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CLINICAL STUDY

The ROX, shock and diastolic shock indexes in the prediction of mortality in COVID-19

Serdal ATES[1], Mehmet OKUMUS[2], Erdal DEMIRTAS[2], Yahya Kemal GUNAYDIN[2], Sertac GULER[2]

Hitit University Erol Olcok Education and Research Hospital, Department of Emergency Medicine, Corum, Turkey.
serdalmd@gmail.com

ABSTRACT
OBJECTIVES: The aim of this study is to determine the role of Respiratory Rate Oxygenation (ROX), shock, and diastolic shock indexes in predicting mortality in coronavirus disease 2019 (COVID-19) patients admitted to the emergency department.
BACKGROUND: The COVID-19 spread worldwide in a short time and caused a major pandemic. The ROX, shock, and diastolic shock indexes are used in various life-threatening clinical situations. The use of these indexes in triage at emergency departments can accelerate the determination of COVID-19 patients' severity.
METHODS: The ROX, shock and diastolic shock indices were calculated and recorded. Patients were divided into three groups; 1) who were discharged from the hospital, 2) who were admitted to the hospital and 3) who were admitted to the intensive care unit.
RESULTS: Increased diastolic shock index and decreased ROX index were found to be independent risk factors for mortality. In the prediction of mortality, the sensitivity and specificity of the diastolic shock index were 61.2% and 60.8%, respectively. However, the sensitivity and specificity of ROX index was 73.1% and 71.5%, respectively.
CONCLUSION: In conclusion, we found that the ROX index had higher sensitivity and specificity than other indexes in predicting mortality in the evaluation of COVID-19 patients *(Tab. 3, Fig. 2, Ref. 18)*. Text in PDF www.elis.sk
KEY WORDS: COVID-19, ROX index, shock index, diastolic shock index.

Introduction

The coronavirus disease 2019 (COVID-19) spread worldwide in a short time and caused a major pandemic after it started in China in December 2019. Severe pneumonia and respiratory failure caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have increased the disease mortality (1).

During the pandemic period, it was observed that emergency department applications were much higher than their capacities. The early recognition of critically ill patients is crucial in the initial evaluation of these patients presenting to the emergency department. Various clinical, laboratory, and radiological risk factors have been identified for these patients. However, prognostic evaluations based on laboratory and radiological examinations may prolong the stay of critically ill patients in the emergency department and delay their hospitalization. Therefore, it is thought that simple parameters at the bedside will accelerate patient management regarding hospitalization and discharge (2).

Numerical parameters obtained from vital signs such as Respiratory Rate Oxygenation (ROX), shock, and diastolic shock indexes are used in various life-threatening clinical situations. ROX index is defined as (SpO_2/FiO_2)/Respiratory Rate. This index is used to predict the need for invasive mechanical ventilation in patients with pneumonia and acute respiratory failure who are admitted to intensive care units (ICU) and begin treatment with a high-flow nasal cannula (HFNC) (3). The shock index was defined in 1967 as the ratio of heart rate to systolic blood pressure. It is used to measure the degree of hypovolemia in cases of hemorrhagic and infective shock (4). Studies have shown that it is a mortality-related factor in various conditions such as sepsis, pulmonary embolism, and pneumonia (5, 6). The diastolic shock index is defined as the ratio of heart rate to diastolic blood pressure. The diastolic shock index is used to determine the severity of the disease and initiate early vasopressor treatment in cases such as septic shock and vasodilator shock (7).

The number of studies investigating the link between the ROX, shock, and diastolic shock indexes and the prognosis of COVID-19 patients is limited. The use of these indexes in triage at emergency departments can accelerate the determination of COVID-19 patients' severity. This can also assist in providing early diagnosis

[1]Hitit University Erol Olcok Education and Research Hospital, Department of Emergency Medicine, Çorum, Turkey, and [2]Health Sciences University, Ankara Training and Research Hospital, Department of Emergency Medicine, Ankara, Turkey

Address for correspondence: Serdal ATES, MD, Hitit University Erol Olcok Education and Research Hospital, Department of Emergency Medicine, Yeniyol Mah. Baltali 1 Sok. 7/32 Merkez, Corum, Turkey.
Phone: +905365537721, Fax: 0364 219 19 38

and treatment to critically ill patients. Therefore, the aim of this study is to determine the role of ROX, shock, and diastolic shock indexes in predicting mortality in COVID-19 patients admitted to the emergency department.

Material and methods

This retrospective observational study was conducted in the emergency department of a training and research hospital. The study was approved by the local ethics committee (No: E-21-782). Our study was conducted in accordance with the latest version of the ''Declaration of Helsinki'' and ''the Good Clinical Practices Directive''.

Patients over the age of 18 who visited the emergency department with suspicion of COVID-19 between March 2020 and March 2021, and whose PCR test was evaluated as positive were included in the study. Patients with a negative COVID-19 PCR test, who were hospitalized due to a non-COVID-19 clinical condition (such as acute coronary syndrome, acute stroke, gastrointestinal bleeding), and who were pregnant were not included in the study.

Vital findings of the patients at the time of admission (blood pressure, pulse, saturation value, fever, respiratory rate), comorbid diseases such as chronic obstructive pulmonary disease (COPD), ischemic heart disease (IHD), chronic kidney failure (CKD), cerebrovascular disease (CVD), congestive heart failure (CHF), diabetes mellitus (DM), hypertension (HT) were recorded. ROX, shock, and diastolic shock index Index values of the patients were calculated and recorded. It was calculated as "ROX Index = (SpO2 /FiO2)/Respiratory Rate", "Shock Index = Heart Rate/Systolic Blood Pressure", and "Diastolic Shock Index = Heart Rate/Diastolic Blood Pressure". Patients' discharge, ward admission, ICU admission, and mortality within the first month were recorded.

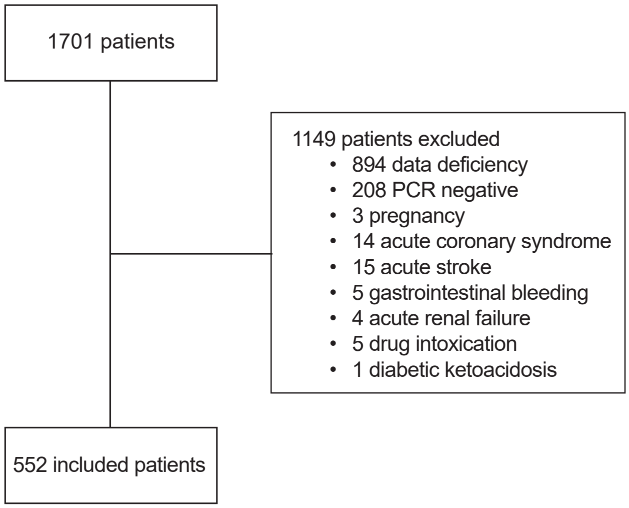

Fig. 1. Flowchart of study design.

Power analysis

When the alpha error was calculated as 0.05, power as 80%, the difference between ROX, shock, and diastolic shock index

Tab. 1. The demographic characteristics, presence of comorbidities, vital signs, indexes of the patients according to mortality status.

	Survivor (n=418)	Non-survivor (n=134)	All patient (n=552)	p
Age, median (IQR 25–75)	58 (48–70)	72 (66–80)	63 (51–73)	**<0.001**
Sex (n,%)				
Male	208 (49.8%)	84 (62.7%)	292 (52.9%)	0.009
Female	210 (50.2%)	60 (37.3%)	260 (47.1%)	
Comorbidities (n,%)				
COPD	46 (11%)	17 (12.7%)	63 (11.4%)	0.594
DM	102 (24.4%)	50(37.3%)	152 (27.5%)	0.004
HT	144 (34.4%)	70 (52.2%)	214 (38.8%)	**<0.001**
CHF	8 (1.9%)	11 (8.2%)	19 (3.4%)	**<0.001**
IHD	50 (12%)	39 (29.1%)	89 (16.1%)	**<0.001**
CRF	6 (1.4%)	8 (6%)	14(2.5%)	0.004
CND	6(1.4%)	5 (3.7%)	11 (2.0%)	0.098
Vital Parameters, median (IQR 25–75)				
SBP (mmHg)	127 (114–142)	124 (110–142)	126 (113–142)	0.272
DBP (mmHg)	73 (65–82)	68 (62–80)	71 (63–82)	0.002
HR(bpm)	89 (79–98)	94 (81–110)	90 (80–100.5)	**<0.001**
RR (bpm)	24 (20–28)	30 (25–37)	25 (20–30)	**<0.001**
SpO_2 (%)	92 (86–95)	82 (68–89)	90 (82–95)	**<0.001**
Temp (°C)	36.7 (36.4–37.2)	36.9 (36.4–37.7)	36.7 (36.4–37.2)	0.081
Indices, median (IQR 25–75)				
SI	0.69 (0.60–0.79)	0.78 (0.64–0.9)	0.72 (0.6–0.82)	**<0.001**
DSI	1.22 (1.04–1.41)	1.36 (1.14–1.6	1.25 (1.06–1.46)	**<0.001**
ROX Index	18.43 (15.08–22.38)	12.22 (9.2–16.2	17.08 (12.8–21.4)	**<0.001**

COPD – Chronic obstructive pulmonary disease, DM – Diabetes mellitus, HT – Hypertension, CHF – Congestive heart failure, IHD – Ischemic heart disease, CRF – Chronic renal failure, CND – Chronic neurological disease, SBP – Systolic blood pressure, DBP – Diastolic blood pressure, HR – Heart rate, RR – Respiratory rate, spO_2 – Blood oxygen saturation, SI – Shock İndex, DSİ – Diastolic shock index, ROX – Rate of Oxygenation, IQR – İnterquartile range

Tab. 2. Factors that predict mortality within the first month.

	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	**p value**	**OR**	**95% CI**	**p**
Age	1.070	1.052–1.088	**<0.001**	1.070	(1.049–1.093)	**<0.001**
Sex (female)	0.590	0.396–0.879	**0.009**			NA
COPD	1.175	0.649–2.128	0.594			NA
DM	1.844	1.217–2.793	**0.004**			NA
HT	2.081	1.403–3.088	**<0.001**			NA
CHF	4.583	1.803–11.648	**0.001**	3.262	1.113–9.564	**0.031**
IHD	3.021	1.878–4.862	**0.001**	2.484	1.408–4.383	**0.002**
CRF	4.360	1.485–12.802	**0.007**	4.980	1.236–20.069	**0.024**
CND	2.661	0.799–8.865	0.111			NA
SBP (mmHg)	0.995	0.987–1.004	0.314			NA
DBP (mmHg)	0.981	0.967–0.995	**0.010**			NA
HR (bpm)	1.024	1.013–1.036	**<0.001**			NA
RR (bpm)	1.113	1.084–1.142	**<0.001**			NA
spO_2 (%)	0.932	0.916–0.948	**<0.001**			NA
Temp (°C)	1.296	1.043–1.611	**0.019**			NA
SI	10.53	3.637–30.491	**<0.001**			NA
DSI	4.892	2.697–8.874	**<0.001**	3.546	1.707–7.367	**0.001**
ROX Index	0.830	0.795–0.866	**<0.001**	0.838	0.797–0.881	**<0.001**

COPD – Chronic obstructive pulmonary disease, DM – Diabetes mellitus, HT – Hypertension, CHF – Congestive heart failure, IHD – Ischemic heart disease, CRF – Chronic renal failure, CND – Chronic neurological disease, SBP – Systolic blood pressure, DBP – Diastolic blood pressure, HR – Heart rate, RR – Respiratory rate, spO_2 – Blood oxygen saturation, SI – Shock İndex, DSİ – Diastolic shock index, ROX – Rate of Oxygenation, OR – Odds ratio, CI – Confidence interval

between the two groups as 10%, and the ratio of the two groups as 1, the sample size was calculated as 162 for a single group with G*Power (2).

Statistical analysis

IBM Statistics Package for the Social Sciences version 23.0 (SPSS ver. 23.0) statistical package program was used for statistical analysis in the study. While descriptive statistics are shown as numbers and percentages in the analyses, distribution statistics are shown as median (25–75% quartiles-Interquartile range (IQR)). For numerical variables, conformity to normal distribution was evaluated with the Kolmogorov–Smirnov test. Mann–Whitney-u test was applied to evaluate whether there was a difference in the distribution of age, vital signs, and indices according to mortality status. The chi-square test was applied to evaluate whether there was a difference in the distribution of gender and comorbid diseases according to the presence of mortality. Stepwise logistic regression analysis was used to determine independent factors predicting mortality in the first month of COVID-19 disease. ROC analysis was performed to determine threshold values for the parameters that were significant in logistic regression. Youden index (sensitivity-(1-specificity)) was used when determining the threshold value. For statistical significance in the analyses, cases with a type 1 error value below 5% were considered significant (p<0.050).

Results

1701 patients who applied to the emergency department between March 2020 and March 2021 were evaluated. 1149 of these patients were excluded from the study because they met the exclusion criteria. 525 patients were included in the study (Fig. 1).

Of the 552 patients included in our study, 292 (52.9%) were men and 260 (47.1%) were women. The median age of the patients was 63 years (IQR 25-75;51-73). The total numbers of patients with DM, HT, COPD, CHF, IHD, CKD, and CVO were 152 (27.5%), 214 (38.8%), 63 (11.4%), 19 (3.4%), 89 (16.1%), 14 (2.5%) and 11 (2.0%), respectively.

Of the 552 patients included in the study, 200 (36.2%) were discharged, 200 (36.2%) were admitted to the ward, and 152 (27.6%) were admitted to the ICU. Among the patients included in our study, 8 (4%) of 200 discharged patients, 37 (18.5%) of 200 patients admitted to the ward, and 89 (58.6%) of 152 patients admitted to the ICU died within the first month. The demographic characteristics, presence of comorbidities, vital signs, indexes of the patients according to their mortality status are given in Table 1.

In the univariate analysis, age and gender of the patients, the presence of comorbid diseases such as DM, HT, CHF, IHD, CKD, and vital signs such as diastolic blood pressure, pulse, respiratory rate, SpO2, shock with fever, diastolic shock and ROX indexes

Tab. 3. Cut-off values for patient age, DSI, and ROX indexes in predicting mortality within the first month.

	Cut-off	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Age	57	0.757	82.9	46.2	36.9	87.7
DSI	1.29	0.637	61.2	60.8	33.3	83
ROX	15.6	0.773	73.1	71.5	45.1	89.2

DSI – Diastolic shock index, ROX – Rate of Oxygenation AUC – Area under the curve, PPV – Positive predictive value, NPV – Negative predictive value were found to be associated with mortality. In the multivariate analysis, age of the patients, the presence of comorbid diseases such as HF, IHD, CKD, diastolic shock index, and ROX index were found to be independent risk factors in predicting mortality in COVID-19 disease (Tab. 2).

The ROC curves of the patients' age, diastolic shock index, and ROX index in predicting the mortality within the first month are shown in Figure 2. The age of patient (AUC: 0.757, 95% CI: 0.713-801, $p<0.001$), the diastolic shock index (AUC: 0.637, 95% CI: 0.583-692, $p<0.001$) and the ROX index (AUC: 0.773, 95% CI: 0.727-819, $p<0.001$) were predictive factors for mortality within the first month in COVID-19 patients (Fig. 2). Threshold values for these parameters in mortality within the first month are shown in Table 3.

Discussion

In our study, the value of diastolic shock, shock, and ROX indexes in the prediction of mortality within the first month in patients with COVID-19 were evaluated. It was found that the ROX index exhibits a higher sensitivity and specificity than the others in the prediction of mortality in COVID-19 patients.

There have been studies on the use of the ROX index in the evaluation of the success of HFNC and non-invasive ventilation in critically ill COVID-19 patients (2, 8, 9). The study by Zaboli et al has shown that as the percentage of lung involvement increases, the ROX index decreases and the risk of ARDS and intubation increases in patients with COVID-19. As a result, the severity and mortality rate of the disease increases. In the study, the median ROX value of the patients who required intubation at the 72nd hour of hospitalization was 15.3, while the median ROX value of patients who did not need intubation was 22.2 (10). Similarly, the prospective study by Gaspic et al has shown that the ROX index was associated with mortality in COVID-19 patients who received HFNC treatment. In the study, while the average ROX value was found to be 2.9 in mortal patients, the average ROX value was found to be 5.25 in surviving patients (11). Additionally, the prospective study by Gianstefani et al has shown that the ROX index could predict hospitalization, need for mechanical ventilation, and mortality in COVID-19 patients. In the same study, the sensitivity was found to be 76.5% when the ROX index cut-off was determined as 25.7 in the prediction of hospitalization in COVID-19 patients (12). In our study, similar to these studies, it was shown that as the severity of the disease increases, the ROX index becomes lower. Moreover, it is an independent risk factor in predicting mortality in COVID-19 patients. When the ROX Index cut-off value for mortality was determined as 15.6, the sensitivity and specificity were found to be 73.1% and 71.5%, respectively.

The study by Avci et al has investigated the effect of the diastolic shock index on prognosis in COVID-19 pneumonia, and a high value of the diastolic shock index was found to be associated with mortality. When the diastolic shock index cut-off value was determined as 1.35 (AUC=0.737), the sensitivity was found to be 70.93% and the specificity was 72.63% (13). Similarly, in our study, a higher diastolic shock index value was found to be associated with mortality. In our study, when the diastolic shock

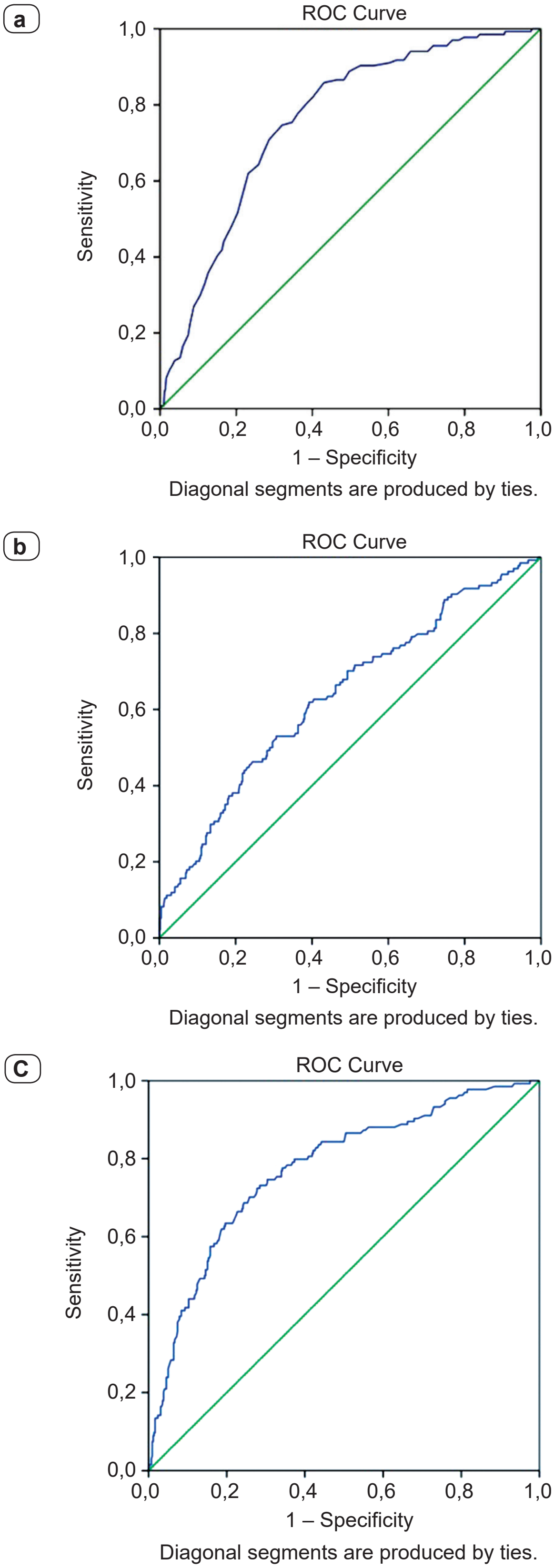

Fig. 2. ROC curves of age (a.), diastolic shock (b.), and ROX (c.) indexes in predicting mortality within the first month.

index cut-off value was determined as 1.29 (AUC=0.637), the sensitivity was found to be 61.8% and the specificity was 60.8%.

Kurt et al have demonstrated that the shock index was higher in COVID-19 patients hospitalized in ICU (14). The study by Van Rensen et al has shown that the shock index calculated at the time of admission to the emergency department in COVID-19 patients has no role in predicting ICU admission or clinical deterioration (15). Doğanay et al have indicated that the shock index is an important parameter in predicting mortality when evaluated together with patient age in COVID-19 patients (16). In our study, while the shock index was statistically significant in univariate analysis, it was not significant in multivariate analysis. The results of our study suggested that the ROX and diastolic shock indexes are better prognostic factors than the shock index.

A meta-analysis showed that the severity of COVID-19 increases with patient age (17). Jain et al have found the relationship between patient age and COVID-19 in their study (18). Similar to these studies, the present study has revealed that advanced patient age is an independent risk factor in predicting mortality within the first month.

This study has two main limitations. Firstly, this study is a retrospective one center study with a limited number of patients. Secondly, since the study was retrospective, approximately 2/3 of the patients brought in with oxygen had to be excluded from the study because it was not known how many liters/minutes of oxygen the patients received.

In conclusion, the use of non-invasive, easily calculated indexes obtained from vital signs in COVID-19 with lung involvement might be useful in the early recognition of critically ill COVID-19 patients.

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