Oxygenation Indicators as a Predictor of Early Mortality in Critically ill Patients with COVID-19

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ABSTRACT

Objective: In the follow-up of Coronavirus disease 2019 (COVID-19), the predictors of prognosis and mortality are important for early initiation of treatments to reduce the severity of disease and for preventing death. There are many biochemical parameters used as early mortality markers in COVID-19 patients. However, there is not a sufficient number of studies on the predictive role of oxygen markers.

Methods: Prospectively designed study which was approved by the local ethics committee (2021/514/200/33) included 122 patients with COVID-19-associated acute respiratory distress syndrome (CARDS). The patients were divided into two groups discharged (Group-D) and deceased (Group-E). Demographic data och oxygenation and biochemical values of the patients, length of stay in intensive care unit (ICU), intubation duration, the status of discharge and mortality were recorded for each patient.

Results: There was no significant difference between the two groups in terms of the values of Oxygen saturation, partial pressure of oxygen, and arterial oxygen content first measured at the ICU. On the other hand, a significant difference was observed between the two groups in the parameters of oxygenation index (OI), oxygenation saturation index (OSI), P/F, S/F, ScvO₂, and the APACHE II and SOFA scores, the number of intubated days, and lactate, ferritin, and IL-6 (p<0.05). ROC curve and logistic regression analyses were performed for these variables and cut-off points were calculated. The OI (>7, AUC: 0.798, p=0.001) and OSI (>4.5, AUC: 0.805, p=0.001) indicators were determined to be the strongest independent variables for mortality. It was observed that mortality increased 23 times when OI \geq 7, and 40 times when OSI \geq 4.5.

Conclusion: OI and OSI were found to be significant independent variables in predicting mortality in ICU admissions with the diagnosis of CARDS. In addition, in our study, it was determined that among these noninvasively studied parameters, the S/F ratio was as valuable as P/F and OI was as a strong predictor as OSI.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory infection caused by the SARS-CoV-2 virus, and one of its most important features is that it causes profound hypoxemia. Even if most of the infected individuals develop mild disease and no significant complications develop afterward, 5% of the cases require hospitalization in the intensive care unit (ICU).^[1,2] Although most of the infected individuals develop the mild disease and also in developing a significant complication afterward, 5% require admission to the ICU.^[1,2]

The need for intubation and mechanical ventilation support in critically ill patients varies between 42% and 100%. $^{[3]}$

It is known that Acute Respiratory Distress Syndrome

(CARDS) developing in patients with COVID-19 who are followed in ICUs has a different course from typical ARDS.^[4] Ground-glass opacities showing interstitial involvement on computed tomography are considered early signs while dense consolidation on tomography image refers to the later stage of the disease. The images are in favor of bilateral multifocal involvement and there is a tendency to involve the lower lobes of the lung.^[5] The main difference between CARDS is the respiratory mechanics, which are relatively protected depending on the severity of hypoxemia.^[6] While lung compliance is generally low in patients who are followed up with typical ARDS, lung compliance may be high or low in CARDS.^[7] In addition, micro and macro thrombosis, pulmonary thrombosis, ventilation-perfusion imbalance due to pulmonary vasoregulation, diffuse intravascular coagulation, and bleeding can be seen in CARDS that progresses with vascular endothelial damage.^[8] As it turned out, ARDS secondary to COVID-19 seems to have worse outcomes than ARDS that develop due to other causes, and the mortality rate in critical cases can rise up to 74%.^[1]

Oxygen saturation (SpO_2) value and partial pressure of oxygen (PaO_2) are commonly used in the monitoring of hypoxemia.^[9] Other invasive or non-invasive methods may also be preferred when identifying hypoxemia. In invasive methods, blood gas is measured from the artery or central catheter. As a result, arterial oxygen content (CaO_2) , Horowitz ratio (PaO_2/FiO_2) (P/F), central venous oxygen saturation $(ScvO_2)$, and oxygenation index (OI) values can be determined. The oxygenation saturation index (OSI) and SpO_2/FiO_2 (S/F) ratio can be monitored using non-invasive methods.

In the light of all this information, it is clear that determining the degree of hypoxemia is important in the diagnosis, follow-up, and treatment of CARDS. However, there is not a sufficient number of studies in the literature addressing the place of oxygen indicators measured with invasive and non-invasive methods in clinical prediction. In this study, we investigated the effectiveness of oxygenation indicators in the detection of hypoxemia during admission to the ICU and their role in the prediction of mortality in severe COVID-19 cases.

MATERIALS AND METHODS

Study design and participants

Our study was conducted at a city hospital that rendered active service during the pandemic with 1100 beds and 140 intensive care beds. Following the approval of the Institutional Ethics Committee (Ethics Committee No: 2021/514/200/33) and the provision of informed consent by all study participants, this prospective observational study was initiated. The study was carried out in line with the ethical principles stated in the Declaration of Helsinki and Good Clinical Practices.

The study included 122 intubated adult patients who were admitted to the ICU between April and September 2021, whose real-time reverse transcriptase-polymerase chain reaction test was positive for SARS-CoV-2 RNA and/or whose chest tomography was compatible with CARDS. The diagnosis of ARDS was made according to the Berlin Diagnostic Criteria.^[10]

ASA III patients with a hematological disease, anemia, heart failure, or severe comorbidity (such as progressive Stage 4 malignancy, pulmonary embolism, diabetic ketoacidosis, advanced chronic kidney disease, acute liver failure, pregnancy, and acute myocardial infarction) were excluded from the study. Death or discharge from the ICU was considered the endpoint of the study. The patients were divided into two groups as Group D and Group E. Group D was consisted of patients that were discharged and Group E was the group of patients that died.

Data collection

Demographic data of the patients, APACHE-II Score, SOFA Score, number of days intubated, length of stay in the ICU, and exitus or discharge status were recorded.

After the patients were admitted to the ICU, their arterial blood gas, central venous blood gas, and complete blood count were simultaneously evaluated.

The following oxygenation parameters were measured and recorded:^[11]

- Peripheral SpO₂
- The PaO₂ in arterial blood
- P/F=PaO₂/FiO₂ (Horowitz ratio)
- S/F=SpO₂/FiO₂
- ScvO₂
- CaO₂ (1.34 × hemoglobin concentration × SpO₂)+ (0.0031 × PaO₂)
- Arterial OI: FiO₂ × mean airway pressure×100/PaO₂
- OSI: FiO₂ × mean airway pressure×100)/SpO₂

Higher OI and OSI values were considered indicators of worse oxygenation. Other elevated parameters were accepted as an indication of good oxygenation. The effects of the variables between the two groups on mortality were determined and cut-off values were calculated for these markers.

Furthermore, the highest Lactate, IL-6, Ferritin, C-reactive protein (CRP), and Procalcitonin values and the lowest Lymphocyte values were recorded in both groups.

Statistical analysis

The IBM SPSS 22 software was used for data analysis. Descriptive statistics (mean, standard deviation, median, frequency) were used in the analysis of the study data. Correlation analysis was performed with the Pearson and Spearman correlation methods. The Student's t test and the Mann–Whitney U test were used for quantitative comparisons of patients that died and those that survived, and the Chi-square and Fisher's exact tests were used for qualitative comparisons. Logistic regression analysis was performed to investigate independent risk factors that are indicative of mortality. Cut-off values of the data were determined by ROC analysis. ROC curves were prepared for important quantitative data, and sensitivity and specificity were calculated. P<0.05 was considered statistically significant.

RESULTS

From April 1, 2021, to September 1, 2021, 424 patients with a diagnosis of COVID-19 were admitted to the ICU. Of those patients, 122 met the inclusion criteria of this study. The average age of patients was 60.09 ± 16.50 years and 63.9% (78 patients) were male. The mean length of stay in the ICU was calculated as 9.32 ± 5.88 days and the

mean number of days they were followed up as intubated was 6.86 ± 5.32 days.

The patients were divided into two groups Group D and Group E, the former consisted of patients that were discharged and the latter was the group of patients that died. No significant difference was observed between the groups regarding their demographics (Tables I and 2). Group E had significantly higher APACHE-II and SOFA scores, and lactate, IL-6, Ferritin, OI, and OSI levels but significantly lower MAP, P/F ratio, S/F ratio, ScvO₂ (p<0.05, Table I). However, there was no significant difference between the two groups in other parameters.

The logistic regression analysis revealed that OI and OSI were independent predictors and the strongest predictors of early mortality (AUC 0.798 and AUC 0.805, Tables 3, 4 and Fig. 1). The optimal cut-off points for prognosis were calculated as 4.5 for OSI and 7 for OI. In patients that had an OSI of >4.5 in the ROC analysis, mortality was ob-



Figure 1. Diagonal segments are produced by ties.

		E (n=31) ality +	-	0 (n=91) arge +	р
	Average	SD	Average	SD	
Age	55.48	14.688	61.66	16.872	.072
Gender					
Female	12		32		.723
Male	19		59		
Comorbidity	14		41		.992
Number of ICU days	9.97	6.205	9.10	5.785	.480
Number of intubated days	9.97	6.205	5.55	4.738	.001***
APACHE-II Score	30.42	3.695	16.37	8.469	.000***
SOFA Score	5.78	1.37	3.13	1.72	.03***
MAP	65.48	9.323	84.46	14.565	.000***
SpO,	89.94	5.910	89.16	4.817	.470
PaO,	61.03	20.183	68.12	21.393	.109
P/F	106.60	61.412	143.84	60.822	.004**
S/F	123.6	50.790	185.8	38.91	.000***
Lactate	4.41	2.475	2.25	1.277	.000***
ScvO ₂	51.15	16.649	65.14	10.968	.000***
CaO	1369.86	296.634	1460.76	297.120	.143
OI	12.89	12.486	4.00	2.133	.000***
OSI	7.21	4.770	2.84	1.392	.000***
IL-6	898.09	1198.497	106.60	164.651	.000***
Ferritin	3810.12	9318.328	851.89	766.731	.003**
CRP	112.15	84.295	96.54	87.437	.388
РСТ	4.73	12.054	2.36	13.976	.401
Lymphocyte	973.61	1742.426	1021.32	861.805	.842
Hgb	12.44	2.268	11.79	2.432	.194
Htc	37.84	6.121	35.41	7.014	.088

 Table 1.
 Factors affecting mortality in the intensive care unit

Student's t test was used for age, SOFA Score, MAP, Spo₂, Chi square test was used for comorbidity and gender, and Mann Whitney U test was used for others. **P<0.01; **P<0.001; P<0.05 statistically significant.

ICU: Intensive care unit; MAP: Mean arterial pressure; PaO₂: Arterial oxygen pressure; SpO₂: Oxygen saturation; OSI: Oxygen saturation index; OI: Oxygen Index; S/F ratio: SpO₂/FiO₂; P/F Ratio: PaO₂/FiO₂; ScvO₂: Central venous oxygen saturation; CaO₂: Arterial oxygen content; APACHE II: Acute Physiology and Chronic Health Evaluation; CRP: C-reactive protein; PCT: Procalcitonin.

Table 2. Median values of	f parameters affe	cting mortality
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	G	iroup D (n=91 Discharge +)	G	roup E (n=3 Mortality +	,	р
	Median	IQR25	IQR75	Median	IQR25	IQR75	
Number of ICU days	7.00	6.00	10.00	9.00	6.00	12.00	.480
Number of intubated days	0.00	0.00	0.00	6.00	3.00	8.00	.001***
APACHE-II Score	14.00	9.00	23.00	31.00	28.00	33.00	.000***
PaO,	63.00	55.00	71.00	60.00	46.00	71.00	.109
P/F	132.00	107.50	162.50	84.00	65.00	150.00	.004**
S/F	2.18	1.72	102.22	116.25	88.00	160.00	.000***
Lactate	1.80	1.40	2.70	3.60	2.10	6.50	.000***
ScvO ₂	65.00	59.00	71.00	55.00	34.00	64.00	.000***
Oİ	3.43	2.56	5.12	8.62	4.22	21.54	.000***
Osi	2.61	1.84	3.17	5.93	3.15	12.50	.000***
IL-6	50.00	20.08	112.95	290.00	111.25	1321.00	.000***
FERRITIN	665.00	313.75	1262.75	1599.00	577.00	3827.00	.003**
CRP	66.50	31.00	140.00	96.00	45.00	163.00	.388
PCT	0.23	0.10	0.65	0.55	0.16	1.55	.401
Lymphocyte	780.00	500.00	1300.00	460.00	320.00	870.00	.842

Mann-Whitney U test. **P<0.01; ***P<0.001; P<0.05 statistically significant.

ICU: Intensive care unit; PaO,: Arterial oxygen pressure; OSI: Oxygen saturation index; OI: Oxygen Index; S/F ratio: SpO,/FiO,; P/F Ratio: PaO,/FiO,; ScvO,: Central venous oxygen saturation; APACHE II: Acute Physiology and Chronic Health Evaluation; CRP: C-reactive protein; PCT: Procalcitonin.

Table 3.	Roc Anal	ysis of the	parameters
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	Area Under the Curve								
Test result variable(s)	Test result variable(s) Area Std. Error ^a Cut-off Asymptotic Sig. ^b Asymptotic 95% Co								
					Lower Bound	Upper Bound			
S/F	.425	.066	125	.000	.754	.896			
ScvO ₂	.259	.055	60	.000	.152	.367			
OI	.798	.053		.000	.694	.903			
OSI	.805	.054		.000	.695	.915			
P/F	.284	.063	95	.000	.160	.408			

ROC analysis. S/F: SpO₂/FiO₂; P/F: PaO₂/FiO₂, ScvO₂; Central venous oxygen saturation; OSI: Oxygen saturation index; OI: Oxygen index.

Table 4.	The performance levels of the tested variables according to the calculated Aucs
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	Sensitivite	Spesifisite	Pozitive predictive value	Negative predictive value	Accuracy
S/F 125	54.8	91.2	68.0	85.6	81.9
P/F 95	58.1	89.0	64.6	86.2	81.2
ScvO ₂ 60	64.5	73.6	45.5	85.9	70.3

served with 64.5% sensitivity and 92.3% specificity. While the OSI value was ≤4.5 in 92.3% of the patients who were discharged, the OSI was 4.5> in 64.5% of the patients who died. In patients that had an OI >7, mortality was observed with a sensitivity of 61.3% and a specificity of 92.3% (Table 5). While OI was <7 in 92.3% of discharged patients, OI was >7 in 61.3% of patients that died.

In the cut-off value analysis, the death risk of those with an OSI of \geq 4.5 was found to be 40 times higher

(p<0.001). The risk of death for those with an OSI of \geq 7 was found to be 23 times higher (Table 6). In addition, it was determined that the OI and OSI values showed a positive correlation with intubation time, stay at the ICU, the APACHE-II score, and the lactate and ferritin levels (p<0.00), but had a negative correlation with age, MAP, SpO₂, PaO₂, and the P/F and S/F ratios, and ScvO₂ (p<0.05). No significant relationship was found with the other markers (Table 7).

	Exi	tus +	Disch	arge +		
OSI	n	%	n	%	Chi-square	Р
4.5<	20	64.5	7	7.7		
<=4.5	11	35.5	84	92.3	43.32	.00
				value: 88.4%; Accuracy: %		.00
	Specificity: 92.3%; Positiv		%; Negative predictive			
	Specificity: 92.3%; Positiv	ve predictive value: 74.1	%; Negative predictive	value: 88.4%; Accuracy: 9		p
Sensitivity: 64.5%;	Specificity: 92.3%; Positiv	ve predictive value: 74. I tus +	%; Negative predictive Disch	value: 88.4%; Accuracy: 9 harge +	^{685.3}	

Chi square test; p<0.05 statistically significant. Accuracy: 84.5%; Sensitivity: 61.3%; Specificity: 92.3%; Positive predictive value: 73.1%; Negative predictive value: 87.5%.

Table 6.	Impac	t of OI and OSI or	n mortality		
	Sig.	OR	95% CI for OR		
			Lower	Upper	
01	.006	23.090	2.436	218.874	
OSI	.002	40.890	4.110	406.852	

Logistic Regression. OSI: Oxygen saturation index; OI: Oxygen index.

DISCUSSION

In this study, we investigated the effectiveness of oxygen indicators in predicting mortality in patients that were followed up with a diagnosis of CARDS and the correlation of non-invasive markers with invasive markers. OI and OSI values measured at the time of admission were significantly higher and the P/F ratio, S/F ratio, ScvO₂ values were found to be significantly lower in patients who developed mortality. OI and OSI were found to be the strongest independent variables of mortality. It was determined that among non-invasive parameters, the S/F ratio was as valuable as P/F and OI was as a strong predictor as OSI.

Several studies are demonstrating that decreased SpO₂ and PaO, levels in patients with COVID-19 are associated with mortality in the ICUs.^[12,13] In a study conducted with 140 patients, the relationship between mortality and hypoxemia was investigated and it was confirmed that SpO₂ was a predictor of mortality.^[3] However, there is a limited number of studies in the literature regarding the relationship between other oxygen indicators and mortality due to COVID-19 in adult patients. In a recent study by Oliynyk et al.^[14] comparing oxygenation indicators (SpO₂, PaO₂, P/F, oxygen delivery, and oxygen consumption) with healthy subjects, patients were divided into two groups as survival and exitus groups and it was determined that the indicators showed a statistically significant difference in the exitus group of patients diagnosed with COVID-19 (p<0.001). In our study, however, no difference was found between the exitus and survival groups regarding the SpO₂, PaO₂, and CaO₂ values, which are frequently used in the follow-up of COVID-19.

Table 7. Relationship of OI and OSI to all markers

	0		OS	I
	r	Р	r	р
OSI	.896**	.000	-	-
Age	282**	.002	295**	.001
APACHE-II	.389**	.000	.489**	.000
Number of ICU days	.189*	.037	.308**	.001
Number of intubated days	.406**	.000	.535**	.000
MAP	329**	.000	421 ^{**}	.000
SpO ₂	304**	.001	210*	.020
PaO ₂	400**	.000	273**	.002
P/F	526**	.000	536**	.000
S/F	422**	.000	326**	.000
Lactate	.467**	.000	.459**	.000
ScvO ₂	529**	.000	492**	.000
CaO ₂	.005	.958	.042	.646
II-6	.134	.144	.159	.083
Ferritin	.331**	.000	.350**	.000
CRP	.052	.566	.021	.818
PCT	.094	.305	.086	.346
Lymphocyte	.056	.537	.070	.447
Hgb	.065	.477	.080	.380
Hct	.122	.182	.143	.115

Pearson Correlation Analysis. ICU: Intensive care unit; MAP: Mean arterial pressure; PaO_2 : Arterial oxygen pressure; SpO_2 : Oxygen saturation; OSI: Oxygen saturation index; OI: Oxygen Index; S/F ratio: SpO_2/FiO_2 ; P/F Ratio: PaO_2/FiO_2 ; ScvO_2: Central venous oxygen saturation; CaO_2: Arterial oxygen content; APACHE II: Acute Physiology and Chronic Health Evaluation; CRP: C-reactive protein; PCT: Procalcitonin.

However, it was thought that we obtained different results because our sample group consisted of severe cases that required follow-up in the ICU and that all patients who were admitted to the ICU with the diagnosis of CARDS were already severely hypoxemic at the time of admission, even if they did not die during their follow-up.

In the retrospective pilot study conducted by Nozari et al.^[15] with 68 patients, the prognostic importance of

the OI, OSI S/F, and P/F parameters in terms of predicting mortality in patients with COVID-19 was investigated and it was demonstrated that all measurements were associated with mortality in patients who were mechanically ventilated. This study emphasized the importance of the time window for future interventions in patients with COVID-19 and pointed out that large-scale studies are needed to confirm the prognostic value of those indices. In addition to this, our study determined the optimal cut-off points for prognosis as >4.5 for OSI and >7 for OI (p<0.001). Additionally, as a result of the analysis, the death risk of those with an OSI of \geq 4.5 was found to be 40 times higher (p<0.001), and the risk of death for those with an OSI of \geq 7 was found to be 23 times higher.

As a result of the study they conducted with 280 critically ill patients with COVID-19, Lu et al.^[16] defined the S/F value as a non-invasive prognostic marker and reported that it increased mortality 1.82 times (95% CI: 1.56–2.13). Rice et al.^[17] reported that S/F ratios were correlated with P/F ratios, and S/F ratios of 235 and 315 units were equivalent to P/F ratios of 200 and 300 units, respectively, in patients with ARDS. Similarly, it was observed in the present study that the S/F ratios were significantly lower in the mortality group and were in parallel with the P/F ratios. Moreover, it was determined that there was a significant negative correlation between OSI and OI value.

ScvO₂ is a parameter that shows the O₂ saturation of the superior vena cava and jugular vein, measured by the insertion of a catheter in the central vein. ScvO₂ has been associated with increased mortality in the follow-up of sepsis. ^[18] A case series of COVID-19 emphasized the importance of ScvO₂ in the evaluation of hypoxemia and underlined that its use in follow-up can help reduce oxygen toxicity. ^[19] In this study, ScvO₂ was found to be significantly lower in the exitus group (mean value: 51) (p=0.000), and it was also shown to be effective in predicting mortality. However, the necessity of inserting a central catheter makes it difficult to obtain a quick and easy measurement.

Since blood lactate levels show whether oxygen is sufficient for aerobic metabolism, it helps the clinician more precisely and better evaluate oxygen balance and tissue hypoxia. Many studies have demonstrated that high lactate levels in patients with COVID-19 are associated with mortality.^[20] Similarly, in our study, the lactate levels measured at the time of admission were statistically significantly higher than in Group E than in Group D.

Many recent studies demonstrated that biochemical markers are guiding for predicting mortality in patients with COVID-19. Two meta-analyses reported that cardiac troponin, CRP, interleukin-6, creatinine, alanine transferase, lymphocyte, thrombocyte, and albumin can be used as mortality markers.^[21,22] In parallel to these results, we observed in our study that lactate, IL-6, and Ferritin measured at the time of admission were significantly higher in Group E than in Group D. Additionally, our study revealed that ferritin value, the APACHE score, and intubation time were correlated with oxygenation parameters (Table 7). In a case series of 1591 patients with COVID-19 who were admitted to ICUs, it was reported that the majority of patients required mechanical ventilation support and the mortality rate in ICU was 26%. Similarly, the overall mortality rate in our study was 25.4%. It was thought that vaccination might also have an effect on the lower mortality rates compared to the early stages of the pandemic.^[23]

Strengths and Limitations of the Study

The fact that the study is prospective research and such a comprehensive evaluation has not been carried out so far is important in terms of contributing to clinical prediction. The sample size in our study was sufficient to demonstrate statistically significant relationships.

The originality of our study is that the whole study population was a homogeneous group consisting of patients admitted to the ICU with the diagnosis of COVID-19. Furthermore, since the ICU with 140 beds is managed by a single clinic and the same treatment algorithms are applied in our institution, the approach to the patients included in the study was standardized.

Being a single-center study and the low number of patients included can be listed as the limitations of the study.

CONCLUSION

Our study revealed that the OSI and OI parameters can be strong independent indicators of mortality in patients with CARDS. Considering the high mortality rates due to this disease, it was concluded that more widespread use of these parameters, which are thought to be effective in predicting the prognosis of patients and regulating their treatment and can be obtained with simple, non-time-consuming, and easily applicable measurements can guide therapeutic interventions. However, although the clinical and prognostic values of oxygenation indices are well established in ARDS, more studies are needed to confirm their value in patients with COVID-19.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 28.04.2021, Decision No: 2021/514/200/33).

Informed Consent

Prospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: A.S.; Design: F.C., G.C.; Supervision: K.T.S.; Fundings: Y.B.; Materials: H.H.; Data: H.H., Y.B.; Analysis: A.S., G.C.; Literature search: Y.B., K.T.S.; Writing: Y.B.; Critical revision: K.T.S., A.S.

Conflict of Interest

None declared.

REFERENCES

- Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single centered retrospective observational study. Lancet 2020;8:475–81. [CrossRef]
- Tosun Y, Akıncı O, Akdoğan O. Is surgery a risk in recovered COVID-19 patients?. Cerrahpaşa Med J 2022;46:30–4. [CrossRef]
- Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 2020;95:1138–47. [CrossRef]
- Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. JAMA 2020;323:2329–30. [CrossRef]
- Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2. [CrossRef]
- Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a "typical" acute respiratory distress syndrome. Am J Respir Crit Care Med 2020;201:1299–300.
- Gattioni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or Not?. BMC Critical Care 2020;24:154. [CrossRef]
- Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. Med J Aust 2020;213:54–6.e1.
- Sengul D, Sengul I. Connection of reactive oxygen species as an essential actor for the mechanism of phenomena; ischemic preconditioning and postconditioning: Come to age or ripening? North Clin Istanb 2021;8:644–9. [CrossRef]
- ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307:2526–33.
- Agarwal P, Warner MB, Reichner C, LazarousDG. Marino's the ICU book. Ann Am Thorac Soc 2014;11:999.
- Shenoy N, Luchtel R, Gulani P. Considerations for target oxygen saturation in COVID-19 patients: are we under-shooting? BMC Med 2020;18:260. [CrossRef]
- Fink DL, Goldman NR, Cai J, El-Shakankery KH, Sismey GE, Gupta-Wright A, et al. Ratio of oxygen saturation index to guide management of COVID-19 pneumonia. Ann Am Thorac Soc

2021;18:1426-8.

- Oliynyk OV, Rorat M, Barg W. Oxygen metabolism markers as predictors of mortality in severe COVID-19. Int J Infect Dis 2021;103:452–6.
- Nozari A, Mukerji S, Vora M, Garcia A, Park A, Flores N, et al. Postintubation decline in oxygen saturation index predicts mortality in covid-19: a retrospective pilot study. Crit Care Res Pract 2021;6682944. [CrossRef]
- Lu X, Jiang L, Chen T, Wang Y, Zhang B, Hong Y, Wang J, Yan F. Continuously available ratio of SpO2/FiO2 serves as a noninvasive prognostic marker for intensive care patients with COVID-19. Respir Res 2020;21:194. [CrossRef]
- Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB. Comparison of the SpO2/FIO2 ratio and the PaO2/ FIO2 ratio in patients with acute lung injury or ARDS. Chest 2007;132:410–7. [CrossRef]
- Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA. Emergency Medicine Shock Research Network (EMShockNet) Investigators. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA 2010;303:739–46.
- Garg RK, Kimbrough T, Lodhi W, DaSilva I. Systemic oxygen utilization in severe covid-19 respiratory failure: a case series. Indian J Crit Care Med 2021;25:215–8. [CrossRef]
- Doğan N, Doğan S, Pekdemir M, Yılmaz S, Emir D, Teke K. Prediction of mortality, hospitalization and mechanical ventilation need of patients with pneumonia in covid-19 outbreak. KOU Sag Bil Derg 2021;7:130–7. [CrossRef]
- Tian W, Jiang W, Yao J, Nicholson CJ, Li R, Sigurslid HH, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. J Med Virol 2020;92:1875–83.
- Henry BM, Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 2020;58:1021–8.
- Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A et al. Baseline characteristics and Outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA 2020;323:1574–81. [CrossRef]

Kritik COVID-19 Hastalarında Erken Mortalitenin Prediktörü Olarak Oksijenasyon İndikatörleri

Amaç: COVID-19 takibinde, hastalığın şiddetli seyretmesi ve ölümle sonuçlanabilmesi nedeniyle, prognoz ve mortaliteyi öngören belirteçlerinin ortaya konulması önem arz etmektedir.COVID-19 hastalarında erken mortalite belirteci olarak biyokimyasal parametrelerin kullanıldığı bilinmektedir ancak oksijen belirteçleri ile yapılan yeterli sayıda çalışma bulunmamaktadır. Bu çalışmada yoğun bakım kabulü yapılan şiddetli COVID-19 hastalarında, mortalite üzerine etkisi olabilecek oksijenasyon indikatörlerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Prospektif olarak planlanan ve yerel etik kurul onayı alınan çalışmamıza (2021/514/200/33) üçüncü basamak yoğun bakım ünitesine, Nisan-Eylül 2021 tarihleri arasında kabulü yapılan COVID-19 bağlı Akut Respiratuvar Distres Sendromu (CARDS) tanılı 122 hasta dahil edildi. Ölüme neden olabilecek komorbiditesi, hematolojik hastalığı olan hastalar çalışma dışı bırakıldı. Hastalar exitus ile sonuçlanan (Grup-E) ve taburcu-discharge edilen olarak (Grup-D) iki gruba ayrıldı. Hastaların demografik verileri, APACHI-II ve SOFA skoru, arteriyel kandaki kısmi oksijen basıncı (PaO₂), oksijen satürasyonu (SpO₂), arteriyel oksijen kontenti (CaO₂), PaO₂/FiO₂ (P/F) oranı, SpO₂/FiO₂ (S/F) oranı, santral venöz oksijen satürasyonu (ScvO₂), arteriyel oksijen indeksi (OI), oksijen satürasyon indexi (OSI), laktat, IL-6 ve ferritin, lenfosit düzeyi, ortalama arter basıncı, yoğun bakım gün sayısı, entübe gün sayısı, taburculuk ve mortalite durumları kaydedildi.

Bulgular: Yatış anında ölçülen SPO₂, PaO₂, CaO₂ değerleri açısından iki grup arasında anlamlı fark yoktu. OI, OSI, P/F, S/F, ScvO₂, APACHEII ve SOFA skoru, entübe gün sayısı, laktat, ferritin, IL-6 parametreleri açısından iki grup arasında anlamlı ilişkili bulundu. Bu değişkenler için ROC ve lojistik regresyon analizi yapıldı, kesme noktaları hesaplandı. OI (>7, AUC: 0.798, p=0.001) ve OSI (>4.5, AUC: 0.805, p=0.001) indikatörlerinin mortalitenin en belirgin bağımsız değişkenleri olduğu tespit edildi. AyrıcaOI≥7 olması durumunda mortalitenin 23 kat, OSI ≥4.5 olması durumunda mortalitenin 40 kat artırdığı görüldü.

Sonuç: CARDS tanısı ileyoğun bakım ünitesine yatışlarda mortaliteyi öngörmedeOI ve OSI'nin anlamlı bağımsız değişkenler olduğu görüldü. Aynı zamanda çalışmamızda bu non-invaziv bakılan parametrelerden S/F oranının; P/F kadar değerli, OI oranının; OSI kadar güçlü bir prediktör olduğu tespit edildi.

Anahtar Sözcükler: ARDS; COVID-19; intensive care units; mortality predictors; oksijenasyon indikatörleri.