The prognostic value of PaO2/FiO2 ratio in predicting clinical outcomes in COVID-19 patients

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Abstract

***Purpose*: The PaO2/FiO2 (P/F) ratio is a parameter used to assess oxygenation in coronavirus disease 2019 (COVID-19) patients. This study aimed to investigate the prognostic value of the P/F ratio in predicting clinical outcomes, including disease severity, length of stay, and mortality.**

***Methods*: A retrospective analysis was conducted on COVID-19 patients admitted to a single center in Houston, Texas between March 2020 and February 2022, where 753 patients were included out of 994 that were admitted. Patients were categorized into four groups based on the Berlin Criteria (P/F ratio): Group 1 (severe) with P/F ratio <100 mmHg, Group 2 (moderate) with P/F ratio 101-200 mmHg, Group 3 (mild) with P/F ratio 201-300 mmHg, and Group 4 (normal) with P/F ratio >300 mmHg. Data analysis was performed using IBM SPSS Statistics version 25.0. Descriptive statistics, chi-square, and logistic regression tests were employed to determine statistical significance.**

***Results*: Seven hundred and fifty-three patients were included in this study. The median age was 56 years (44-66.50), the median length of stay was 7 days (4-13), and the P/F was 252 (149-328.50). Four hundred and thirty-three (57.5%) were male, and 320 (43,5%) patients survived.**

There were 125 (16.6%) patients in Group 1, 166 (22%) in Group 2, 196 (26%) in Group 3, and 266 (35.3%) in Group 4. A chi-square analysis revealed a significant correlation between P/F and clinical outcomes (p<0.0001). As far as mortality, 74 (48.7%) patients in Group 1, 47 (30.9%) in Group 2, 17 (11.2%) in Group 3, and 14 (9.2%) in Group 4 died. There was a correlation between P/F and gender (p<0.0001). There were 108 (72%) patients in Group 1, 94 (55%) patients in Group 2, 133 (61.6%) patients in Group 3, and 155 (49.2%) patients in Group 4 were male.

In the logistic regression analysis, where significance was determined at p<0.05 and a confidence interval (CI) of 95%, it was observed that being male was strongly associated with a higher risk of mortality within these groups (p=0.041). Group 1 was also significantly linked to increased mortality (p<0.001). Belonging to Group 2 showed an association with the risk of death (p<0.001), while in Group 3, the Wald test score was 0.800 and indicated a lower likelihood of mortality, suggesting a protective factor (p=0.371). We found that with an increase in the length of stay, the probability of mortality rose (p=0.007). Of all the variables belonging to Group 1 exhibited the strongest association with mortality, as evidenced by a Wald test score of 59.075, with a p-value of <0.001.

***Conclusions*: In our cohort, there was a strong association between the P/F ratio, clinical outcomes, gender, and the length of hospital stay in COVID-19 patients. Those patients with more severe P/F ratio impairment experienced higher mortality rates and longer hospital stays.**

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Introduction

The onset of the coronavirus disease 2019 (COVID-19) pandemic, began as an outbreak in Wuhan, China, in December 2019. The virus responsible for COVID-19, known as severe acute respiratory syndrome virus 2 (SARS-CoV-2), has led to over 1.2 million deaths from December 2019 to March 2024 in the United States of America. (1) The pandemic of COVID-19 had an unprecedented impact on the global healthcare system. (2) COVID-19 primarily targets the respiratory system, often resulting in pneumonia and acute respiratory failure (ARF). Its clinical presentation varies widely, from cases without symptoms to critical, potentially fatal conditions. There are many tools that can be used to calculate the possible prognosis in these patients. However, the ratio of partial pressure of arterial oxygen (PaO2) to a fraction of inspired oxygen concentration (FiO2) has appeared as a critical parameter. (3) The PaO2/FiO2 (P/F) ratio is used to classify the severity of acute respiratory distress syndrome (ARDS), and it reflects the efficacy with which oxygen is exchanged in the lungs and thus, serves as an important value to determine the severity of respiratory distress and clinical management. (4)

The P/F ratio offers the basics regarding the foundation of respiratory physiology and represents the efficacy of oxygenation and the possible degree of lung injury. (5) When comparing PaO2 and FiO2, patients can then be divided into different categories, ranging in severity of respiratory dysfunction: normal, mild, moderate, and severe. (6) Severe respiratory dysfunction represents the diffuse alveolar damage and impaired gas exchange that is taking place within the lungs. (7) Taking this into account, the clinical outcome in these cases is suboptimal, the monitoring of this condition with P/F ratio is imperative to improve the prognosis of patients.

This study aimed to investigate the prognostic significance of the P/F ratio as a predictive value for clinical outcomes, such as disease severity, length of stay, and mortality among four distinct groups of hospitalized COVID-19 patients.

Methods

Study design and participants

This was a retrospective cohort analysis conducted at a single-center hospital in Houston, Texas, from March 2020 to February 2022. Inclusion criteria included adult patients aged 18 years and above who were hospitalized for COVID-19 infection with P/F ratio data on admission as well as Ichikado, Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation (APACHE) II scores on admission. Patients under the age of 18, and/or without P/F ratio data on admission were excluded.

Data collection

We utilized the Meditech™ electronic medical record system within the hospital to compile patient data for the research. This dataset included various information such as demographic details, clinical data, laboratory results, severity assessments, imaging records, treatment specifics, length of hospitalization, and patient results.

To confirm the diagnosis of COVID-19, we employed various techniques, including reverse transcription polymerase chain reaction (RT-PCR), SARS Antigen Fluorescent Immunoassay (SOFIA), or IgG/IgM rapid tests, alongside clinical evaluation and chest imaging. Demographic and clinical information taken into account encompassed factors such as age, gender, ethnicity, pre-existing medical conditions, and body mass index (BMI).

Patients were categorized into four groups based on the Berlin Criteria (P/F ratio): Group 1 (severe) with P/F ratio <100 mmHg, Group 2 (moderate) with P/F ratio 101-200 mmHg, Group 3 (mild) with P/F ratio 201-300 mmHg, and Group 4 (normal) with P/F ratio >300 mmHg. APACHE II scores were categorized into 8 groups: Group 1 (0-4 points), Group 2 (5-9 points), Group 3 (10-14 points), Group 4 (15-19 points), Group 5 (20-24 points), Group 6 (25-29 points), Group 7 (30-34 points) and Group 8 (>34 points). SOFA scores were also categorized into 8 groups: Group 1 (0-1 points), Group 2 (2-3 points), Group 3 (4-5 points), Group 4 (6-7 points), Group 5 (8-9 points), Group 6 (10-11 points), Group 7 (12-14 points), and Group 8 (>14 points). Patients were divided into 2 groups based on their admission Ichikado CT score: Group 1 (<172 points) and Group 2 (>172 points).

Our protocol and research adhered to ethical standards and received approval from the hospital's Institutional Review Board prior to data collection. Patient data was anonymized and treated with utmost confidentiality to safeguard individual privacy.

Statistical analysis

We used IBM SPSS ™ Statistics version 24 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (SD), while categorical data were presented as frequencies and percentages. Descriptive statistics were used to summarize the demographic and clinical characteristics of both patient groups, as well as the chi-square test and logistic regression analysis. All authors collected and analyzed the data.

Results

This study included a total of 753 patients; 320 (43.5%) were female, and 433 (57.5%) were male. The median age was 56 years (44-66.50), median BMI was 29.50 (26.22-34.87), and the median length of stay was 7 days (4-7). One hundred and thirty-eight (18.3%) patients were Caucasian, 442 (58.7%) were Hispanic, 138 (20.6%) were African-American, and 27 (3.6%) were identified as other races. The mean first recorded P/F ratio was 252 (149-328.50).

The most common comorbidities were hypertension with 285 (37.8%) patients, 270 (35.9%) had ventricular or atrial enlargement, 193 (25.6%) with diabetes mellitus, 22 (2.9%) had chronic obstructive pulmonary disease (COPD), 18 (2.4%) had chronic kidney disease, 23 (3.1%) had peripheral vascular disease, and 21 (2.8%) had congestive heart failure (CHF).

The most common adverse events during hospitalization were disseminated intravascular coagulation with 125 (16.6%) patients, pulmonary embolism with 68 (9%) patients, and pulmonary hypertension with 66 (8.8%) patients. Out of the 753 patients, 79.8% survived.

The median SOFA score on admission was 2 (1-3), the median APACHE II score on admission was 9 (6-13), and the median Ichikado CT score on admission was 150 (120-200). There were 125 (16.6%) patients in P/F Group 1, 166 (22%) in P/F Group 2, 196 (26%) in P/F Group 3, and 266 (35.3%) in P/F Group 4.

A significant association between clinical outcome and P/F groups was encountered (**Table 1**). Out of the 152 patients that died, 74 (48.7%) were in Group 1, 47(30.9%) in Group 2, 17 (11.2%) in Group 3, and 14 (9.2%) in Group 4 ($p<0.001$).

Regarding the severity scores, a significant association was found between the P/F groups and APACHE II, SOFA, and Ichikado scores ($p<0.001$). Patients with a mild or normal P/F ratio tend to have a low severity score with low mortality, and vice versa, patients with a moderate or severe P/F ratio tend to have high severity scores with a high percentage of mortality.

Speaking specifically about the APACHE II score, a total of 111 patients were in Group 1 with 0-4 points, of which 60 (54.1%) had a normal P/F ratio. A total of 289 patients were in Group 2 with 5-9 points, of which 123 (42.6%) had a normal P/F ratio. There were 205 patients in Group 3 with 10-14 points, of which 56 (27.3%) had a normal P/F ratio. A total of 68 patients were in Group 4 with 15-19 points, of which 20 (29.4%) had a severe P/F ratio. Thirty-four patients were in Group 5 with 20-24 points, of which 14 (41.2%) had a severe P/F ratio. Thirty-four patients were in Group 6 with 25-29 points, of which 16 (47.1%) had a severe P/F ratio. Seven patients were in Group 7 with 30-34 points, of which 2 (28.6%) had a severe P/F ratio. Finally, 5 patients were in Group 8 with >34 points, of which 3 (60%) had a severe P/F ratio ($p<0.001$) (**Table 2**).

When the SOFA score was analyzed, a total of 200 patients were in Group 1 with 0-1 points, of which 169 (84.5%) had a normal P/F ratio. A total of 403 patients were in Group 2 with 2-3 points, of which 159 (39.5%) had a mild P/F ratio. There were 78 patients in Group 3 with 4-5 points, of which 26 (33.3%) had a severe P/F ratio. A total of 33 patients were in Group 4 with 6-7 points, of which 14 (42.4%) had a moderate P/F ratio. Thirty patients were in Group 5 with 8-9 points, of which 23 (76.7%) had a severe P/F ratio. Six patients were in Group 6 with 10-11 points, of which 5 (83.3%) had a severe P/F ratio. One patient was in Group 7 with 12-14 points, which had a severe P/F ratio. Two patients were in Group 8 with >14 points, of which both (100%) had a moderate P/F ratio ($p<0.001$) (**Table 3**).

The analysis for the Ichikado CT score was also revealing. Four hundred and fifty-nine patients were in Group 1 with <172 points, of which 228 (49.7%) had a normal P/F ratio, in comparison with Group 2 with >172 points with 294 patients in total, of which the majority was in the severe P/F ratio group with 96 (32.7%) patients ($p<0.001$) (**Table 4**).

In a logistic regression analysis, we found that being male was strongly associated with a higher risk of mortality within these groups ($p=0.041$). Group 1 was also significantly linked to increased mortality ($p<0.001$). Group 2 also yielded an association with the risk of death ($p<0.001$), while in Group 3, we found a lower likelihood of mortality, suggesting a protective factor ($p=0.371$). We also found that with an increase in the length of stay, the probability of dying increased ($p=0.007$).

Discussion

The PaO2/FiO2 ratio emerged as the most reliable independent prognostic biomarker for predicting the progression of severity in COVID-19 patients in our cohort. While the current study identified that being male, having a low P/F ratio, an increased hospital stay, and a high severity score were strongly associated with a higher risk of mortality, it was also noted that certain underlying conditions in patients may likely play a role in this.

Consistent with findings in existing literature, prevalent comorbidities observed in this population included hypertension, diabetes, stroke, coronary ar-

tery disease, and chronic liver disease. (8,9) These likely contributed to the elevated mortality rate in this group, as mortality among COVID-19 patients with such comorbidities tends to be higher due to pre-existing inflammatory conditions in chronic diseases, and heightened vulnerability to cellular immune responses and humoral activation, particularly involving tumor necrosis factor and interleukin 6. (10)

Our study demonstrated a strong correlation between a low P/F ratio and elevated mortality rates in COVID-19 patients. A study by Sinatti and collaborators showed that a P/F ratio could be considered a reliable prognostic biomarker for patients with COVID-19, with a cut-off value of <274 mmHg. (3) In other clinical conditions, the P/F ratio has demonstrated efficacy in predicting hospital mortality. (11) A multicenter study by Casillas and coinvestigators also revealed the association of the P/F ratio with an increased risk of mortality. (12) Therefore, while alternative metrics may exist, the P/F ratio seems to be a reasonable predictor of clinical outcomes in COVID-19 and other conditions. Furthermore, Santus and coworkers found that a decrease in the P/F ratio was independently correlated with an increase in the risk of intra-hospital mortality. (13)

While the P/F ratio is valuable in this clinical setting, other prognostic tools also merit consideration. For instance, Chen and associates utilized several laboratory markers such as white blood cell (WBC) count, platelets, albumin, urea nitrogen, myocardial enzymes, creatinine kinase (CK), lactate dehydrogenase (LDH), lactate, and calcium to predict the need for invasive mechanical ventilation. (14)

In addition, Zhou and collaborators found that cardiac complications, such as new or exacerbated congestive heart failure, dysrhythmias, or myocardial infarction, were common in their population. (15) In comparison, complications in our population encompassed pulmonary issues, including disseminated intravascular coagulation, pulmonary embolism, and pulmonary hypertension.

Severity scores play a crucial role in determining the clinical severity and outcome of patients. (16) This establishment of severity allows for a more refined treatment of patient illness. Such a relationship was apparent in our results, as we found that patients with moderate to severe P/F ratios were likely to have higher severity scores with higher predictive mortality rates. In two studies, the APACHE II score was higher and the P/F ratio was lower, indicating a strong discriminative ability to predict mortality among COVID-19 patients admitted to the ICU. (14,17)

In a study conducted by Yang and coworkers the median SOFA score of severe patients was higher in male and older age patients. (8) This is consistent with our findings. Additionally, several studies have linked not only the SOFA score but also age, d-dimer levels, high-sensitivity C-reactive protein, body temperature, albumin levels, diabetes, and interleukin 6 levels as predictors of severity in patients with COVID-19. (15,18)

Lastly, our results are aligned with the findings of Araiza and coworkers, who found that an Ichikado score >172 points was a strong predictor for mortality in patients hospitalized for COVID-19. (19)

Conclusions

Our study highlights the importance of the P/F ratio as a key prognostic indicator in COVID-19 patients. It shows a clear link between lower P/F ratios and increased mortality risk, emphasizing its predictive value across different patient groups. Additionally, factors like gender, length of stay, and severity scores further contribute to mortality risk. The study suggests integrating the P/F ratio into routine care for better patient management.

Conflicts of interest

The authors have no conflicts of interest in the preparation of this manuscript. This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

This study was partially presented as a poster presentation at the American Thoracic Society Congress in San Diego, California, May 20, 2024.

Table 1. P/F groups denote severity levels based on the PaO2/FiO2 (P/F) ratio, with corresponding mortality percentages and total patient counts

Clinical outcome	Percentages (%)	Group 1 (severe)	Group 2 (moderate)	Group 3 (mild)	Group 4 (normal)	Total	p-value
Dead	# of patients	74	47	17	14	152	<0.001
	% within the outcome	48.7%	30.9%	11.2%	9.2%	100%	
	% within the total population	9.8%	6.2%	2.3%	1.9%	20.2%	
Alive	# of patients	51	119	179	252	601	
	% within the outcome	8.5%	19.8%	29.8%	41.9%	100%	
	% within the total population	6.8%	15.8%	23.8%	33.5%	79.8%	

Table 2. APACHE II score groups are indicated alongside predicted mortality rates, with corresponding mortality percentages within each P/F group and total patient counts

APACHE II score groups	Predicted mortality rate	Percentages (%)	Group 1 (severe)	Group 2 (moderate)	Group 3 (mild)	Group 4 (normal)	Total	p-value
Group 1 (0-4 pts)	4%	# of patients	5	10	36	60	111	<0.001
		% within APACHE groups	4.5%	9%	32.4%	54.1%	100%	
		% within the total population	0.7%	1.3%	4.8%	8%	14.7%	
Group 2 (5-9 pts)	8%	# of patients	23	55	88	123	289	<0.001
		% within APACHE groups	8%	19%	30.4%	42.6%	100%	
		% within the total population	3.1%	7.3%	11.7%	16.3%	38.4%	
Group 3 (10-14 pts)	15%	# of patients	42	57	50	56	205	0.177
		% within APACHE groups	20.5%	27.8%	24.4%	27.3%	100%	
		% within the total population	5.6%	7.6%	6.6%	7.4%	27.2%	
Group 4 (15-19 pts)	25%	# of patients	20	19	11	18	68	<0.001
		% within APACHE groups	29.4%	27.9%	16.2%	26.5%	100%	
		% within the total population	2.7%	2.5%	1.5%	2.4%	9%	
Group 5 (20-24 pts)	40%	# of patients	14	15	2	3	34	<0.001
		% within APACHE groups	41.2%	44.1%	5.9%	8.8%	100%	
		% within the total population	1.9%	2%	0.3%	0.4%	4.5%	
Group 6 (25-29pts)	55%	# of patients	16	8	5	5	34	<0.001
		% within APACHE groups	47.1%	23.5%	14.7%	14.7%	100%	
		% within the total population	2.1%	1.1%	0.7%	0.7%	4.5%	
Group 7 (30-34 pts)	73%	# of patients	2	2	2	1	7	<0.001
		% within APACHE groups	28.6%	28.6%	28.6%	14.3%	100%	
		% within the total population	0.3%	0.3%	0.3%	0.1%	0.9%	
Group 8 (>34 pts)	85%	# of patients	3	0	2	0	5	<0.001
		% within APACHE groups	60%	0%	40%	0%	100%	
		% within the total population	0.4%	0%	0.3%	0%	0.7%	

Legend: APACHE=Acute Physiology and Chronic Health Evaluation.

Table 3. SOFA score groups are listed with their corresponding predicted mortality rates, alongside mortality percentages within each P/F group and total patient count

SOFA score groups	Predicted mortality rate	Percentages (%)	Group 1 (severe)	Group 2 (moderate)	Group 3 (mild)	Group 4 (normal)	Total	p-value
Group 1 (0-1 pts)	0%	# of patients	5	13	13	169	200	0.008
		% within SOFA groups	2.5%	6.5%	6.5%	84.5%	100%	
		% within the total population	0.7%	1.7%	1.7%	22.4%	26.6%	
Group 2 (2-3 pts)	6.4%	# of patients	57	113	159	74	403	0.035
		% within SOFA groups	14.1%	28%	39.5%	18.4%	100%	
		% within the total population	7.6%	15%	21.1%	9.8%	53.5%	
Group 3 (4-5 pts)	20.2%	# of patients	26	21	13	18	78	0.252
		% within SOFA groups	33.3%	26.9%	16.7%	23.1%	100%	
		% within the total population	3.5%	2.8%	1.7%	2.4%	10.4%	
Group 4 (6-7 pts)	21.5%	# of patients	8	14	9	2	33	0.785
		% within SOFA groups	24.2%	42.4%	27.3%	6.1%	100%	
		% within the total population	1.1%	1.9%	1.2%	0.3%	4.4%	
Group 5 (8-9 pts)	33.3%	# of patients	23	2	2	3	30	<0.001
		% within SOFA groups	76.7%	6.7%	6.7%	10%	100%	
		% within the total population	3.1%	0.3%	0.3%	0.4%	4%	
Group 6 (10-11pts)	50%	# of patients	5	1	0	0	6	0.037
		% within SOFA groups	83.3%	16.7%	0%	0%	100%	
		% within the total population	0.7%	0.1%	0%	0%	0.8%	
Group 7 (12-14 pts)	95.2%	# of patients	1	0	0	0	1	<0.001
		% within SOFA groups	100%	0%	0%	0%	100%	
		% within the total population	0.1%	0%	0%	0%	0.1%	
Group 8 (>14 pts)	95.2%	# of patients	0	2	0	0	2	<0.001
		% within SOFA groups	0%	100%	0%	0%	100%	
		% within the total population	0%	0.3%	0%	0%	0.3%	

Legend: SOFA=Sequential Organ Failure Assessment.

Table 4. Ichikado score groups association with mortality rates within each P/F group, total patient counts

Ichikado score groups	Predicted mortality rate	Percentages (%)	Group 1 (severe)	Group 2 (moderate)	Group 3 (mild)	Group 4 (normal)	Total	p-value
Group 1 (<172 pts)	<79%	# of patients	29	73	129	228	459	<0.001
		% within the outcome	6.3%	15.9%	28.1%	49.7%	100%	
		% within the total population	3.9%	9.7%	17.1%	30.3%	61%	
Group 2 (>172 pts)	>79%	# of patients	96	93	67	38	294	
		% within the outcome	32.7%	31.6%	22.8%	12.9%	100%	
		% within the total population	12.7%	12.4%	8.9%	5%	39%	

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