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The Role of Oxygenation Index as an Outcome Predictor in Mechanically Ventilated Acute Respiratory Distress Syndrome Patients

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Abstract **Original Research Article**

Background: Acute respiratory distress syndrome (ARDS) is associated with a significant mortality rate and a high likelihood of failing to wean from mechanical ventilation. Predicting such outcomes in such patients is crucial for the modification of appropriate treatment approaches and for facilitating family communication. Several studies have found that the oxygenation index is an early predictor of outcomes. This study aimed to assess the role of OI assessed on day 1 for predicting weaning outcomes and mortality within 28 days. ***Methods:*** This prospective observational study was done at Dhaka Medical College Hospital (DMCH) over a year. A total of 122 patients with ARDS admitted to the non-COVID intensive care unit (ICU) at the Department of Anesthesia, Pain, Palliative & Intensive Care were included in the study based on selection criteria, using a non-probability sampling technique after receiving informed written consent from the patient's attendants. On day one, the oxygenation index (OI) was measured, and the outcomes were recorded. ***Results:*** An oxygenation index of ≥16.01 cm of H2O substantially increased the risk of mortality by 295.211 (95% confidence interval (CI): 28.163-3094.528) times and predicted mortality with 88.06% sensitivity and 87.27% specificity. The oxygenation index (≥11.11 cm of H2O) was found to independently and significantly increase the chance of weaning outcome (failure) by 35.094 (95% CI: 4.041-304.762) times and weaning failure was predicted with 95.45% sensitivity and 70.27% specificity. ***Conclusion:*** In ARDS patients on mechanical ventilation, the OI measure at day one can be used as a highly accurate, and independent predictor of death and weaning failure.

Keywords: ARDS, Oxygenation index, Mortality, Weaning.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) represents an acute, ubiquitous, inflammatory type of lung damage and a life-threatening situation in severely ill individuals [1]. Diagnostic criteria for ARDS were established by the American-European Consensus Conference (AECC) in 1992. These criteria were revised in 2012 to form the Berlin definition of ARDS in adults [2,3]. Approximately ten percent of patients in intensive care units across the globe suffer from ARDS which is typically caused by pneumonia, sepsis, or severe trauma. Despite significant progress, mortality remains high, reaching 30-40% in most studies [4]. Early prediction of such patients' outcomes allows for quick adjustment of treatment plans and more efficient use of medical resources [5,6], and family communications [5], potentially contributing to lower ARDS death rates. Several severity-scoring techniques are commonly used in the ICU to evaluate severity and predict outcomes [6,7]. Despite their widespread use, there are several limitations, some of the scoring systems require a variety of laboratory data and physiologic parameters for equation calculation and thus difficulties arise in their use. However, there is no scoring system has incorporated the effect of ventilator parameters, such as positive end-expiratory pressure (PEEP) and mean airway pressure (mPaw), on patient outcome [6]. In critically ill patient outcome prediction plays a major role in appropriate treatment decisions and family communication. For early prediction of outcome and to ensure more efficient resource allocation, variables such as the PaO2/FiO2 ratio, the oxygenation index (OI), the influence of co-morbidities, and some clinical scores (SAPS, SOFA), were screened in ARDS patients [5,8,9]. Balzer et al., (2016) reported that OI was a more accurate metric with predictive validity than the AECC on ARDS, the Berlin definition, and the P/F ratio [5]. The oxygenation index (OI) is calculated by adding mean airway pressure (Pmaw) to paO2/FiO2 and multiplying by 100. Several research has shown that OI has stronger predictive powers than pO2/FiO2 [10–12]. A study conducted by Rsovac et al., 2020 indicated that OI at day 3 had a much higher predictive value for mortality than day 1 [13]. Another study by Huber et al., (2020) found that OI on days 1 and 2 of mechanical ventilation was the strongest predictor of 28-day death [14]. Kao et al., (2013) found that OI is associated with weaning outcomes (AOR=0.792, 95% CI 0.62-1.02, P=0.069) [6]. This study was planned to evaluate the role of the oxygenation index (OI) measured on the first day in predicting the failure of weaning from mechanical ventilation and mortality within 28 days.

MATERIALS AND METHODS

This prospective observational study took place from November 2021 to October 2022 at Dhaka Medical College Hospital (DMCH) in Dhaka, Bangladesh. Patients with ARDS admitted to the non-COVID ICU at the Department of Anesthesia, Pain, Palliative & Intensive Care were invited to participate in the study after their attendant was told of the study's objective and aim. The diagnosis of ARDS was based on the Berlin criteria.[2] The study comprised patients aged 18 or older who had mechanical ventilation. The study excluded patients with lung cancer or any other malignancy, COPD, asthma or Interstitial lung disease (ILD), stroke, or neurosurgery. The study enlisted 122 participants using a non-probability sampling technique. The attendants of the patients provided informed written consent. Data were collected utilizing a semi-structured data collection form. The demographic profile, etiology of ARDS, ventilator parameters, oxygenation index (OI), and outcomes were documented. The study received ethical approval from Dhaka Medical College's Ethical Review Committee (Ref: ERC-DMC/ECC/2022/139).

Oxygenation index and Outcome detection

On day 1 of mechanical ventilation, an arterial blood gas analysis was performed utilizing the ABL-80 Flex-Blood gas analyzer to determine PaO2. The corresponding ventilator parameters (PEEP, TI, TE, PIP, Ttot, and FIO2) were monitored and recorded on the same day. Patients were in assist control mode (volume control) with sufficient sedation while ventilator parameters were recorded. For ventilator parameters, the study used Lowenstein elisa-300 and Puritan Bennett 980 series ventilators. The attending intensivist decided to set the mechanical ventilator, wean the patient, and extubate him.

After collecting baseline data, the mean airway pressure was computed using the formula mPaw/MAP = (Ti × PIP) + (TE × PEEP) / Ttot. "The oxygenation index (OI) was computed as OI= [mean airway pressure (MAP) × fraction of inspired oxygen (FiO2) ×100/partial pressure of oxygen in arterial blood (PaO2)]" [8].

Patients were monitored for 28 days to determine the result (mortality and weaning success/failure). Weaning success was defined as successfully removing a breathing tube without the need to restart artificial ventilation within 48 hours of removal. "Weaning failure is defined as one of the following: (1) An unsuccessful spontaneous breathing trial (SBT); (2) Reinsertion of the breathing tube and/or restart of artificial ventilation within 48 hours of extubation" [15].

Statistical Analysis

Following the collection of data, data entry was done. Before any analysis, the acquired data was scrutinized for completeness, accuracy, and consistency. The Statistical Program for Social Sciences (SPSS) version 23 was used in the analysis. The normality of the data was verified using the Shapiro-Wilk test. The means and standard deviations of continuous variables were utilized to summarize the data. A summary of the categorical variables was obtained through the use of frequency distributions. The difference in oxygenation index between the survivors and the dead; weaning success and failure were determined using an independent sample t-test or a Mann-Whitney U test, depending on the nature of the data. The chi-squared test or Fisher's exact test was used to determine the association between categorical variables. The diagnostic/prognostic utility of the Oxygenation index (OI) for mortality and weaning outcome (failure) was determined by computing the cut-off value using receiver operating characteristic (ROC) curve analysis. The predictive utility of OI was determined using both univariate and multivariate logistic regression. We examined the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of OI for mortality and weaning outcomes (failure). The confidence interval and statistical significance criterion were set at <0.05 and 95%, respectively.

RESULTS

The majority of the ARDS patients were from 51-60 years and >60 years of age followed by 41-50 years. The Mean age of the participants was 48.11±14.13 years. More than half of the ARDS patients were male (Table 1).

Table 1: Distribution of patients according to demographic characteristics (N=122)

Demographic characteristics		Frequency	Percentage
Age (years)	18-30	21	17.2
	31-40	15	12.3
	41-50	22	18.0
	51-60	32	26.2
	>60	32	26.2
	Mean ± SD	48.11±14.13	
	Median (range)	51 (18-77)	
Gender	Male	67	54.9
	Female	55	45.1

Data were presented as mean ± SD, frequency (percentage)

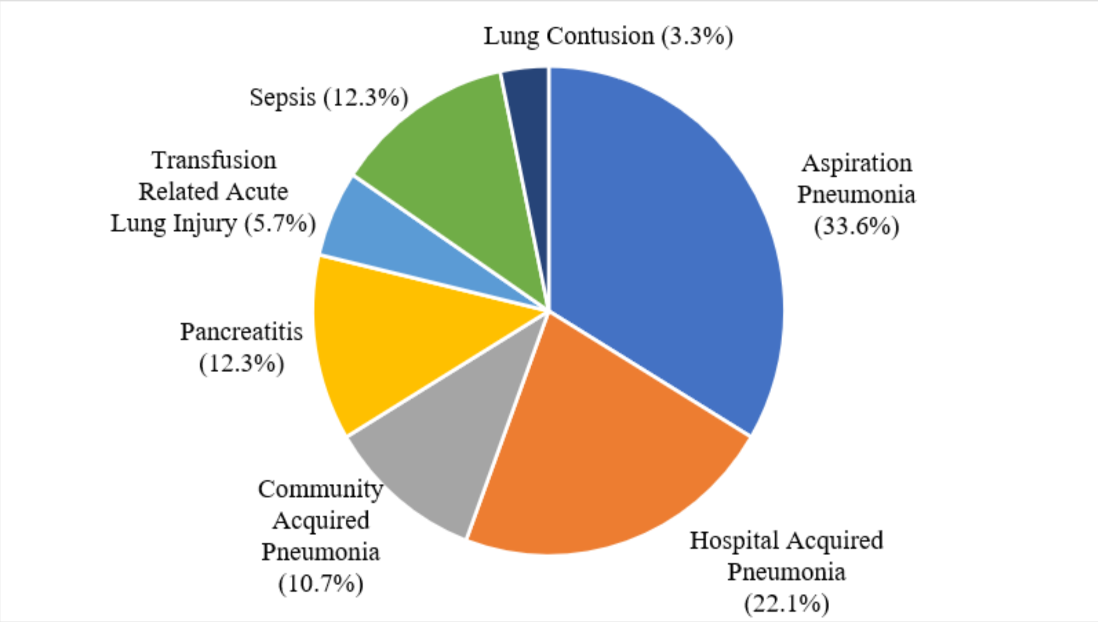

Figure 1: Etiology among ARDS patients (N=122)

The most prevalent cause of ARDS was aspiration pneumonia (33.6%), followed by hospital-acquired pneumonia (22.1%), pancreatitis (12.3%), sepsis (12.3%), and community-acquired pneumonia (10.7) (Figure 1).

Table 2: Distribution of oxygenation index at day 1in different outcomes

Outcomes		Oxygenation index (OI) (cm of H_2O/mm of Hg) Mean ± SD	Median (range)	P value
Weaning outcome	**Successful (n1=37)**	11.26±3.18	9.77 (8.17-18.63)	<0.001
	Failure (n2=22)	14.40±1.80	14.73 (10.36-17.59)	
Mortality	**Yes (n1=67)**	15.30±2.18	15.64 (12.33-17.59)	<0.001
	No (n2=55)	12.22±3.10	11.14 (8.17-18.63)	

Mann Whitney U test was done
S= significant
Data were presented as mean ± SD, Median (range)

The oxygenation index was significantly higher in the weaning failure group (14.40±1.80 cm of H_2O) of participants than in the weaning success participant group (11.26±3.18 cm of H_2O) (p-value: <0.001). Similarly, the oxygenation index was significantly higher among participants who died (15.30±2.18 cm of H_2O) of participants than alive (12.22±3.10 cm of H_2O) (p-value: <0.001) (Table 2).

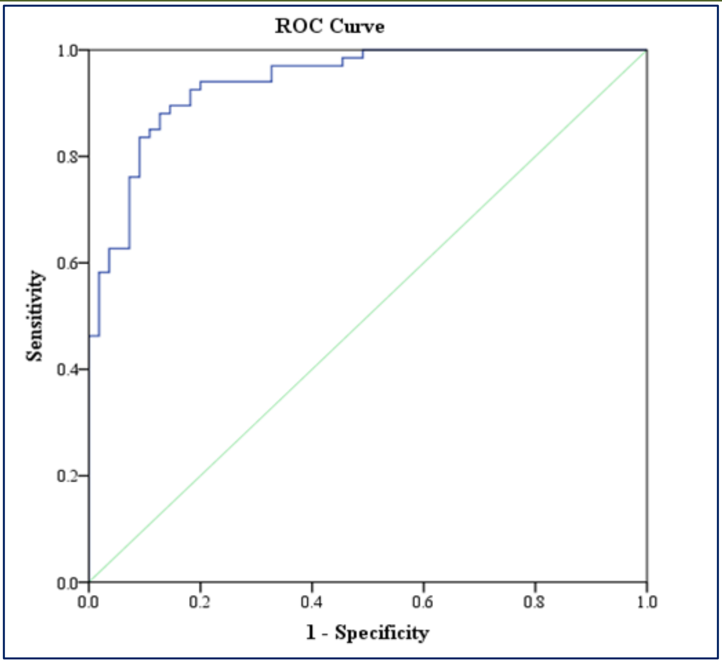

Figure 2: ROC analysis of first-day oxygenation index for prediction of short-term mortality

ROC analysis of oxygenation index level to predict death found an AUC value of 0.940 (95% CI 0.901-0.979) which was statistically significant (P value: <0.001) (figure 2). Based on the Youden index, the cut-off of OI for predicting mortality was determined to be ≥16.01 cm of H_2O.

Table 3: Association of mortality with derived cut-off value of oxygenation index

Oxygenation index (cm of H_2O)	**Death**		**Total**	**Univariate analysis** **Odds ratio (95% Confidence Interval)**	**P value**
	Yes	**No**			
≥16.01	59	7	66	50.571 (17.113-149.448)	<0.001
<16.01	8	48	56		
Total	67	55	122		

Univariate logistic regression was done

Data presented as odds ratio (95% confidence interval)

Oxygenation index (≥16.01 cm of H_2O) significantly increases the odds of mortality by 50.571 (95% Confidence Interval: 17.113-149.448) times (Table 3).

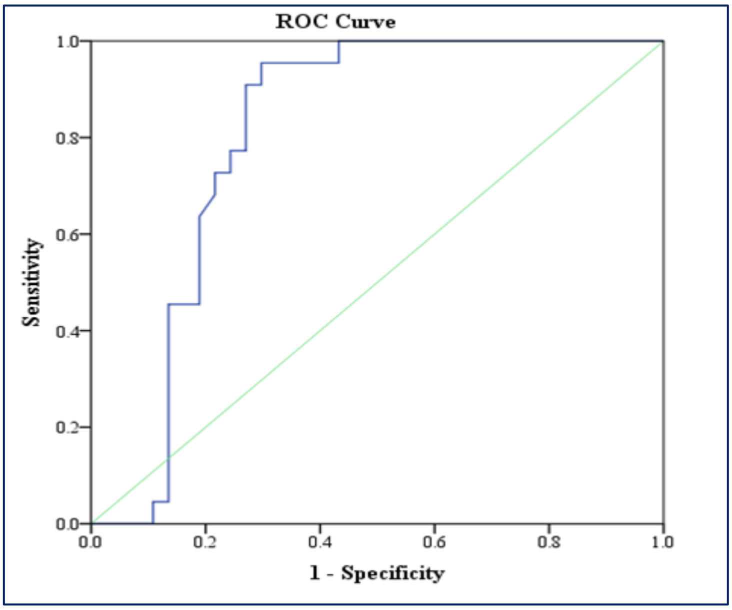

Figure 3: ROC analysis of first-day oxygenation index for prediction of weaning failure

ROC analysis of oxygenation index level to predict weaning outcome (Failure) found an AUC value of 0.805 (95% CI 0.689-0.921) which was statistically significant (P value: <0.001) (figure 2). Based on the Youden index, the cut-off of OI for predicting weaning outcome (Failure) was determined to be ≥11.11 cm of H_2O (Figure 3)

Table 4: Cross-tabulation of the weaning outcome of ARDS patient with oxygenation index value based on derived cut-off value

Oxygenation index (cm of H_2O)	Weaning outcome		Total	Univariate analysis Odds (95% Confidence Interval)	P value
	Failure	Success			
≥11.11	21	11	32	49.636 (5.920-416.161)	<0.001
<11.11	1	26	27		
Total	22	37	59		

Univariate logistic regression was done

Data presented as odds ratio (95% confidence interval)

The oxygenation index (≥11.11 cm of H_2O) significantly increases the odds of mortality by 49.636 (95% Confidence Interval: 5.920-416.161) times (Table 4).

Table 5: Multivariate logistic regression on factors influencing hospital mortality within 28 days and weaning from mechanical ventilation

Outcomes	Variables	Odds ratio (95% Confidence interval)	P value
Mortality	Age (>50 years)	5.231 (0.691-39.570)	0.109
	Sex(male)	2.995 (0.730-12.294)	0.128
	Diabetes mellitus	0.956 (0.180-5.073)	0.958
	Hypertension	35.545 (3.167-398.893)	0.004
	Ischemic heart disease	0.013 (0.001-0.299)	0.007
	Chronic kidney disease	1.118 (0.094-13.253)	0.930
	OI ≥16.01	295.211 (28.163-3094.528)	<0.001
Weaning outcome (failure)	Age (>50 years)	3.165 (0.233-42.989)	0.387
	Diabetes mellitus	2.992 (0.300-29.822)	0.350
	Hypertension	1.543 (0.133-21.039)	0.745
	OI ≥11.11	35.094 (4.041-304.762)	0.001

Multivariate logistic regression was done

Data presented as odds ratio (95% confidence interval)

Oxygenation index (≥16.01 cm of H_2O) was found to independently and significantly increase the odds of mortality by 295.211 (95% Confidence Interval: 28.163-3094.528) times. Hypertension was found to be an independent predictor of mortality also with odds of 35.545 (95% Confidence Interval: 3.167-398.893) times. The oxygenation index (≥11.11 cm of H_2O) is found to independently and significantly increase the odds of weaning outcome (failure) by 35.094 (95% Confidence Interval: 4.041-304.762) times (Table 5).

Table 6: Sensitivity, specificity, PPV, NPV, and accuracy gained by the derived cutoff of oxygenation index with a 95% confidence interval for predicting mortality

Statistic	Value	(95% Confidence Interval)
Sensitivity	88.06%	77.82% to 94.70%
Specificity	87.27%	75.52% to 94.73%
PPV	89.39%	80.75% to 94.42%
NPV	85.71%	75.65% to 92.05%
Accuracy	87.70%	80.53% to 92.95%

Sensitivity [88.06% (95% Confidence Interval: 77.82% to 94.70%)] and specificity [87.27% (95% Confidence Interval: 75.52% to 94.73%)] found from the derived cutoff supported that the derived cutoff of Oxygenation index can predict mortality with about 87.70% accuracy (Table 6).

Table 7: Sensitivity, specificity, PPV, NPV, and accuracy gained by the derived cutoff of oxygenation index with a 95% confidence interval for predicting weaning outcome (failure)

Statistic	Value	(95% Confidence Interval)
Sensitivity	95.45%	77.16% to 99.88%

Specificity	70.27%	53.02% to 84.13%
PPV	65.62%	53.57% to 75.96%
NPV	96.30%	79.11% to 99.44%
Accuracy	79.66%	67.17% to 89.02%

Sensitivity [95.45% (95% Confidence Interval: 77.16% to 99.88%)] and specificity [70.27% (95% Confidence Interval: 53.02% to 84.13%)] found from the derived cutoff supported that the derived cutoff of Oxygenation index can predict weaning outcome (failure) with about 79.66% accuracy (Table 7).

DISCUSSION

The oxygenation index has been mentioned as a way to predict outcomes for newborns, like death [16]. After that, this attribute was found to be a distinct risk factor for death among those with ARDS [5,6,17]. This study sought to evaluate the oxygenation index's ability to predict death and weaning outcomes in patients with ARDS who were receiving mechanical ventilation. We observed that the oxygenation index on the first day of mechanical ventilation in patients is an independent predictor for the outcomes indicated in ARDS. The oxygenation index (OI) was found to be considerably higher in patients who experienced weaning failure and in patients who did not survive. It was also found that OI can predict mortality and weaning outcomes with high sensitivity, specificity, and accuracy. Increasing age is a recognized risk factor for mortality in patients with ARDS, and older individuals have a greater likelihood of death compared to younger ones [18,19]. In this study, the majority of the participants were >50 years of age with male predominance. Almost similar age distribution was reported by DesPrez et al., (2017), a relatively higher age distribution was reported by Chen et al., (2018), and a relatively lower age was reported in a study conducted in India, where the mean age was 46.86 ± 15.81 years. [20] Kao et al., (2018) demonstrated that elderly patients (≥65 years old) diagnosed with ARDS had a worse rate of survival compared to their younger counterparts (<65 years old) also diagnosed with ARDS [21]. However, in this study, it was found that patients with age ≥50 were insignificantly at risk of mortality. In ARDS, mortality is the most commonly reported consequence. A majority of the patients in the study (54.9%) passed away within 28 days. This result is consistent with the findings of Sharif et al., (2013), who documented a mortality rate of 56.5% [22]. Nonetheless, an extremely reduced mortality rate was also noted. Villar et al., (2023)reported that within 28 days of developing ARDS, more than one-third (38.6%) of the patients in their study passed away [24]. Prompt prediction of outcomes such as mortality and weaning failure in these patients facilitates more effective allocation of medical resources and enables timely adjustments to treatment strategies [6]. Consequently, this may enhance patient survival rates in intensive care units. Multiple parameters were assessed, including the Berlin definition, P/F ratio, and OI. Among these, the OI was found to be the most precise predictive parameter for outcomes [5,10,12]. The OI was significantly higher in patients who did not survive (15.30±2.18) compared to those who survived (12.22±3.10) in this study. Vadi et al., (2023) documented a comparable result, indicating that OI levels were considerably diminished in survivors (9.8±4.7) relative to non-survivors (16.1±8.2) [25]. DesPrez et al., (2017) found no statistically significant difference in OI levels between survivors [11(7-20)] and non-survivors [13(8-26)] in their study [26].

During the study, an OI measurement of ≥16.01 cm of H2O on day 1 was associated with a 295.211 times higher risk of mortality (95% CI: 28.163-3094.528). Using this OI cutoff, mortality prediction had a sensitivity of 88.06% and specificity of 87.27%. The oxygenation index cutoff value of 13.5 on day 1 showed the highest predictive accuracy, indicating that patients with an OI >13.5 had seven times the chance of death compared to those with an OI < 13.5 [25]. Kao et al., (2013) revealed that 3rd day OI was an independent risk factor for hospital mortality. OI is a strong predictor of death, demonstrating superior sensitivity, specificity, and accuracy [6]. Kao et al., (2013) revealed that early OI (within three days) and the Sequential Organ Failure Assessment (SOFA) score were predictive of death in cases of severe acute respiratory failure. Additionally, other studies have revealed that the oxygenation index (OI) on the first or third day can also predict mortality [6]. A study by Rsovac et al., (2020) investigated the predictive value of OI at Day 3 for death, showing 97.4% sensitivity and 87.1% specificity [13]. As with off-weaning outcome prediction, the predictive capacity of OI for mortality on day 1 versus day 3 may differ due to the dynamic nature of the patient's condition, treatment response, changes in ventilator management, complication development, and the underlying pathogenesis of ARDS. Multiple studies have investigated the relationship between OI and the weaning outcomes. According to Tseng et al.'s study, a high initial oxygenation index value is an independent predictor of ventilator dependency in patients with ventilator-associated pneumonia [27]. The study conducted by Gajic et al., (2007) revealed that age, OI, and cardiovascular failure three days after intubation are factors that can predict either death or the need for extended mechanical breathing [17]. This study revealed that an OI ≥11.11 cm of H2O was associated with a 35.094 times increased probability of weaning failure on regression analysis (95% CI: 4.041-304.762). Using this parameter, weaning failure may be predicted with 95.45% sensitivity and 70.27% specificity. Kao et al., (2013) showed that variations in the Oxygenation index from day 1 to day 3 were linked to the result of weaning. The group that did not successfully weaned showed a non-significant decrease in OI improvement compared to the group that successfully weaned (-1.06 versus -3.32, $P = 0.008$) [6]. The study was conducted in a tertiary medical college hospital with a limited sample size, which limits generalizability. Moreover, ventilator parameters, such as PaO2/FiO2, might fluctuate due to patient-ventilator asynchronies, poor sedation, airway secretions, and post-suctioning. And, when the PEEP Requirement increases, doctors typically adopt lung protective methods to reduce plateau pressure, which in turn inhibits the growth in mPaw. Such a situation might have resulted in a variation of the OI and may have influenced the predictive capability of OI.

CONCLUSION

More than half of the patients died from ARDS. Those who died had a greater oxygenation index than those who survived, as did those who failed to wean. The OI evaluated on Day 1 was found to be a significant predictor of weaning failure and death within 28 days. The Oxygenation Index (OI) shows promise in accurately predicting mortality and weaning failure within the first day of mechanical breathing to the ICU following standardized ARDS treatment. However, a multicenter study encompassing additional hospitals and a larger sample size is required to investigate the predictive ability of OI on day 1, as well as OI on day 3.

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