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Unveiling the Power of P/FPE: A Game-Changer in Predicting Outcomes for COVID-19-Associated ARDS

P/FPE İndeksinin Gücü: COVID-19'a Bağlı ARDS'de Sonuçların Öngörülmesinde Yeni Bir Yaklaşım

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ABSTRACT

Objective: COVID-19-related acute respiratory distress syndrome (C-ARDS) brings some tough challenges because it often leads to issues like damaged blood vessel linings and failure in multiple organs. The standard way to measure oxygen levels the PaO_2/FiO_2 (P/F) ratio is not always reliable at predicting the severity of ARDS. That's why researchers have suggested a new tool called the P/FPE ratio, which combines the P/F with positive end-expiratory pressure (PEEP) to give a clearer picture of how severe the condition really is. This study evaluates the prognostic utility of the P/FPE ratio, measured at 24 and 72 hours of admission, in predicting intensive care unit (ICU) mortality and ventilator free days (VFD) in mechanically ventilated patients with moderate to severe C-ARDS.

Method: The analysis was conducted on 400 C-ARDS ICU patients at Bakırköy Dr. Sadi Konuk Training and Research Hospital between March 2020 and June 2022, who underwent orotracheal intubation within 72 hours. Patients were classified by P/FPE scores (mild: <20, moderate: 20–40, severe: >40). Demographic, hemodynamic, mechanical ventilation and laboratory parameters were analyzed. T-test, Mann-Whitney U test, and Cox regresssion test were used for statistical analyses, statistical significance was set at $p<0.05$.

Results: At 24 hours, the non-survivor group had significantly lower P/F (155 vs. 180.9, $p<0.001$) and P/FPE (17.4 vs. 21.8, $p<0.001$) ratios and higher PEEP (8.8 vs. 8.4, $p=0.005$) compared to survivors. No significant differences were observed at 72 hours. P/FPE>16 showed the highest sensitivity (70.9%) and specificity (47.3%) for predicting mortality (Positive predictive value: 53.1%, Negative predictive value: 30.6%). P/FPE >16 was associated with shorter ICU stays ($p<0.001$) but not with VFD ($p>0.05$). P/FPE-based severity classification correlated with higher mortality rates across all ARDS categories compared to the P/F ratio.

Conclusion: The P/FPE ratio at 24 hours outperforms the P/F ratio in predicting ICU mortality, offering improved risk stratification. Its association with shorter ICU stays highlights its potential to guide early therapeutic decisions. Multicenter studies are needed to validate these findings across diverse ARDS populations.

Keywords: Acute respiratory distress syndrome, COVID-19, mechanical ventilation, P/F ratio, P/FPE index, intensive care unit

ÖZ

Amaç: COVID-19 ilişkili akut solunum sıkıntısı sendromu (C-ARDS), endotel disfonksiyonu ve çoklu organ yetmezliği nedeniyle kompleks bir klinik duruma sebep olur. Geleneksel PaO_2/FiO_2 (P/F) oranının, C-ARDS sonuçlarını öngörmede kısıtlılıkları mevcuttur. Pozitif End Ekspiratuar Basınç (PEEP) ile P/F oranını birleştiren P/FPE oranı, daha doğru bir mortalite indeksi olarak önerilmiştir. Bu çalışma, orta ve ağır C-ARDS tanılı, mekanik ventilasyon uygulanan hastalarda, yoğun bakım ünitesine (YBÜ) yatış sonrası 24 ve 72 saatte ölçülen P/FPE oranının YBÜ mortalitesini ve ventilatörsüz günleri (VFD) öngörmedeki prognostik faydasını incelemeyi planlamaktadır.

Yöntem: Mart 2020 ile Haziran 2022 arasında Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi'nde YBÜ'ye yatırılan ve 72 saat içinde entübe takip edilen 400 C-ARDS hastası üzerinde retrospektif bir analiz yapıldı. Hastalar, P/FPE skorlarına göre sınıflandırıldı (hafif: <20, orta: 20–40, ağır: >40) ve hastalar hayatta kalan ile hayatta kalmayan gruplara ayrıldı. Demografik, hemodinamik, mekanik ventilasyon ve laboratuvar parametreleri analiz edildi. İstatistiksel analizler t-testleri, Mann-Whitney U testleri ve Cox regresyonunu içeriyordu; anlamlılık $p<0,05$ olarak belirlendi.

Bulgular: 24 saatte, hayatta kalmayan grupta P/F (155'e karşı 180,9; $p<0,001$) ve P/FPE (17,4'e karşı 21,8; $p<0,001$) oranları anlamlı derecede düşük, PEEP ise daha yüksekti (8,8'e karşı 8,4; $p=0,005$). 72 saatte anlamlı fark gözlenmedi. P/FPE >16, mortaliteyi öngörmede en yüksek duyarlılık (%70,9) ve özgüllük (%47,3) gösterdi (Pozitif prediktif değer: %53,1, Negatif prediktif değer: %30,6). P/FPE >16, daha kısa YBÜ kalış süresi ile ilişkiliydi ($p<0,001$), ancak VFD ile ilişkili değildi ($p>0,05$). P/FPE temelli şiddet sınıflandırması, tüm ARDS kategorilerinde P/F oranına kıyasla daha yüksek mortalite oranları ile korelasyon gösterdi.

Sonuç: 24 saatte ölçülen P/FPE oranı, C-ARDS'de P/F oranına kıyasla YBÜ mortalitesini öngörmede daha duyarlı bir göstergedir ve daha iyi risk sınıflandırması sunar. Daha kısa YBÜ kalış süresi ile ilişkisi, erken tedavi kararlarını yönlendirme potansiyelini göstermektedir. Bulguların farklı ARDS popülasyonlarında doğrulanması için çok merkezli çalışmalar gereklidir.

Anahtar sözcükler: Akut solunum sıkıntısı sendromu, COVID-19, mekanik ventilasyon, P/F oranı, P/FPE indeksi, yoğun bakım ünitesi

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) kicks in suddenly, causing severe breathing problems with low oxygen levels and lung inflammation on both lungs—things that can't be blamed entirely on heart issues or plevral effusion (1,2). Throughout the COVID-19 pandemic, we've come to see COVID-19-linked ARDS (C-ARDS) as its own unique type, marked by serious damage to the inner linings of blood vessels, tiny blood clots, and widespread effects that can cause failure on multiple organs (3-6). Mortality rates from ARDS climb with its severity, from about 35% in milder cases up to 46% when it's severe (7). The criteria for gauging ARDS severity is still the PaO_2/FiO_2 (P/F) ratio, which is defined as arterial oxygen pressure against the amount of oxygen being given. It can fluctuate over time and doesn't always predict outcomes reliably. Checking the P/F ratio again at least a day after diagnosis can help to predict survival better, since people whose ratios improve tend to have a survival chance (8,9). That said, a one-time P/F snapshot often doesn't line up well with what actually happens to patients, which is why we need better tools to guide ARDS treatment (10,11). The P/FPE index, which multiplies the PaO_2/FiO_2 by positive end-expiratory pressure (PEEP) and fits right into the Berlin guidelines for ARDS (12). Studies show that tracking P/FPE from the start gives a better view of ARDS severity than the old P/F alone (12).

Our main goal in this study was to see how the P/FPE ratio that has been—checked at 24 and 72 hours after patients arrived in the intensive care unit (ICU) affects death rates in the intensive care unit for patients with moderate to severe C-ARDS. These were patients who needed tracheal intubation and mechanical ventilation (MV). On top of that, we planned to investigate whether this ratio ties into how many days patients could go without the ventilator (known as ventilator-free days, or VFD).

MATERIAL and METHODS

Study Design

The study was approved by the Ethics Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital (Protocol No. 2022-19-05), and a retrospective analysis was conducted on 429 patients diagnosed with C-ARDS who were admitted to the general ICU between March 1, 2020, and June 1, 2022. Patient data were extracted from the ImdSoft Metavision/QlinICU Clinical Decision Support System (ImdSoft, Israel) using structured query language queries. Patients aged 18 years and older, who were admitted to the ICU and diagnosed with C-ARDS and orotracheally intubated within the first 72 hours, were included in the study. The diagnosis of COVID-19 was confirmed using real-time reverse transcription polymerase chain reaction (RT-qPCR) on nasopharyngeal swab specimens, employing the Bio-Speedy Direct RT-qPCR SARS-CoV-2 assay (Bioeksen, Turkey). In cases where PCR testing was unavailable or inconclusive, the diagnosis was supported by chest computed tomography findings consistent with COVID-19 pneumonia. Acute respiratory distress syndrome (ARDS) was diagnosed based on the Berlin Definition (2012), which requires: (1) onset within one week of a known clinical insult or worsening respiratory symptoms; (2) bilateral opacities on chest imaging not fully explained by effusions, lobar collapse, or nodules; (3) respiratory failure not fully attributable to cardiac failure or fluid overload; and (4) a PaO_2/FiO_2 ratio ≤300 mmHg with a minimum PEEP or continuous positive airway pressure (CPAP) of 5 cmH_2O. Acknowledging more recent developments in the ARDS literature, we also considered the "Global Definition of ARDS" (2023), which extends the Berlin criteria by incorporating oxygenation assessment via the SpO_2/FiO_2 ratio, including patients on high-flow nasal oxygen support, and accepting broader imaging modalities, such as lung ultrasound, as diagnostic alternatives. However, to ensure consistency across our cohort and facilitate comparability with prior studies, we adopted the classical Berlin Definition as the primary diagnostic criterion.

Pregnant patients, individuals under 18 years of age, patients diagnosed with non C-ARDS, those not requiring orotracheal intubation within the first 72 hours or those intubated but extubated within the same period, as well as a total of 29 patients with incomplete data in the electronic medical record system, were excluded from the study.

Patients and Methods

The demographic characteristics of the patients like age, sex, body mass index (BMI), predictive body weight (PBW), sequential organ failure assessment (SOFA) and acute physiology and chronic health evaluation (APACHE-II) score, oxygen saturation (SpO_2), MV parameters (expiratory tidal volume (TVe), positive end-expiratory pressure (PEEP), FiO_2, respiratory rate (RR), peak airway pressure, driving pressure, and dynamic compliance, arterial blood gas (ABG)parameters [pH, partial pressure of carbon dioxide, partial pessure of oxygen (PaO_2), and lactate, laboratory parameters (c-reactive Protein (CRP), procalcitonin (PCT) were analyzed.

Mechanical ventilation parameters for C ARDS patients were continuously recorded in the electronic medical record at one minute intervals during the first 24 and 72 hours post intubation. For each patient and time point, the P/FPE index was calculated. PEEP values were individualized for each patient based on arterial blood gas (ABG) results and lung and diaphragm-protective ventilation strategies. Specifically, PEEP titration was designed to achieve target oxygenation levels (SpO_2 88–95% or PaO_2 55–80 mmHg), minimize driving

pressure, prevent alveolar overdistension, and preserve diaphragm function. Ventilator free days were defined as the number of days free from invasive MV within the first 28 days after ICU admission; patients who died before day 28 were assigned zero VFD. For each patient and time point, the P/FPE index was calculated using the following formula:

$P/FPE=PaO_2 / FiO_2 \times PEEP$

Where PaO_2 is the arterial oxygen partial pressure (mmHg), FiO_2 is the fraction of inspired oxygen (expressed as a decimal between 0 and 1), and PEEP is the applied positive end-expiratory pressure (cmH_2O). This approach follows the method proposed by Palanidurai et al (13).

The ARDS severity was then stratified according to predefined P/FPE thresholds (12):

- Mild: P/FPE < 20
- Moderate: P/FPE 20–40
- Severe: P/FPE > 40

Patients were subsequently dichotomized into survivor and non survivor groups for outcome analysis.

Statistical Analysis

Patient data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp., USA). The normality of data distribution was evaluated using the Kolmogorov–Smirnov test. Continuous variables were expressed as median (interquartile range, IQR: 25^{th}–75^{th} percentile), and categorical variables as frequencies and percentages. Between-group comparisons of continuous variables (survivor vs. non-survivor) were performed using the Mann–Whitney U test for non-normally distributed data and the independent t-test for normally distributed data. Paired (within-group) analyses between 24 h and 72 h values were conducted using the Wilcoxon signed-rank test. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Receiver Operating Characteristic (ROC) curve analysis was used to determine optimal cutoff values for mortality prediction. The Area Under the Curve (AUC) with 95% confidence intervals (CIs) was calculated using the DeLong method. Variables identified as potential predictors in the univariable analyses were subsequently included in the multivariable logistic regression model, and results were expressed as odds ratios (Exp(B)) with 95% confidence intervals. Statistical significance was set at $p<0.05$ for all tests.

RESULTS

Baseline Characteristics

Baseline demographic, clinical, and laboratory characteristics of the 400 patients are summarized in Table I. Among them, 186 (46%) were survivors and 214 (54%) non-survivors. The median (IQR) age was 58.5 years (44-70), and 58.3% were male. The median APACHE-II and SOFA scores were 23 (18-28) and 10.1 (7-13), respectively. Median CRP and PCT values were 129 (59-209) mg L^{-1} and 0.8 (0.3-2.9) ng mL^{-1} (Table I).

ICU Outcomes

Median (IQR) ICU length of stay was 12.8 days (6.9-20.5), median duration of MV was 10.6 days (5.6-16.8), and median VFD was 1.2 (0.3-3.7) (Table II).

Oxygenation and Ventilation Parameters

At 24 hours, survivors exhibited significantly higher P/F ratio and P/FPE index and lower $PaCO_2$ compared with non-survivors (all $p<0.001$). PEEP was slightly higher in non-survivors ($p=0.004$). At 72 hours, differences in P/F ratio, P/FPE index, and PEEP were no longer significant, while $PaCO_2$ remained

Table I. Baseline Demographic and Laboratory Characteristics of Patients within the First 24 Hours of ICU Admission (n=400)

Gender n (%)	
Female	167 (41.7)
Male	233 (58.3)
Age (year)	58.5 (44-70)
BMI (kg m^{-2})	27.3 (25-30)
APACHE-II	23 ± 7.3
SOFA	10.1 ± 3.6
CRP (mg L^{-1})	129 (59-209)
PCT (ng mL^{-1})	0.8 (0.3-2.9)

Data are expressed as median (interquartile range, **IQR:** 25^{th}–75^{th} percentile) and mean ± standard deviation (SD).
IQR: Interquantile range, **SD:** Standard deviation, **BMI:** Body mass index, **APACHE:** Acute physiology and chronic health evaluation, **SOFA:** Sequential organ failure assessment, **CRP:** C-reactive protein, **PCT:** Procalcitonin.

Table II. The ICU Outcomes: Length of Stay, Duration of Mechanical Ventilation, and Ventilator-free Days

Parameters	Median (IQR)
ICU length of stay (day)	12.8 (6.9 – 20.5)
MV duration (day)	10.6 (5.6 – 16.8)
VFD (day)	1.2 (0.3 – 3.7)

IQR: Interquantile range, **ICU:** Intensive care unit, **MV:** Mechanical ventilation, **VFD:** Ventilator-free days.

Table III. Comparison of Oxygenation and Ventilation Parameters Between Survivor and Non-Survivor Groups at 24 h and 72 h

	24 hour			72 hour			p (24h vs 72h)
Parameters	**Survivors (n=186)**	**Non-survivors (n=214)**	**p**	**Survivors (n=186)**	**Non-survivors (n=214)**	**p**	
P/F ratio	181 (132–238)	155 (110–201)	<0.001*	175 (128-229)	186 (130-241)	0.326	0.214
PEEP (mmHg)	8.4 (6.7–10.1)	8.8 (7.0–10.5)	0.004*	8.6 (6.8-10.3)	8.8 (7.1-10.4)	0.819	0.371
P/FPE	21.8 (15.2–29.3)	17.4 (12.0–24.6)	<0.001*	20.4 (14.5-27.1)	20.9 (14.8-26.5)	0.354	0.179
$PaCO_2$ (mmHg)	49 (41–57)	55 (46–66)	<0.001*	46 (39-54)	49 (42-59)	<0.001*	0.032*

Data are expressed as median (interquartile range, IQR: 25^{th}–75^{th} percentile). Comparisons between survivors and non-survivors at each time point were performed using the Mann–Whitney U test. Within-group (24 h vs 72 h) comparisons were performed using the Wilcoxon signed-rank test. ***:** significant at 0.05 level.
P/F: Partial oxygen pressure/ fraction of inspired oxygen, **PEEP:** Positive end-expiratory pressure, **P/FPE:** Partial oxygen pressure/ fraction of inspired oxygen x Positive end-expiratory pressure, **$PaCO_2$:** Partial carbon-dioxide pressure.

Table IV. Receiver Operating Characteristic (ROC) Analysis of P/FPE Cut-Off Values for Predicting ICU Mortality in C-ARDS Patients

P/FPE	Sens	Spe	PPV	NPV
>14	81.3	28.6	72.0	18.7
>16	70.9	47.3	53.1	30.6
>18	61.5	52.9	47.3	38.5
>20	56.7	61.2	40.0	44.7
>22	49.5	68.0	31.2	50.5

P/FPE: Partial oxygen pressure/ fraction of inspired oxygen x Positive end-expiratory pressure, **Sens:** Sensitivity, **Spe:** Specificity , **PPD:** Positive predictive value, **NPD:** Negative predictive value.

higher in non-survivors (p<0.001). Within-group (24 h vs 72 h) comparisons showed modest but non-significant improvements in oxygenation indices in both groups (p>0.05). Detailed comparisons are presented in Table III.

ROC Analysis for Mortality Prediction

The ROC curve analysis identified a P/FPE cutoff > 16 as the optimal threshold for predicting ICU mortality, providing a sensitivity of 70.9% and specificity of 47.3% (Table IV). This cutoff yielded a positive predictive value of 53.1% and a negative predictive value (NPV) of 30.6%.

Predictive Performance of Ventilatory Parameters

Among conventional ventilatory indices, P/F > 150, PEEP ≥ 8 cmH_2O, and work of breathing (WOB) ≥ 1.1 J min^{-1} had comparable discriminative capacities.

The highest AUC value was observed for P/FPE > 16 (AUC = 0.61, 95% CI = 0.56–0.67), followed by P/F > 150 (AUC = 0.61, 95% CI = 0.56–0.67) and TVe/PBW ≥ 7 mL kg^{-1} (AUC = 0.60, 95% CI = 0.55–0.66) (Table V).

Multivariable Logistic Regression Analysis

Binary logistic regression revealed that P/FPE > 16, PEEP ≥ 8 cmH_2O, and P/F > 150 were independently associated with ICU length of stay.

Among these, P/FPE > 16 demonstrated a significant protective effect (Exp(B) = 0.575, 95% CI 0.379–0.873, p<0.001), whereas P/F > 150 was associated with markedly shorter stays (Exp(B) = 0.099, 95% CI 0.059–0.167, p<0.001) (Table VI).

Parameters such as WOB ≥ 1.1 J min^{-1} and TVe/PBW ≥ 7 mL kg^{-1} did not reach statistical significance (p>0.05).

When patients were stratified by ARDS severity mild (P/FPE < 20), moderate (P/FPE 20–40), and severe (P/FPE > 40) mortality rates within each stratum were consistently higher when classified by the P/FPE index than by the conventional P/F ratio. This finding suggests that the P/FPE index may afford greater sensitivity for identifying high risk patients across the full spectrum of ARDS severity (Figure 1).

Among these three parameters, it was determined that patients with P/FPE > 16 in both the survivor and non-survivor groups had statistically significantly shorter ICU stays (p<0.05) (Figure 2).

The effects of MV and oxygenation parameters (PEEP ≥ 8, P/F > 150, WOB ≥ 1.1, TVe/PBW ≥ 7, P/FPE > 16) on VFD were found to be statistically insignificant.

DISCUSSION

The Berlin criteria remain the current standard for diagnosing ARDS; however, their prognostic utility, particularly in C-ARDS, has been increasingly questioned (14-16). This study sought to evaluate whether the P/FPE ratio, a novel severity index incorporating both oxygenation and ventilatory support parameters, offers improved predictive accuracy for mortality

Table V. Comparison of the Hourly Mean Values of Conventional Parameters and the P/FPE Parameter in Terms of Their Sensitivity, Specificity, PPV, and NPV for Predicting Mortality

Parameters	Results (%)					
	Sens	Spe	PPV	NPV	AUC	95% CI
P/F >150	66.8	47.4	53.6	33.1	61.2	55.6-66.8
PEEP ≥ 8 (cmH_2O)	60.4	31.0	73.4	39.8	42.0	36.3-47.7
WOB ≥ 1.1 ($J\ min^{-1}$)	67.0	28.2	82.2	32.8	33.6	28.2-38.9
TV_e/PBW ≥ 7 ($mL\ mg^{-1}$)	64.3	51.0	51.1	35.5	60.3	54.7-65.9
P/FPE > 16	70.9	47.3	53.1	30.6	61.4	55.8-66.9

Sens: Sensitivity, **Spe:** Specificity, **PPV:** Positive predictive value, **NPV:** Negative predictive value, **AUC:** Area under curve, **CI:** Confidence interval, **P/F:** Partial oxygen pressure/fraction of inspired oxygen, **PEEP:** Positive end-expiratory pressure, **WOB:** Work of breathing, **TV_e:** Expiratory tidal volume, **P/FPE:** Partial oxygen pressure/ fraction of inspired oxygen x Positive end-expiratory pressure.

Table VI. Impact of Mechanical Ventilation and Oxygenation Parameters on ICU Length of Stay

	ß	SE	Wald	df	p	Exp (B)	%95CI	
							Lower	Upper
PEEP≥8 (cmH_2O)	-0.688	0.139	24.362	1	***0.021***	0.503	0.382	0.661
WOB≥1.1 ($J\ min^{-1}$)	-0.040	0.147	0.076	1	*0.783*	0.960	0.720	1.280
TVe/PBW≥7 ($mL\ mg^{-1}$)	0.082	0.138	0.354	1	*0.552*	1.086	0.828	1.420
P/FPE>16	-0.554	0.213	6.758	1	***<0.001***	0.575	0.379	0.873
P/F>150	-2.309	0.264	76.549	1	***<0.001***	0.099	0.059	0.167

CI: Confidence interval, **PEEP:** Positive end-expiratory pressure, **WOB:** Work of breathing, **P/F:** Pao_2/Fio_2, **Tve:** Expiratory tidal volume, **PBW:** Predictive body weight, volume, **P/FPE:** Partial oxygen pressure/fraction of inspired oxygen X positive end-expiratory pressure, **P/F:** Partial oxygen pressure/ fraction of inspired oxygen.

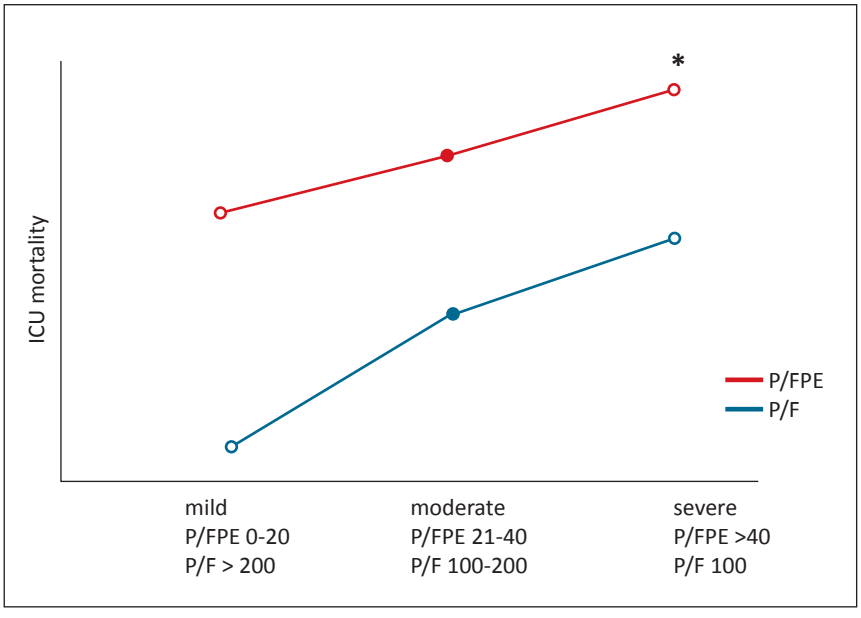

Figure 1. Mortality rate across P/F and P/FPE categories (Mild, Moderate, Severe). p-values from chi-square test, *p<0.05.

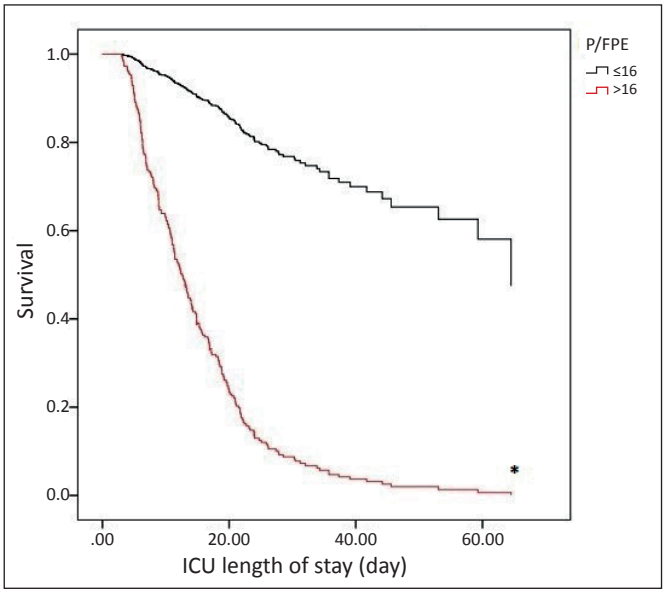

Figure 2. Survival probability over ICU length of stay (days) for P/FPE groups (e.g., Group A and Group B). p-values from log-rank test, *p<0.05.

and ICU outcomes in C-ARDS patients compared to the traditional P/F ratio.

Sayed et al. demonstrated that the P/FPE ratio significantly outperforms the conventional P/F ratio of the Berlin definition for ARDS severity assessment, recommending its adoption across all severity categories to achieve more granular stratification in C ARDS patients; they further identified a mortality predictive cutoff with both high sensitivity and specificity (12). In concordance with these findings, our study showed that a P/FPE ratio > 16 was strongly associated with ICU mortality and offered greater prognostic sensitivity than either the P/F ratio or PEEP values alone. These results underscore the importance of integrating PEEP into oxygenation indices to enhance prognostic precision and refine severity classification in patients with C ARDS. Given the enhanced capacity of the P/FPE index to stratify ARDS severity and predict mortality, we subsequently evaluated its relationship with two secondary outcomes: ICU length of stay and VFD. In our cohort, survivors exhibited significantly longer ICU length of stay and greater VFD compared with non survivors. Stratification by a P/FPE cutoff of > 16 revealed that patients regardless of survival status demonstrated a statistically significant reduction in ICU duration of stay; however, no significant association emerged between a P/FPE > 16 and VFD. Although a P/FPE ratio > 16 was predictive of ICU mortality, it did not correlate with the duration of MV. This discrepancy likely reflects the multifactorial determinants of ventilator weaning including sedation protocols, and comorbid conditions which are not fully captured by oxygenation based indices alone. In a study by Li et al. the non-survivor group demonstrated longer durations of both ICU stay and MV compared to the survivor group (17). Conversely, Gupta B et al. reported that in patients with C-ARDS, the mean ICU stay was 14.2 ± 6.80 days, with no significant differences in either ICU length of stay or MV duration between the survivor and non-survivor groups (18). Our mortality analysis stratified by P/FPE levels demonstrated a clearer gradation in outcomes than traditional P/F categories, reinforcing its role as a more discriminative tool for risk stratification in C-ARDS.

Gutierrez-Zamudio et al. reported that PaO_2 values measured during ICU stays in patients with ARDS were not associated with mortality (19). In contrast, Sartini et al. demonstrated significant differences in P/F ratio values between the survivor and non-survivor groups in patients with C-ARDS (20). Consistent with prior studies, our findings showed that P/F ratio alone was not predictive of mortality, underscoring the need for composite indices like P/FPE.

In a large cohort study by Tiruvoipati et al., involving over 250,000 ARDS patients receiving MV, the development of hypercapnic acidosis (defined as pH < 7.35 and $PaCO_2$ > 65 mmHg) within the first 24 hours was associated with significantly higher mortality compared to patients with compensated hypercapnia or normocapnia (21). Consistent with these findings, our study also demonstrated higher $PaCO_2$ levels in the non-survivor group, suggesting a potential link between early hypercapnia and adverse outcomes.

This study has several limitations. First, it is a single-center retrospective analysis, which may limit the generalizability of the findings. Additionally, the study cohort only included patients with C-ARDS, which may restrict the applicability of the P/FPE ratio to other ARDS etiologies. Finally, dynamic changes in ventilator settings beyond the 72-hour and other adjunctive therapies (e.g., extracorporeal membrane oxygenation, corticosteroids, or neuromuscular blockade) were not evaluated, which could have influenced both oxygenation parameters and clinical outcomes.

CONCLUSION

The P/FPE ratio enables a more detailed assessment and classification of disease severity in patients with C-ARDS, achieving a cut-off value with sufficiently high sensitivity and specificity for predicting mortality. Incorporating this index into routine clinical assessment may enhance prognostication and guide early therapeutic decisions.

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AUTHOR CONTRIBUTIONS

Conception or design of the work: ZC, PR
Data collection: ZC
Data analysis and interpretation: PR
Drafting the article: EO
Critical revision of the article: FT
Other (study supervision, fundings, materials, etc): FT
The author (EO, PR, FT, ZC) reviewed the results and approved the final version of the manuscript.

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