Prognostic Performance of Shock Index, Diastolic Shock Index, Age Shock Index, and Modified Shock Index in COVID-19 Pneumonia

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Original Research

Abstract

Objective: We aimed to compare the prognostic accuracy of shock indexes in terms of mortality in patients hospitalized with coronavirus disease 2019 (COVID-19) pneumonia.
Methods: Hospitalized patients whose COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) test results were positive, had thoracic computed tomography (CT) scan performed, and had typical thoracic CT findings for COVID-19 were included in the study.
Results: Eight hundred one patients were included in the study. Chronic obstructive pulmonary disease, congestive heart failure, chronic neurological diseases, chronic renal failure, and a history of malignancy were found to be chronic diseases that were significantly associated with mortality in patients with COVID-19 pneumonia. White blood cell, neutrophil, lymphocyte, C reactive protein, creatinine, sodium, aspartate aminotransferase, alanine aminotransferase, total bilirubin, high sensitive troponin, d-dimer, hemoglobin, and platelet had a statistically significant relationship with in-hospital mortality in patients with COVID-19 pneumonia. The area under the curve (AUC) values of shock index (SI), age shock index (aSI), diastolic shock index (dSI), and modified shock index (mSI) calculated to predict mortality were 0.772, 0.745, 0.737, 0.755, and Youden Index J (YJI) values were 0.523, 0.396, 0.436, 0.452, respectively.
Conclusions: The results of this study show that SI, dSI, mSI, and aSI are effective in predicting in-hospital mortality.

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The coronavirus disease 2019 (COVID-19) pandemic (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) appears to be the most important health crisis of the 21st century and remains a serious problem for global health, given its high rate of transmission, morbidity and mortality.[1] As of March 28, 2022, since its first appearance in Wuhan City, China in December 2019, more than 480 million confirmed cases have been detected worldwide and more than 6.1 million people have died.[2]

The shock index (SI), obtained by dividing heart rate (HR) by systolic blood pressure (SBP), is considered a predictor of mortality in different clinical conditions. Modified shock index (mSI), defined as HR divided by mean arterial pressure (MAP), diastolic shock index (dSI), defined as HR divided by diastolic blood pressure (DBP), and age shock index (aSI), defined as age multiplied by SI, are 3 different SI derivatives.[3] By adding the theoretical benefits of including DBP and age, it is intended to create more efficient derivatives of SI. mSI has been reported as a good predictor of disease severity of patients admitted to the emergency department.[4] The age shock index is a new index that was first studied to predict mortality in elderly trauma patients.[5]

SI, dSI, mSI, and aSI have been studied with different populations, and their accuracy has been confirmed.[3,6–9] In addition, although SI and mSI have been studied in COVID-19 patients,[10,11] there is no study comparing these 4 markers. In this study, we aimed to compare the prognostic accuracy of SI, mSI, dSI, and aSI in terms of mortality in patients hospitalized with COVID-19 pneumonia.

Methods

Study Design

This study was approved by the Local Clinical Research Ethics Committee (Institutional Review Board) of the Antalya Education and Research Hospital with the registration number of 5/12 on April 15, 2021. This retrospective observational study was conducted with patients who presented to tertiary-care hospital and diagnosed with COVID-19, between March 11, 2020, and January 13, 2021. In Turkey, the first COVID-19 patient was diagnosed on March 11,

2020, and the first volunteer person was vaccinated on January 14, 2021. To prevent COVID-19 vaccines from affecting the study population, the study patient admission deadline was set before the first vaccination date.

Patient Selection

Hospitalized patients (both the inpatient unit and the intensive care unit) older than 18 y of age whose COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) test results were positive, had been performed thoracic computed tomography (CT) scan and had typical thoracic CT findings for COVID-19 included in the study. Patients with negative RT-PCR test results, unable to have laboratory tests, incomplete or partial laboratory test results, without thoracic CT scan, without typical thoracic CT findings, referred to another hospital, undergoing cardiopulmonary resuscitation in the emergency department, and patients with recurrent admissions were excluded from the study. According to the COVID-19 Adult Patient Management Guideline of Turkish Ministry of Health on March 25, 2020, patients who had respiratory rate <30/min, spontaneous SpO2 level >90%, and pneumonia findings in posterior-anterior chest X-ray or thorax CT were hospitalized to the inpatient unit. Patients who had respiration rate ≥ 30, signs of dyspnea or respiratory distress, SpO2 level <90% despite nasal oxygen support of 5 L/min and above, partial oxygen pressure <70 mmHg despite nasal oxygen support of 5 L/min and above, PaO2/FiO2 level <300, lactate level >4 mmol/L, bilateral infiltrations or multilobar involvement on chest X-ray or thorax tomography, hypotension (SBP <90 mmHg, >40 mmHg decrease from usual SBP, MAP <65 mmHg), skin perfusion disorder, kidney or liver function test disorder, thrombocytopenia, organ dysfunction such as change of consciousness, an immunosuppressive disease, an uncontrolled comorbidity with more than 1 feature, elevated troponin level, or arrhythmia were hospitalized to the intensive care unit.[12] The presence of typical thoracic CT findings for COVID-19 was determined using criteria described in previous studies including ground-glass opacity, crazy-paving pattern, and consolidation.[13,14]

Data Record

Data included patient demographics (age and sex), past medical history, HR, SBP, DBP, pulse oximeter, body temperature, hemogram (white blood cell [WBC], neutrophil, lymphocyte, hemoglobin, and platelet) and biochemistry (C-reactive protein [CRP], blood urea nitrogen, creatinin, sodium, potassium, aspartate aminotransferase [AST], alanine aminotransferase [ALT], total bilirubin, high sensitive troponin [HS troponin] and d-dimer) parameters studied at the time of the first admission to the hospital, thoracic CT scan interpretation and in-hospital mortality. In-hospital mortality was defined as death occurring during the hospital stay. Vital findings at the time of the first admission to the hospital (before the start of treatment) were used to calculate shock indices.

Definitions

The SI and dSI were calculated as a ratio of HR to SBP and HR to DBP, respectively. The MAP was calculated as (SBP + 2 × DBP) /3 and mSI was calculated as a ratio of HR to MAP. The aSI was calculated as Age × SI.

Table 1. Gender, comorbidities, and categorical descriptive statistics of the study population

Variable	Category	Survivors (N=464)		Non-survivors (N=337)		Sig.*
		n	%	n	%	P-Value
Sex	Male	242	53.3	212	46.7	0.002
	Female	222	64.00	125	36.00	
COPD	No	435	60.30	286	39.70	<0.001
	Yes	29	36.30	51	63.70	
DM	No	365	57.80	266	42.20	0.927
	Yes	99	58.20	71	41.80	
HT	No	320	56.80	243	43.20	0.337
	Yes	144	60.50	94	39.50	
AF	No	458	58.30	327	41.70	0.095
	Yes	6	37.50	10	62.50	
CHF	No	444	59.90	297	40.10	<0.001
	Yes	20	33.30	40	66.70	
IHD	No	418	58.20	300	41.80	0.625
	Yes	46	55.40	37	44.60	
CND	No	452	59.30	310	40.70	<0.001
	Yes	12	30.80	27	69.20	
CRF	No	446	59.20	307	40.80	0.003
	Yes	18	37.50	30	62.50	
Malignancy	No	455	58.60	321	41.40	0.024
	Yes	9	36.00	16	64.00	

Note: Categorical data were analyzed with the chi-squared test.
*Asymptotic 2-sided significance between groups.
Abbreviations: CHF, congestive heart failure; CND, chronic neurological disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CT, computed tomography; DM, diabetes mellitus; HT, hypertension; IHD, ischemic heart disease; PE, physical examination.

Data Analysis

Statistical analysis was performed using IBM SPSS Statistics Version 26.0 and MedCalc Statistical Software Version 19.0.6. Total study population was divided survivor group and nonsurvivor group for statistical analysis and the groups were compared. Continuous and ordinal data were analyzed with the Mann Whitney U-test, and categorical data were analyzed with the chi-squared test. Continuous data were reported as medians and interquartile ranges (25th-75th). Categorical data were presented as frequency and percentage. A P value less than 0.05 was considered statistically significant.

Receiver operating characteristic (ROC) analysis was performed using the Delong method to evaluate and compare the mortality prediction performance of SI, aSI, mSI, and dSI values.[15] AUC and Youden Index J (YJI) were calculated to compare the predictive performance of these 4 different indices. YJI analysis was used to determine the threshold value with the highest performance in terms of predicting mortality risk.[16] Sensitivity, specificity, PPV, NPV values of indices were calculated using the threshold value determined by YJI.

Results

After applying the inclusion and exclusion criteria, this study continued with the data of the remaining 801 patients. The study population consisted of 347 women and 454 men. There was a statistically significant difference between the groups in terms of gender, and the mortality risk was higher in male gender (Table 1). The median

Table 2. Descriptive statistics for age, vital parameters, laboratory measurements, and severity scores

Variable	All patients (*n*=801)	Survivor (*n*=464)	Non-survivor (*n*=337)	*P*-Value*
Age, median (25th-75th)				
Age	69 (58-78)	69 (56-77)	70 (61-80)	0.005
Vital signs, median (25th-75th)				
SBP (mmHg)	120 (110-133)	124 (113-140)	115 (109-123)	<0.001
DBP(mmHg)	72 (65-81)	77 (66- 85)	71 (65-78)	<0.001
MAP (mmHg)	88. 7 (80.5-98.3)	92 (82.7-101.7)	85.7 (79.3-92.5)	<0.001
HR (bpm)	96 (81-107)	88 (77-100)	105 (93-113)	<0.001
spO2 (%)	92 (86-96)	95 (91-97)	87 (81-93)	<0.001
RR (bpm)	20 (15-28)	16 (14-20)	28 (21-37)	<0.001
Temp (ºC)	36.7 (36.3-37.2)	36.7 (36.2-37.1)	36.7 (36.3-37.4)	0.059
Laboratory measurements, median (25th-75th)				
WBC (10^3/mm^3)	8.5 (6.2-13.1)	7.7 (5.6-11.8)	9.8 (7.0-14.4)	<0.001
Neutrophil (10^3/mm^3)	6.5 (4.3-10.6)	5.7 (3.8-9.8)	7.3 (5.3-12.1)	<0.001
Lymphocyte (10^3/mm^3)	1.1 (0.6-1.7)	1 (0.6-1.6)	1.2 (0.7-1.8)	0.039
Hemoglobin (g/dL)	12.1 (10.6-13.3)	12.4 (11.0-13.4)	11.6 (10.0-13.0)	<0.001
Platelet (10^3/mm^3)	201 (137-266)	206.5 (151.3-268)	187 (97-262.5)	<0.001
CRP (mg/L)	118.9 (50.2-189.8)	96.3 (35-173.2)	147.2 (76.7 -220.8)	<0.001
BUN (mg/dL)	39 (25-57)	40 (28-57)	36 (22-62)	0.107
Creatinin (mg/dL)	1.18 (0.85-2.1)	0.99 (0.76-1.73)	1.60 (1.04-2.30)	<0.001
Sodium (mmol/L)	137 (133-141)	136 (133-140)	138 (133-144)	<0.001
Potassium (mmol/L)	4.3 (3.8-4.8)	4.24 (3.9-4.7)	4.3 (3.8-5)	0.080
AST (U/L)	45 (28-95)	37 (26-74.75)	58 (35-119.5)	<0.001
ALT (U/L)	37 (19-95)	31 (16-67)	49 (24-126)	<0.001
Total bilirubin (mg/dL)	0.6 (0.4-0.8)	0.5 (0.3-0.79)	0.67 (0.5-0.99)	<0.001
HS troponin (ng/L)	23 (11-54)	18 (9-38)	36 (16-67)	<0.001
D-dimer (ug/L)	645(411.5-993.5)	607.5 (375-925.3)	727 (491.5-1089.5)	<0.001
Severity scores, median (25th-75th)				
SI	0.78 (0.64-0.91)	0.69 (0.59-0.83)	0.91 (0.77-1.0)	<0.001
aSI	52.25 (41.17-64.85)	46.33 (36.6-56.6)	61.3 (50.71-74.24)	<0.001
dSI	1.31 (1.07-1.54)	1.16 (1-1.38)	1.46 (1.27-1.66)	<0.001
mSI	1.07 (0.87-1.26)	0.96 (0.81-1.13)	1.22 (1.06-1.34)	<0.001

Note: Continuous and ordinal data were analyzed with the Mann Whitney U test.
*Asymptotic 2-sided significance between groups.
Abbreviations: aSI, age shock index; CRP, c-reactive protein; DBP, diastolic blood pressure; dSI, diastolic shock index; HR, heart rate; HS troponin, high sensitive troponin T; mSI, modified shock index; SBP, systolic blood pressure; SI, shock index; spO2, blood oxygen saturation.

ages of the total study population, survivor group, and nonsurvivor group were 69 (58-78), 69 (56-77), 70 (61-80), respectively. A statistically significant difference was found between the groups in terms of age, and advanced age was found to be associated with high mortality (Table 2). In our study population, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), chronic neurological diseases (CND), chronic renal failure (CRF), and a history of malignancy were found to be chronic diseases that were significantly associated with mortality in patients with COVID-19 pneumonia (Table 1).

WBC, neutrophil, lymphocyte, CRP, creatinine, sodium, AST, ALT, total bilirubin, HS troponin, and laboratory parameters of d-dimer, hemoglobin and platelet had a statistically significant relationship with in-hospital mortality in patients with COVID-19 pneumonia. Hemoglobin and platelet were lower in the nonsurvivor group, while other parameters were higher (Table 2).

The performances of the SI, aSI, dSI, and mSI variables were analyzed by ROC analysis in terms of predicting the mortality

risk of patients with COVID-19 pneumonia. The AUC values of SI, aSI, dSI, and mSI calculated to predict mortality were 0.772, 0.745, 0.737, 0.755, and YJI values were 0.523, 0.396, 0.436, 0.452, respectively (Table 3; Figure 1). When ROC curves were compared in pairs, there were statistically significant differences between the SI and each of the other 3 indices to predict mortality. Table 4 shows that this significant difference favors SI.

Limitations

The prominent limitations of this study are its retrospective and single-center design. Another limitation of our study is the relatively high mortality rate in the study population. The fact that the COVID-19 pandemic peaks and relatively mild patients are followed at home is effective in this situation. In addition, the exclusion of patients who did not have typical pneumonia findings on CT and had missing data on vital signs or laboratory findings may also have affected this situation.

Table 3. Predictive performance of SI, aSI, dSI, and mSI in terms of in-hospital mortality for COVID-19 patients

Variable	Sensitivity (CI 95%)	Specificity (CI 95%)	PPV (CI 95%)	NPV (CI 95%)	AUC (CI 95%)	YJI (CI 95%)	Criterion of YJI	P-Value
SI	67.36 (62.1-72.3)	84.91 (81.3 - 88.0)	76.4 (72.1 - 80.3)	78.2 (75.4 - 80.8)	0.772 (0.742- 0.801)	0.523 (0.463-0.577)	>0.87	<0.001
aSI	60.53 (55.1-65.8)	79.09 (75.1 - 82.7)	67.8 (63.3 - 71.9)	73.4 (70.6 - 76.0)	0.745 (0.713 - 0.775)	0.396 (0.330-0.450)	>58.3	<0.001
dSI	70.92 (65.8-75.7)	72.63 (68.3 - 76.6)	65.3 (61.5 - 68.9)	77.5 (74.3 - 80.4)	0.737 (0.705 - 0.767)	0.436 (0.376-0.498)	>1.35	<0.001
mSI	67.66 (62.4-72.6)	77.59 (73.5 - 81.3)	68.7 (64.6 - 72.5)	76.8 (73.7 - 79.5)	0.755 (0.723 - 0.784)	0.452 (0.387-0.512)	>1.14	<0.001

Note: ROC analysis was performed using the Delong method.
Abbreviations: aSI, age shock index; AUC, area under the curve; CI, confidence interval; dSI, diastolic shock index; mSI, modified shock index; NPV, negative predictive value; PPV, positive predictive value; SI, shock index; YJI, Youden J Index.
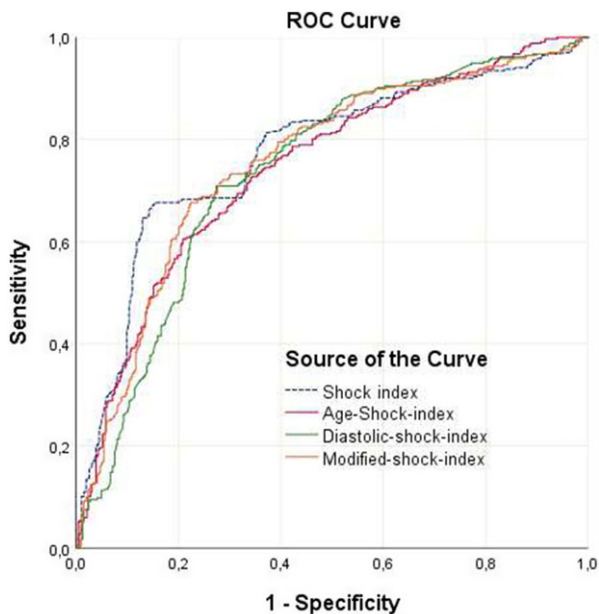
Figure 1. ROC curves of shock index, age shock index, diastolic shock index, and modified shock index.

Table 4. Pairwise comparisons of ROC curves

Comparisons	DBA	95% CI	z statistic	P-Value
SI-aSI	0.0273	0.00112 to 0.0536	2.043	0.0410
SI-dSI	0.0350	0.0163 to 0.0538	3.665	0.0002
SI-mSI	0.0176	0.00613 to 0.0291	3.008	0.0026
aSI-dSI	0.00771	-0.0218 to 0.0372	0.513	0.6081
aSI-mSI	0.00974	-0.0174 to 0.0369	0.703	0.4819
dSI-mSI	0.0174	0.00889 to 0.0260	3.994	0.0001

Note: ROC analysis was performed using the Delong method.
Abbreviations: aSI, age shock index; CI, confidence interval; DBA, difference between areas; dSI, diastolic shock index; mSI, modified shock index; SI, shock index.

Discussion

In this study, we compared the prognostic performance of SI, dSI, mSI, and aSI in terms of in-hospital mortality in patients hospitalized with COVID-19 pneumonia. We concluded that these 4 scorings may be useful in predicting in-hospital mortality. For our study population, we found the performance of SI to predict in-hospital mortality was higher than the other 3 scores.

SI, dSI, mSI, and aSI are noninvasive measurements, and important markers for early evaluation of hemodynamics and tissue perfusion.[17] SI score has been studied in cases such as pulmonary embolism, geriatric patients with influenza, sepsis, ectopic pregnancy, shock, early detection of transfusion need, mortality risk in myocardial infarction, mortality risk in patients with gastrointestinal bleeding, and the need for intensive care in patients admitted to the emergency department, and it has been found to be a successful prognostic marker.[18–26] In studies examining the relationship between COVID-19 and mortality risk, the ideal cutoff value for SI was reported as 0.93 by Doğanay et al.,[10] 0.86 by van Rensen et al.,[27] and 0.72 by Kurt and Bahadırlı.[11] A novel study compared 4 different cutoff value of SI in COVID-19 for predicting of ICU requirement and 30-d mortality. The authors concluded that the most useful threshold value for the SI in predicting the prognosis of COVID-19 patients is 0.9 in both situations.[28] In our study, the ideal cutoff value for SI was found to be 0.87, and the sensitivity of this cutoff value in terms of predicting mortality was 67%, the specificity was 85%, PPV 76%, NPV 78%, and YJI 0.523.

In a study in which all patients admitted to the emergency department were included in the study population, it was reported that the mSI threshold value of 1.3 was associated with increased intensive care unit (ICU) admission and increased risk of death.[4] Two other studies compared SI with mSI to predict prognosis in emergency patients and reported that mSI was a better predictor of mortality.[8,29] In another study, it was reported that a 1.4 threshold value of mSI was a successful indicator in predicting the risk of 7-d all-cause mortality and major cardiac problems in STEMI patients. This study also compared SI with mSI and concluded that mSI is better for predicting prognosis.[30] Smischney et al. found the best cutoff point as 1.8 for mSI to predict in-hospital mortality in ICU patients.[31] Jayaprakash et al. reported that mSI value higher than 1.3 measured in the early period in sepsis patients was associated with an increased risk of myocardial damage and mortality.[32] Another study found that patients with an mSI greater than 1.3 were more likely to be admitted to the ICU and to die. In this study, both SI and mSI were found to be associated with increased mortality risk and length of stay in the ICU.[33]

In a study comparing different shock indexes to determine the need for transfusion in trauma patients, the ideal threshold value was calculated as 0.95 for SI, 1.15 for mSI, and 36.95 for aSI.[7] In another study comparing SI, aSI, and mSI in predicting mortality risk in geriatric trauma patients, the prognostic performance of aSI was found to be the best. In the same study, ideal threshold values

were calculated as 1.05 for SI, 1.40 for mSI, and 80 for aSI.[6] Ospina-Tascón et al. demonstrated that progressive increases in dSI before vasopressor treatment in sepsis patients were associated with increased 90-day mortality risk.[34] Kurt and Bahadırlı investigated in-hospital mortality in COVID-19 patients and reported that a cut-off value of 1 for mSI gave the highest sensitivity.[11] In our study, we investigated the relationship among 4 different indexes and in-hospital mortality in patients hospitalized with the diagnosis of COVID-19 pneumonia. We found that the ideal thresholds of SI, dSI, mSI, and aSI were 0.87, 1.35, 1.14, and 58.3, respectively, and all 4 of them performed well in predicting mortality risk. We would like to emphasize that for our study population, SI had the highest AUC and YJI for these 4 markers and was superior to the others.

Descriptive data of patients such as age, gender, and comorbid diseases will be useful in predicting the need for hospitalization and determining risk groups in terms of mortality, especially in cases where health services are limited. In the literature, there are articles reporting the effects of age, gender, and comorbidity in terms of need for intensive care and mortality risk in patients with a diagnosis of COVID-19.[10,11,27,31,35–39] In our study, advanced age, male gender, COPD, CHF, CND, CRF, and history of malignancy were found to be closely associated with mortality, in line with the literature.

Ruan et al.[35] showed that there were significant differences in WBC, lymphocyte, platelet, albumin, total bilirubin, blood urea nitrogen, creatinine, myoglobin, cardiac troponin, CRP, and interleukin-6 values between the living and dying groups of COVID-19 patients. In a study conducted in Wuhan, the origin of COVID-19, CRP, procalcitonin, WBC, and neutrophil counts were found to be higher in the death group.[36] In another study, it was found that age, WBC, neutrophil count, blood urea nitrogen, creatinine, AST, potassium, CRP, and d-dimer may be higher in the clinically severe patient group. Lymphocyte counts, albumin, and sodium levels were found to be lower in the clinically severe patient group.[37] A recent study reported that there were significant differences between survivor and non-survivor groups regarding WBC, neutrophil, lymphocyte, hemoglobin and platelet levels.[38] In our study, WBC, neutrophil, lymphocyte, CRP, creatinine, sodium, AST, ALT, total bilirubin, HS troponin, and d-dimer were higher in the group who died due to COVID-19 disease; while hemoglobin and platelet were found at lower levels.

Conclusions

The results of this study show that SI, dSI, mSI, and aSI are effective in predicting in-hospital mortality. The performance of SI to predict in-hospital mortality is higher than the other 3 scores. In addition, these indexes can identify patients who may have a worse prognosis, enable closer monitoring, and increase the level of alertness against possible complications.

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