ratio, mean PaO_2/FiO_2 ratio in the first 3 days; mean PEEP, mean PEEP in the first 3 days; mean TV/kg IBW, mean TV/kg IBW in the first 3 days; PaO_2/FiO_2 ratio, the ratio of partial pressure arterial oxygen and fraction of inspired oxygen; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; TV, tidal volume
*Statistical significance

7 days, and average daily calories during the first week were independent predictors for 28-day mortality (**Table 3**). Furthermore, the patients who received average daily calories during the first week of <60% of estimated daily energy requirement had a greater risk of death (OR = 3.28, 95% CI 1.79–6.01, $P < 0.001$). Moreover, interestingly, the risk of death within 28 days increased with increasing 7-day cumulative fluid balance as shown in **Figure 1**.

Discussion

This study demonstrated that the 28-day mortality of the ARDS patients admitted in our medical ICUs was high, compared with the mortalities in other studies [15–19] (**Table 4**). We postulated that the higher mortality rate resulted from limited ICU beds, delayed ICU admission, delayed sedative and neuromuscular blockade administration, and shortage of medical staff. Our mortality rate tended to be increasing with the greater ARDS severity; however, it was not significant. It might be explained that there were multiple factors affecting the mortality rate such as ventilator-induced lung injury, ventilator-associated pneumonia, and positive cumulative fluid balance. Noticeably, 42.3% of our patients received TV greater than 8 mL/kg IBW on the first day, compared with 30% of the patients in the PRoVENT study [19]. Moreover, there were limited data of the Pplat in our study (4%), compared with 17.2% in ALIEN [18], 40% in

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Table 3. Multivariate analysis for 7- and 28-day mortalities

Multivariate analysis	7-day mortality†			28-day mortality‡		
	Adjusted HR	95% CI	*P*	Adjusted HR	95% CI	*P*
Age (years)	1.004	0.985–1.023	0.70	1.002	0.979–1.027	0.63
ARDS severity						
Mild	1			1		
Moderate	1.608	0.308–8.388	0.57	7.65	0.878–66.662	0.66
Severe	1.835	0.204–16.539	0.59	14.00	0.715–274.194	0.82
APACHE II	1.050	0.995–1.108	0.94	1.151	1.073–1.235	<0.01*
PaO_2/FiO_2 ratio, day 1	1.003	0.995–1.011	0.50	1.003	0.994–1.013	0.46
Mean PaO_2/FiO_2 ratio	0.988	0.981–0.994	<0.01*	0.997	0.989–1.006	0.55
TV/kg IBW, day 1				1.001	0.997–1.004	0.68
PIP, day 1				1.037	0.966–1.114	0.32
Neuromuscular blockade				1.218	0.524–2.832	0.65
I/O balance, day 1 (L/day)	0.984	0.818–1.182	0.86	0.816	0.666–0.998	0.048*
Total I/O balance in 3 days (L/day)	1.192	1.102–1.289	<0.01*	0.969	0.802–1.169	0.74
Total I/O balance in 7 days (L/day)	1.061	0.979–1.150	0.15	1.103	1.026–1.186	<0.01*
7-day AVG enteral calories (kcal/day)	0.998	0.997–0.999	<0.01*	0.999	0.998–1	<0.01*

APACHE II, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; AVG, average; BMI, body mass index; CI, confidence interval; HR, hazard ratio; IBW, ideal body weight; I/O, intake/output; mean PaO_2/FiO_2 ratio, mean PaO_2/FiO_2 ratio in the first 3 days; PaO_2/FiO_2 ratio, the ratio of partial pressure arterial oxygen and fraction of inspired oxygen; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; TV, tidal volume

†Adjusted age, ARDS severity, APACHE II score, mean PaO_2/FiO_2 ratio during the first 3 days, fluid balance on day 1 and cumulative fluid balance during the first 3 and 7 days, and AVG daily calories during the first week for 7-day morality

‡Adjusted age, ARDS severity, APACHE II score, PaO_2/FiO_2 ratio on day 1, mean PaO_2/FiO_2 ratio during the first 3 days, TV/kg IBW on day 1, PIP on day 1, neuromuscular blockade use, fluid balance on day 1 and cumulative fluid balance during the first 3 and 7 days, and AVG daily calories during the first week for 28-day mortality

*Statistical significance

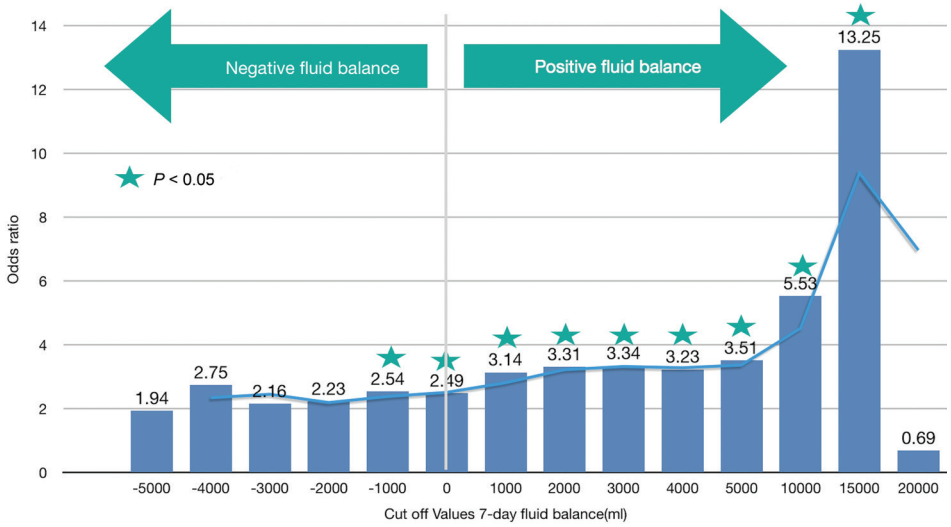

Figure 1. The increasing OR of 28-day mortality in patients who had more positive 7-day cumulative fluid balance. OR, odds ratio

Table 4. Comparison of 28-day mortality of ARDS patients and factors possibly associated with mortality between our study and other studies including ALIEN, LUNG SAFE, PRoVENT, and APRONET

Study period	Our study 2010–2014	ALIEN [18] 2008–2009	LUNG SAFE [15] 2014	PRoVENT [19] 2014–2015	APRONET [20] 2016–2017
28-day mortality					
All severity of ARDS	69.2%	42.7%	34.8%	29%	NA
Mild ARDS	51.6%	NA	29.6%	NA	NA
Moderate ARDS	69.5%	NA	35.2%	NA	NA
Severe ARDS	73.5%	NA	40.9%	NA	NA
Factors					
TV (mL/kg IBW) on day 1	8.56 ± 2.48	7.2 ± 1.1	7.6	7.6	6.7
Percentage of patients with TV >8 mL/kg IBW on day 1	42.3%	NA	NA	30%	NA
Percentage of Pplat measurement	4%	17.2%	40%	41%	90.7%
Percentage of patients with prone position (in severe ARDS)	4%	NA	16%	NA	32.9%
Percentage of patients receiving neuromuscular blockage	35.3%	NA	21.7%	NA	NA
Percentage of patients with recruitment maneuver	48.1%	NA	20.9%	NA	NA
Percentage of patients with ECMO	0%	NA	3.2%	NA	1.9%
Percentage of patients with HFOV	1.5%	NA	1.2%	NA	NA
Percentage of patients with APRV	5.63%	NA	NA	NA	NA

APRV, airway pressure release ventilation; ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; HFOV, high-frequency oscillatory ventilation; IBW, ideal body weight; Pplat, plateau pressure; TV, tidal volume; NA, not available

LUNG SAFE [15], 41% in PRoVENT [19], and 90.7% in APRONET [20]. These findings might indicate that the physicians less concerned about ventilator-induced lung injury. Furthermore, the prevalence of prone position in our severe ARDS patients was only 4%, compared with 16% in LUNG SAFE [15] and 32.9% in APRONET [20]. Prone position was infrequently used in our study because of different study periods. The PROSEVA [6] reported the mortality benefit of prone position in 2013, but we retrospectively reviewed the data between 2010 and 2014. In addition, the prevalence of the use of neuromuscular blocking agent was 35.3% in our study, higher than LUNG SAFE (21.7%) [15] due to the higher proportion of severe ARDS patients in our study. Despite the greater use of neuromuscular blockade, the mortality rate was higher, which might be from inadequate doses of this medication and no ventilator asynchrony monitoring. Recruitment maneuver was performed to 48.12% of the patients, which was quite high, compared with 20.9% in the LUNG SAFE [15]. Despite the fact that the recruitment maneuver potentially increased the risk of barotrauma and death [21, 22], our study did not show the association between the procedure and the complications. Finally, similar to other studies, there were low prevalence of HFOV, APRV, and extracorporeal membrane oxygenation (ECMO) use, which less affected the ARDS outcomes [7, 8, 23–29].

According to the ventilator complications, barotrauma was not different between ARDS survivors and non-survivors. Nevertheless, ventilator-associated pneumonia was higher in the non-survivors group (18.4% vs 13.4%).

Besides, most of the patients had positive cumulative fluid balance, which contributed to the significantly greater mortality in our study (**Figure 1**). Compared with FACTT [10], our ARDS patients had cumulative fluid balance over 7 days close to the fluid balance of the patients in the liberal fluid management group (6,634.97 ± 6,718.06 mL in our study vs 6,992 ± 502 in liberal FACTT), who had worse clinical outcomes, including less ventilator-free days and deteriorated oxygenation index and lung injury score. Nevertheless, FACTT did not demonstrate the mortality risk from liberal fluid management. The different findings might be explained by the fact that there were limited data of hemodynamic status, which possibly confounded to the significantly higher mortality rate in our study.

Furthermore, our study showed that the patients receiving daily calories less than 60% of the estimated daily caloric need during the first week had higher mortality. This result was different from the findings in the EDEN study [30], which demonstrated that initial trophic enteral feeding for up to

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6 days in patients with acute lung injury resulted in similar ventilator-free days, 60-day mortality, and infectious complications, compared with full enteral feeding. It might be explained that our patients with lower caloric intake possibly had more severe conditions such as hemodynamic instability or severe lung injury treated with prone position, which had an impact on mortality outcome.

Our study had limitations. Due to the retrospective design, the information was obtained from the recorded documents. Thus, there were some missing data such as height, body weight, Pplat, and driving pressure. In addition, there might be uncontrolled factors confounding to the mortality rate such as inadequate antibiotics and source control, inappropriate resuscitation of shock, or the different severity of comorbidities.

Conclusion

The 28-day mortality of ARDS was high. In addition, the average TV and fluid balance were greater than the protective limits. These findings indicated the potential improvement of ARDS outcomes in our hospital. The educational program focusing on ARDS management, follow-up, and feedback activities should be provided to our medical personnel.

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