Original Article

Predictive Value of P_{50} in the Clinical Outcome of the Patients with Severe COVID-19 Pneumonia: A Retrospective Cohort Study

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Abstract

Background: The oxygen tension at half-saturation (P50) was found to be increased in patients with respiratory distress. However, the roles of P50 calculated upon hospital admission in predicting the prognosis of severe COVID-19 patients are not well-investigated. Thus, this study aimed to investigate whether P50 values obtained from hypoxic severe COVID-19 patients upon admission were associated with a later need of invasive mechanical ventilation (IMV). This study also aimed at finding independent predictors of IMV.

Materials and Methods: 151 patients with confirmed severe COVID-19 were enrolled in this study between August and December 2020. Overall, 63 (41.7%) progressed to IMV, and 88(58.2%) did not need IMV. Demographic data, clinical outcome, and laboratory measurements were recorded, and P50 was calculated. P50 that discriminated patients required IMV and patients did not require IMV was determined using the ROC curve. The risk factors for the need for IMV were identified through logistic regression.

Results: The calculated P50 of all patients was higher than the normal value (P<0.005). Moreover, P50 was significantly higher in patients who required IMV (P=0.002). ROC curve verified the discriminatory ability of P50, providing an area under the ROC curve of 0.647(95%CI 0.558-0.736; P=0.002) for a cutoff of 29.29mmHg. Calculated P50≥29.29mmHg was a risk factor for the need of IMV (OR=3.306, 95%CI 1.676-6.525; P=0.001). In multivariate analysis, the independent predictors of the need for IMV were older age, male sex, high P50, high aspartate transaminase, and low PO2 (P<0.05).

Conclusion: Calculated P50 on hospital admission might serve as a promising predictor of IMV in severe COVID-19.

Keywords: COVID-19, Mechanical ventilation, P50, Pneumonia

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Introduction

Pneumonia caused by coronavirus originated in Wuhan, China in late 2019 has spread around the world, becoming a pandemic (1). Clinical records have ranged from febrile respiratory symptoms without hypoxemia, progression to invasive mechanical ventilation, even organ dysfunction, and death (2). In

recent studies, around 5% of patients with COVID-19 were admitted to the intensive care unit (ICU), and 2.3% of patients required invasive mechanical ventilation (IMV) (3). Another study reported that 63.2% of patients admitted to the ICU with covid-19 pneumonia needed IMV (4).

Major risk factors for IMV are old age, male sex, and comorbidities, such as diabetes, cardiac arrhythmias, and renal disease (5). Another retrospective study found that the use of glucocorticoid and increased neutrophil count and lactate dehydrogenase were predictive indicators of IMV among patients with COVID-19 (6). Identifying the early predictors of IMV upon hospital admission becomes critically significant as it could identify high-risk patients requiring closer monitoring for signs of deterioration to decrease progression to respiratory distress and improve patients' prognosis (5).

The oxyhemoglobin dissociation curve (ODC) relates the hemoglobin oxygen saturation (SO_2) to the partial pressure of oxygen (PO_2) in the blood to describe how the hemoglobin molecule acquires and releases oxygen. P_{50} is the oxygen tension at 50% saturation of hemoglobin which is used to indicate hemoglobin oxygen affinity. Low-affinity hemoglobin is higher than P_{50}, and high-affinity hemoglobin a lower than P_{50} (7).

A previous study had suggested that the P_{50} is significantly increased with shifted ODC to the right in patients with acute respiratory distress syndrome (ARDS), which is considered a protective mechanism against tissue hypoxia by decreasing hemoglobin oxygen affinity (8).

To our knowledge, the roles of P_{50} calculated on hospital admission in predicting the prognosis of severe COVID-19 patients are not well-investigated, and there are no sufficient data about the change in oxygen affinity that occurs early in severe COVID-19 pneumonia.

Thus, this study evaluated whether P_{50} levels obtained from hypoxic patients with severe COVID-19 on admission to our hospital were associated with the later need of IMV. We also hypothesized that providing a cutoff point for P_{50} on admission may aid the intensivists in differentiating between severe COVID-19 patients regarding the need for IMV, which could help improve patients' prognoses.

Methods

Study design: This retrospective, cohort observational study was conducted following STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations. Ethical approval for this study (approval number R.20.12.1112) was provided by our university's Institutional Research Board (IRB) on Dec 15, 2020. The patient's informed consent was waived as the study carried neither potential risk nor disregarded the patient's privacy.

Patients: Adult patients aged 18 years or older with a positive result for real-time PCR (polymerase chain reaction) assay for COVID-19 RNA from pharyngeal swab samples were included in the study. The patients were admitted to one ICU at the University Isolation Hospital between August and December 2020. Patients intubated on arrival to ICU, pregnant females, and children with COVID-19 infection did not meet the eligibility criteria of this study.

All patients of the study had been diagnosed with severe COVID-19 before admission to the ICU by a respiratory therapist based on these criteria: $SaO_2 \leq 92\%$ in room air, PaO_2/FiO_2 (arterial oxygen partial pressure/fraction of inspired oxygen) less than 300, a respiratory rate more than 30 breaths/min, or radiological evidence (CT) of more than 50% lung infiltrates. Non-severe COVID-19 patients and patients with missing data were excluded from the analysis.

The patients were allocated into two groups: patients who required IMV and patients who did not require IMV. The latter included either non-mechanical ventilation (simple face mask and non-rebreathing reservoir mask) or noninvasive mechanical ventilation [high-frequency nasal cannula, continuous positive airway pressure (CPAP), biphasic intermittent positive airway pressure (BIPAP)]. A consultant intensivist made decisions on the need for IMV when oxygen therapy (≥10 l/min) with target O_2 saturation (90%-94%) and noninvasive mechanical ventilation were ineffective and when the respiratory rate was> 25 breaths/min, with signs of acute respiratory failure despite maximal oxygen therapy.

Collected data: Data regarding age, sex, and

comorbidities (hypertension, diabetes, ischemic heart disease, renal dysfunction) were recorded upon hospital admission. Initial routine laboratory parameters were checked for each participant: complete blood count (CBC); arterial blood gases (ABG) [pH, arterial carbon dioxide tension ($PaCO_2$), arterial oxygen tension (PaO_2), arterial O_2 saturation (SaO_2)]; liver function tests [albumin, total bilirubin, aspartate transaminase (AST), alanine transaminase (ALT)]; and coagulation profile [prothrombin time, international normalized ratio (INR), D-dimer].

P_{50} was calculated according to the Hill equation (9, 10). Calculated P_{50} would be compared to the standard value of 26.7 mmHg (11).

$$P_{50}= PO_2\times \left[\frac{1-SO2}{SO2}\right]^{1/n} \quad \text{where n = 2.711}$$

End Point: The primary endpoint of this study was to evaluate the value of the initial P_{50} calculated upon hospital admission to predict the need for IMV and to define a cutoff point for P_{50} to aid clinicians in risk stratification of patients regarding the progression of IMV. This study also aimed to find other predictors that help detect severe COVID-19 patients with a high risk for IMV as a secondary endpoint.

Statistical analysis: Statistical Package for the Social Science (SPSS) software (version 25.0) was used to analyze the entered data. The Chi-square test was used for categorical variables to analyze Differences between the two groups. The Kolmogorov-Smirnov test initially tested the normality of continuous variables with data being normally distributed if P-value more than 0.05. We used independent samples t-test to compare normally distributed continuous variables, whereas the Mann–Whitney U-test was used for the non-normally distributed data. One sample Wilcoxon test was used to compare calculated P_{50} to a standard value of 26.7mmHg in severe COVID-19 patients.

A receiver-operating characteristic (ROC) curve was applied for evaluating the accuracy of the calculated P_{50} for predicting the need for IMV (12). The optimal cutoff point of the P_{50} (at which sensitivity and specificity would be maximal and false-positive results would be minimal) was defined. Standard (univariate) logistic regression was applied to predict the likelihood of the need for IMV using only one predictor. To create a prediction model, the multivariate logistic regression model was applied to detect significant "independent" predictors with their OR (95% CI) using significant variables at the univariate analysis. Results were considered statistically significant for any used tests if P-value was less than 0.050.

Power analysis for P_{50} cutoff value: Using PASS 2020 software for Windows, a sample of 63 from the positive group (with IMV) and 88 from the negative group (without IMV) achieved 95% power to identify a difference of 0.1470 between the area under the ROC curve (AUC) under the null hypothesis of 0.5000 and an AUC under the alternative hypothesis of 0.6470 using a one-sided z-test at a significance level of 0.050. The data were continuous responses. The AUC was computed between false-positive rates of 0.000 and 1.000. The ratio of the standard deviation of the responses in the negative group to the standard deviation of the responses in the positive group was 1.000.

Results

Patients' characteristics: 170 ICU patients were eligible for enrollment (Fig. 1). Of these, 19 patients were excluded (12 patients were diagnosed as moderate COVID-19 upon hospital admission, and seven patients had missing initial ABG on the day of hospital admission), leaving 151 severe COVID-19 patients included in our cohort study. Overall, 63 (41.7%) progressed to IMV, and 88 (58.2%) did not need IMV.

Table 1 shows the differences between patients who progressed to IMV and patients who did not need IMV. There were no significant differences in age and frequency of comorbidities between the two groups (P>0.05). Male patients were more prone to IMV than females (P=0.005). Patients who required IMV tend to have rapid RR than other patients (median 28 vs. 24 breaths/min, P=0.01). Of the IMV group, there were 61 patients (96.8%) died at the final follow-up of this study, whereas only 2 patients died (2.3%) among patients who did not need IMV (P<0.005).

Regarding laboratory data, PO_2 and SO_2 were

Table 1: Comparison between patients who required IMV and patients who did not require IMV

parameter	All patients (n=151)	Invasive mechanical ventilation (n=63)	Without invasive mechanical ventilation (n=88)	P
Age (years)	63 [56 to 70]	64 [57 to 73]	61 [55 to 67]	*0.06
Sex				
Male	83(54.9%)	43(68.3%)	40(45.5%)	**0.005
Female	68(45.1%)	20(31.7%)	48(54.5%)	
Respiratory rate (breaths/min)	24 [22 to 28]	28 [22 to 30]	24 [22 to 25]	*0.01
Clinical outcome				
Dead	63(41.8%)	61(96.8%)	2(2.3%)	**<0.005
Improved	88(58.2%)	2(3.2%)	86(97.7%)	
Arterial blood gases				
PH	7.4 [7.34 to 7.44]	7.4[7.32 to 7.47]	7.4 [7.35 to 7.44]	*0.105
PCO_2 (mmHg)	38.3 [33.0 to 44.0]	40[33 to 47.5]	37.9 [33.1 to 42]	*0.1
PO_2 (mmHg)	56.6 [42 to 70.1]	45.6[37.8 to 60.9]	63.3 [47.4 to 80.1]	*<0.005
SO_2 (%)	86.8 [69 to 92.6]	73.1[60 to 88.8]	89.9 [78.3 to 94.7]	*<0.005
Na^+ ($mmol.l^{-1}$)	140 [136 to144]	141[136 to146]	140 [135 to 143]	*0.225
K^+($mmol.l^{-1}$)	3.7 [3.4 to 4.3]	3.8[3.5 to 4.4]	3.7 [3.4 to 4.2]	*0.201
Complete blood count				
RBCs ($m.ul^{-1}$)	4.55±0.772	4.48±0.745	4.60±0.790	***0.346
Hb ($g.dl^{-1}$)	12.43±2.7	12.29±2.09	12.52±12.15	***0.616
Hct (%)	37.75±5.93	37.99±6.1	37.595±5.85	***0.696
WBCs ($\times 10^3 ml^{-1}$)	9.5 [7.0 to13.2]	9.5 [7.0 to 12.8]	9.5 [7.1 to13.15]	*0.582
Lymphocyte ($\times 10^{3.} ml^{-1}$)	1.34 [0.99 to 1.8]	1.3 [0.90 to 1.7]	1.4 [1 to 2.18]	*0.095
Lymphocyte (%)	14.3 [9.6 to	14.1 [9.1 to 20]	14.5 [9.9 to 20.8]	*0.507

	20.4]			
Platelet ($k.ul^{-1}$)	202 [158 to 271]	199 [156 to 257]	210 [162 to 298]	*0.313
Liver function tests				
Serum albumin ($g.dl^{-1}$)	3.4 [3 to 3.6]	3.3 [2.9 to 3.6]	3.5 [3.2 to 3.7]	*0.214
ALT($U.l^{-1}$)	35 [23 to 52.5]	43 [28.5 to 72.5]	30 [20.5 to 43.5]	*<0.005
AST($U.l^{-1}$)	39.7 [28.7 to 55.5]	40 [32.5 to 74.5]	39([26 to 49.5]	*0.02
Serum total bilirubin ($mg.dl^{-1}$)	0.7 [0.6 to 0.8]	0.8 [0.6 to 0.8]	0.7 [0.6 to 0.8]	*0.12
Coagulation profile				
Prothrombin time (sec)	14.6 [13 to 15.9]	14.7 [13 to 16.5]	14.3 [13 to15.9]	*0.314
INR	1.1 [1 to 1.2]	1 [1 to 1.2]	1 [1 to1.2]	*0.823
D-dimer ($ng.ml^{-1}$)	420 [210 to 1350]	720 [400 to 2070]	320 [190 to715]	*0.01
Comorbidities				
Hypertension				
Yes	74(49%)	33(52.4%)	41(46.6%)	**0.483
NO	77(51%)	30(47.6%)	47(53.4%)	
DM				
Yes	59(34.5%)	20(31.7%)	39(44.3%)	**0.118
NO	92(65.5%)	43(68.3%)	49(55.7%)	
IHD				
Yes	17(11.3%)	7(11.1%)	10(11.4%)	**0.961
NO	134(88.7%)	56(88.9%)	78(88.6%)	

CKD				
Yes	5(3.3%)	0(0.0%)	5(5.7%)	**0.054
NO	146(96.7%)	63(100%)	83(94.3%)	

P-value by *Mann–Whitney U test [data are presented as median (IQR)]; P-value by **Chi-square test [data are presented as count (percentage)]; P-value by ***Independent samples t-test [data are presented as mean ± SD]. Abbreviations: df, degree of freedom; ALT, alanine transaminase; AST, aspartate transaminase; INR; international normalized ratio; DM, diabetes mellitus; IHD, ischaemic heart disease; CKD, chronic kidney disease).

statistically significantly lower in patients who needed IMV (P<0.005). Moreover, there was a significant increase in ALT (P<0.005), AST (P=0.02), and D-dimer (P=0.01) in patients who required IMV. Simultaneously, other laboratory variables were comparable in both groups (P>0.05).

Analysis of P_{50} and its cut-off value via Receiver-operator characteristic curve: The calculated P_{50} was statistically significantly higher in the total severe patients than the standard P_{50} value [median 29.12mmHg (IQR: 26.32 to 32.12), P<0.005] using one-sample Wilcoxon test. Furthermore, P_{50} was significantly increased in patients who progressed to IMV [median 31.1mmHg (IQR: 27.28 to 32.99) than patients who did not need IMV [median 28.4mmHg (IQR: 25.94 to 31.34); P= 0.002) (Table 2).

The area under the ROC curve (AUC) for calculated P_{50} was 0.647 (95% CI 0.558 to 0.736; P= 0.002), suggesting that this test had a reasonably good capability to predict the need of IMV (Figure 2), with a sensitivity of 65%, and a specificity of 63% for a cutoff point of 29.29. Patients with calculated P_{50} ≥29.29 mmHg had nearly three times higher odds to exhibit the need for IMV (Table 2).

Table 2: Comparison between patients who required IMV and patients who did not require IMV as regards P50, and the cut-off point of P50.

Parameter	**Invasive mechanical ventilation (n=63)**	**Without invasive mechanical ventilation (n=88)**	**P1**	**Crude OR 95%CI**	**P2**
P50,mmHg	31.1 [27.28 to 32.99]	28.4 [25.94 to 31.34]	*0.002	--	--
P50 cut off value of ≥ 29.29mmHg	41 (65.1%)	33(37.5%)	**0.001	3.306 [1.676 to 6.525]	0.001
P50 cut off value of < 29.29mmHg	22 (34.9%)	55(62.5%)			

P-value by *Mann–Whitney U test [data are presented as median (IQR)]; P1value by **Chi-square test [data are presented as count (percentage)]; P2value by binary logistic regression analysis for predicting the likelihood of the need of IMV. Abbreviations: crude OR, crude odds ratio; 95% CI, 95% confidence interval.

Table 3: Univariate logistic regression analysis for predicting the likelihood of the need for IMV among severe COVID-19 patients.

Parameter	Crude OR	95% CI		P
		Lower	Upper	
Age	1.036	1.003	1.070	0.03
Sex	2.447	1.207	4.959	0.01
RR	1.308	1.044	1.639	0.02
P50	1.083	1.006	1.067	0.034
PO_2	0.936	0.910	0.963	<0.005
SO_2	0.937	0.913	0.962	<0.005
ALT	1.008	0.998	1.017	0.114
AST	1.024	1.008	1.040	0.003
D-dimer	1.000	1.000	1.000	0.555

P-value by univariate logistic regression analysis. Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; RR, respiratory rate; Crude OR, crude odds ratio; 95% CI, 95% confidence interval.

Risk factors for invasive mechanical ventilation

Univariate logistic regression analysis illustrated that older age (P=0.03), male sex (P= 0.01), increased RR (P=0.01), high P_{50} (P=0.034), and increased AST (P=0.003) were denoted to be significant positive predictors of the need of IMV among severe COVID-19 patients, whereas PO_2 (P<0.005), and SO2 (P<0.005) were displayed to be negative predictors of the need of IMV (Table 3).

The multivariable logistic regression model posed statistical significance, $\chi^2(df) = 67.873(7)$, P<0.005. The model correctly classified 75.4% of cases. Specificity and NPV were 80.2%, whereas sensitivity and PPV were 67.3%. Older age, male sex, high P_{50}, high AST, and low PO_2 remained significantly associated with the need for IMV. The odds ratio of IMV increased 1.050-fold for older age (95%CI 1.006 to1.097; P=0.027), 2.893-fold for the male sex (95%CI 1.075 to 7.790; P=0.027), 1.254-fold for the high P_{50} (95%CI 1.005 to 1.226; P=0.019), and 1.035-fold for the increased serum AST (95%CI 1.013 to 1.059; P=0.002), whereas PO_2 was a significant negative independent predictor of IMV; PO_2 had 0.840 times lower odds to exhibit the need of IMV (95%CI, 0.750 to 0.942; P=0.003) (Table 4).

Discussion

In this retrospective study of severe COVID-19 patients, age, sex, frequency of comorbidities, CBC, ABG, liver function tests, and coagulation profile were compared between patients who progressed to IMV and patients who did not progress to IMV.

The median age of severe patients of this study was 63 years [IQR: 56 to70], which is similar to the results of a study of the characteristics of COVID-19 patients (13). This study also reported that males were more vulnerable to IMV than females (P=0.005), suggesting that males are more prone to the bad prognosis and fatality associated with IMV and more likely to develop severe complications. This result was

Table 4: Predictors of the likelihood of the need for IMV among severe COVID-19 patients.

Predictor	Partial regression coefficient B	S.E.	Wald	P	OR [95%CI]
Age	0.049	0.022	4.914	0.027	1.050 [1.006 to 1.097]
Sex					
Female					2.893
Male	1.062	0.505	4.420	0.036	[1.075 to 7.790]
RR	0.043	0.025	2.799	0.094	1.044 [0.993 to 1.097]
P50	0.227	0.097	5.518	0.019	1.110 [1.005 to 1.226]
PO_2	-0.174	0.058	8.942	0.003	0.840 [0.750 to 0.942]
SO_2	0.101	0.056	3.296	0.069	1.107 [0.992 to 1.234]
AST	0.035	0.011	9.325	0.002	1.035 [1.013 to1.059]

P-value by Binomial (multivariate) logistic regression analysis. Abbreviations: AST, aspartate transaminase; RR, respiratory rate; SE, standard error; OR, odds ratio.

consistent with other studies that demonstrated that males might be more susceptible to receiving mechanical ventilation (6, 14) and more vulnerable to lethality (15).

In this study, patients who progressed to IMV tend to have more rapid RR than patients who did not progress to IMV. These results are consistent with other studies showing that rapid RR is associated with the risk of clinical deterioration (16-18).

Regarding ABG, our study demonstrated no significant differences in PH and PCO_2 between severe patients who progressed to IMV and other patients. pH and pCO_2 are recognized to influence the hemoglobin oxygen affinity and the ODC (19), so the difference in P_{50} observed between both groups was not attributed to the change in pCO_2 and pH.

In this study, PO_2 and SO_2 are statistically significantly lower in severe COVID-19 patients who needed IMV, demonstrating that patients requiring IMV had worse oxygenation. This result agreed with other studies which showed that SO_2 was significantly lower in severe patients than non-severe patients (20) and patients requiring mechanical ventilation (5).

This study demonstrated higher initial ALT and AST levels for patients who progressed to IMV, suggesting more severe liver chemistry abnormalities. This finding is consistent with the result of a meta-analysis that disclosed that elevated serum activity of aminotransferase is associated with severe COVID-19, and higher mortality (21). Direct viral cytotoxicity by way of angiotensin-converting enzyme-2, use of hepatotoxic medications, an immune-related injury, and passive hepatic congestion may explain hepatic injury recognized among patients with COVID-19

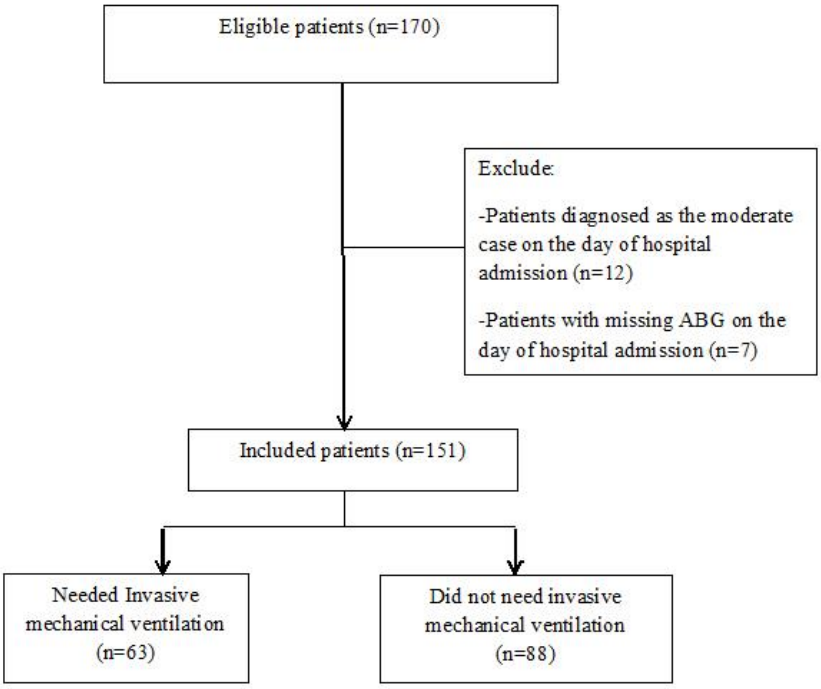

Figure 1. Flowchart of study participants.

infection (22).

Regarding calculated P_{50}, P_{50} was found to be increased in all patients in the study (median 29.11 mmHg) than the normal value (26.7mmHg), reflecting a right shift of ODC (i.e. lower Hb-O_2 affinity). Furthermore, calculated P_{50} was significantly higher in patients who progressed to IMV than patients who did not need IMV (P=0.002). This finding suggested that higher levels of calculated P_{50} upon hospital admission might function as a prognostic indicator of COVID-19 severity as patients with higher P_{50} were more susceptible to receiving IMV. Likely, the change in Hb-O_2 affinity that occurs early in COVID-19 infection may suggest the severity of the disease, even if clinical deterioration occurs later on.

This result was consistent with the study done by Clerbaux et al. (8) on patients with non-COVID ARDS, as they found higher levels of P_{50} with the right shift of ODC. In such a patient, hypoxia was likely severe enough to stimulate the 2,3-diphosphoglycerate (2,3-DPG) synthesis and induce a right shift of the ODC.

In contrast to our results, a retrospective study conducted on intubated and ventilated COVID-19 patients in an ICU had found a lower P_{50} than the standard value (i.e. left shift of the ODC) (23). The left shift in the ODC in this study (i.e. higher Hb-O_2 affinity) may be attributed to adaptation to a long period of hypoxia because blood samples were collected in the ICU after a long time of the disease process.

Another study compared the ODC of 21 critically ill COVID-19 patients to 21 non-COVID-19 respiratory distress patients admitted to ICU and results demonstrated no abnormality in ODC and Hb-O_2 affinity in patients with COVID-19 (24). This discrepancy might be due to the response to the period of hypoxia because their samples were also collected late in ICU, making them less useful in predicting later outcomes than admission values.

Furthermore, our ROC curve analysis demonstrated that the P_{50} level with a cutoff value

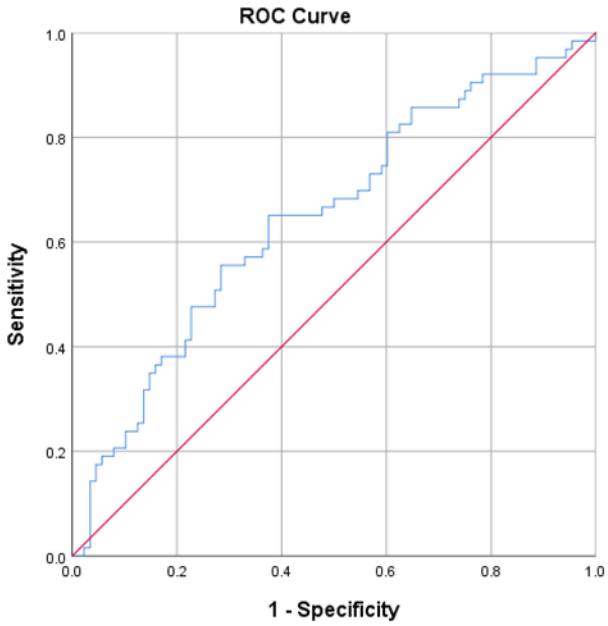

Figure 2. ROC curve analysis for the calculated P50 for predicting the need of IMV, with an area under ROC curve of 0.647, P=0.002.

of≥29.29 mmHg could discriminate between severe COVID-19 patients who progressed to IMV and other severe patients who did not require IMV upon hospital admission. Early discrimination between them will guide the clinicians to emphasize providing full and accurate care to patients with high calculated P_{50}≥29.29 mmHg. Our results can only be considered preliminary hypotheses, and hence, further studies with a larger sample size are needed to confirm these results.

As the health burden of the COVID-19 pandemic increases, the need to predict the progression to IMV among severe COVID-19 patients increases so that the hospitals can deal efficiently with the pandemic by providing necessary medical resources, ICU beds, and mechanical ventilators. Toward this direction, we had created a prediction model in which the univariate and multivariate analysis revealed that older age and male sex were independent predictors of IMV. Multiple studies had illustrated that old age and male sex were predictive indicators of IMV [5] and death in COVID-19 patients (25,26).

Moreover, our data demonstrated that a higher level of P_{50} was a risk factor for the need of IMV in severe COVID-19 patients with 1.11 times higher odds for IMV; this observation raises the possibility of using P_{50}, at the time of hospital admission, as a marker to identify patients who are more likely to progress to IMV; however, this finding requires validation in a larger cohort before they can become clinically applied.

Besides, the multivariable logistic regression model demonstrated that low PO_2 is a significant predictor of the need for IMV. This result was in line with a study carried out by singer et al.(27), which demonstrated that hypoxemia was an independent predictor of IMV in patients with COVID-19.

Additionally, increased AST level on admission was a risk factor for IMV in patients with severe COVID-19 pneumonia with 1.035 times higher odds for IMV, whereas ALT was dropped out during the univariate regression. This finding was following a study of children ventilated for respiratory syncytial virus bronchiolitis in which elevated AST levels on admission (but not elevated ALT levels) were associated with more severe disease measured by duration of mechanical ventilation and length of ICU admission (28). This would suggest that AST prioritizes conditions involving systemic injury because AST is widely expressed in many tissues involving skeletal muscles, heart, lung, and

erythrocytes, while ALT is predominantly from the liver.

RR is a contributing factor to the prognosis of COVID-19 patients as ICU admission and mortality are associated with significantly higher RR values (17, 18), while in this study, it was dropped out during the multivariate regression analysis.

Obtaining these promising results concerning the calculated P_{50} may open the way for a more in-depth analysis of the significance of calculated P_{50} upon hospital admission as a novel marker for COVID-19 severity. Our study just shed light on the role of P_{50} in the risk stratification of patients with COVID-19 that should be taken into consideration.

Conclusion

This study concluded that severe COVID-19 patients with higher admission P_{50} values were more likely to end up receiving IMV during their hospitalization or, at the least, calculated P_{50} may help guide clinicians for aggressive supportive care for the high-risk group. This study also noticed that older age, male sex, high P_{50}, high AST, and low PO_2 were independently predictive of the need for IMV among patients with severe COVID-19 pneumonia.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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