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The Usefulness of Shock Index and Modified Shock Index in Predicting the Outcome of COVID-19 Patients

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Abstract

Objective: The aim of this study is to investigate the accuracy of shock index (SI) and modified shock index (mSI) in predicting the intensive care unit (ICU) requirement and in-hospital mortality among coronavirus disease (COVID-19) patients who are admitted to the emergency department (ED). Likewise, the effects of patients' conditions such as age, gender, and comorbidity on prognosis will be analyzed.
Methods: The files were retrospectively scanned for all COVID-19 patients over the age of 18 years who were admitted to the ED and hospitalized between January 1, 2021, and March 15, 2021. The area under the receiver operating characteristic curve and the area under the curve (AUC) were used to assess each scoring system discriminatory for predicting in-hospital mortality and ICU admission.
Results: There were 464 patients included in this study. The mean age of the patients was 62.4 ± 16.7, of which 245 were men and 219 were women. The most common comorbidity in patients was hypertension (200; 43.1%), followed by chronic obstructive pulmonary disease (174; 37.5%), and coronary artery disease (154; 33.2%). In terms of in-hospital mortality, the AUC of SI, and mSI were 0.719 and 0.739, respectively. In terms of an ICU requirement, the AUC of SI, and mSI were 0.704 and 0.729, respectively.
Conclusion: In this study, it was concluded that SI and mSI are useful in predicting in-hospital mortality and ICU requirement in COVID-19 patients. In addition, another important result of the study is that advanced age, male gender, and hypertension may be associated with a poor prognosis.

Introduction

In December 2019, a new coronavirus, emerged in Wuhan, China, identified severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it quickly spread around the world.[1] The World Health Organization named this infection *coronavirus disease* (*COVID-19*) and announced it as a pandemic.[2] The epidemic caused a serious mortality and morbidity problem worldwide, causing approximately 140 million cases – as a result, 3 million deaths as of April 24, 2021.[3] The clinical spectrum of COVID-19 infection can change from asymptomatic to the most severe disease (acute respiratory distress syndrome [ARDS], acute heart injury and acute kidney injury, etc.).[4] While 32% of all patients with a test of positive require an ICU, many of these patients may die.[5] Early recognition is important in patients at risk of serious illness and who may have potentially life-threatening conditions. Therefore, it is important to reach an early diagnosis of patients who will require critical care.

Shock index (SI) is a ratio that is obtained by dividing the heart rate by systolic blood pressure, a simple and easy-to-use formula to determine the changes in cardiovascular performance prior to systemic hypotension. Allgöwer and Buri first introduced this ratio in 1967 as a simple and effective way of measuring the degree of hypovolemia in cases of hemorrhagic and infectious shock.[6] Although SI is a non-invasive measurement, it is an important marker for the early evaluation of hemodynamics and tissue perfusion.

Ye-Cheng Lıu et al., in their study, considering that SI uses only systolic blood pressure and has an undeniable importance in determining the clinical severity of the patient in diastolic blood pressure, they defined the modified shock index (mSI) in 2012, by adding diastolic blood pressure to SI.[7]

The aim of this study is to investigate the accuracy of SI and mSI in predicting ICU requirement and in-hospital mortality in COVID-19 patients admitted to the emergency department (ED). Additionally, the effects of patients' conditions such as age, gender, and comorbidity on prognosis will be analyzed.

Materials and Methods

Study Design

In the study, patients who were admitted to the Beylikdüzü Public Hospital ED between January 1, 2021, and March 31, 2021, and diagnosed with COVID-19 were examined. The institutional review board approved the analysis and issued a waiver of consent.

Selection of Patients

All patients who were admitted to the ED with COVID-19 complaints, who had oropharyngeal/nasopharyngeal swabs, and who were hospitalized between January 1 and March 31, 2021, were included in the study. Patients whose reverse transcriptase polymerase chain reaction test results were negative and whose SI and mSI could not be calculated were excluded from the study. In addition, patients who were admitted to the ED due to cardiac arrest and those who received inotropic support at the time of the admission were not included in the study.

Measurements

Data were collected from electronic medical hospital records and patients' ambulance forms. Data collected included age, sex, vital signs (body temperature, heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], respiratory rate [RR], mean arterial pressure [MAP], blood oxygen saturation [SpO2], body temperature [Temp]), and SI-mSI. MAP was calculated as $MAP = [SBP + (2 \times DBP)]/3$. SI was calculated as the ratio of HR to SBP (SI = HR/SBP). The mSI was calculated as the ratio of HR to MAP (mSI = HR/MAP). The formulas were calculated using the vital findings at the time of first admission to the ED.

Outcomes

The primary outcome was in-hospital mortality. The secondary outcome is to determine the relationship between SI-mSI and ICU requirement. Outcomes were assessed respectively by reviewing of the hospital medical database. For in-hospital mortality, active cases were excluded from the analysis. For the ICU requirement, all the patients in the cohort at the cutoff date were included in the analysis.

Statistical Analysis

Categorical variables were presented as frequency and percentage. Continuous variables were presented as mean ± standard deviation. The compliance of the data with normal distribution was checked using Kolmogorov-Smirnov and Shapiro-Wilk tests. Patients were divided into 2 groups according to ICU admission requirement. All variables were compared for these two groups using the Pearson's chi-square test, Fisher's exact test, Student's t-test, and Mann–Whitney U test as appropriate. Receiver operating characteristic (ROC) analyses were performed to determine the predictive power of indexes. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of both cut-points were found. The cutoff point that achieves the maximum Youden's index is referred to as the *optimal cut-point*. The odds ratios of indexes with the determined cutoff points were calculated for the outcomes. The area under the curve (AUC) of ROC curves of indexes was compared with a DeLong's test. A 2-sided *P*-value of 0.05 was regarded as statistically significant. All data analyses were performed using SPSS version 23.0 software (SPSS Inc., Chicago, IL).

Ethical Approval and Availability of Data and Materials

The principles outlined in the Declaration of Helsinki have been followed. This study was approved by the local ethics committee. Written informed consent was not required because no patient data have been included in the manuscript.

The data and materials in the manuscript are available from the authors.

Results

After applying the inclusion and exclusion criteria, the study was completed with 464 patients. The mean age of the patient group included in the study was 62.4 ± 16.7, which 245 (52.8%) were male and 219 (47.2%) were female. In-hospital mortality was observed in 73 (15.7%) of the patients. ICU was required in 165 (35.6%) of the patients. The mean age of the ICU requirement group was 74.5 ± 13.0, whereas the mean age of the ICU non-requirement group was 55.8 ± 14.7. The mean age of the 2 groups was significantly higher in the ICU requirement group (< 0.001).

The most common comorbidity in the patients was hypertension (200; 43.1%), followed by chronic obstructive pulmonary disease (174; 37.5%), and coronary artery disease (154; 33.2%). Other demographic and comorbidity data of the study population are presented in Table 1.

According to Youden's index, the optimal cutoff value for predicting in-hospital mortality was 0.72 for SI (sensitivity, 71.2; specificity, 69.6; PPV, 30.4; NPV, 92.8; AUC, 0.719), whereas it was 1 for mSI (sensitivity, 74; specificity, 72.4; PPV, 33.3; NPV, 93.7; AUC, 0.739) (Table 2).

The optimal cutoff values obtained for both scores were found to be significant in predicting in-hospital mortality (odds ratio SI 5.660–mSI 7.395) ($P < 0.001$) (Table 3). The optimal cutoff value for the ICU requirement for SI was 0.73 (sensitivity, 61.2; specificity, 78.3; PPV, 60.8; NPV, 78.5; AUC, 0.704), whereas it was 0.98 for mSI (sensitivity, 65.5; specificity, 78.9; PPV, 63.2; NPV, 80.6; AUC, 0.729). The optimal cutoff values obtained for both scores are significant in predicting the ICU requirement (odds ratio SI 5.681–MSI 7.098) ($P < 0.001$).

In the ROC analysis, which was performed to evaluate the ability of indices to predict in-hospital mortality, the AUC value of SI was 0.719 ± 0.037 (95% CI: 0.647–0.791), whereas that of mSI was 0.739 ± 0.036 (95% CI: 0.669–0.809) (for both, $P < 0.001$) (Figure 1).

When the predictive power of these outcomes was compared, there was a statistically significant difference between the AUCs of the 2 indices, and the mSI was slightly better than SI (AUC difference: −0.020, $P = 0.003$, DeLong's test). In predicting the requirement of ICU admission, the AUC value of SI was 0.704–0.027 (95% CI: 0.651–0.757), whereas the AUC value of mSI was 0.729 ± 0.026 (95% CI: 0.677–0.781) ($P < 0.001$) (Figure 2). Comparing the predictive power of SI and mSI for ICU requirement, there was again a significant difference between the 2 indexes and mSI was slightly more successful (AUC difference: −0.025, $P < 0.001$, DeLong's test). The ROC analysis results for in-hospital mortality and ICU admissions of SI and mSI are presented in Table 4.

Discussion

In this study, we compared the prognostic performance of SI and mSI in terms of in-hospital mortality and ICU admission in

Table 1. Baseline characteristics of the patients

Variables	Total n (%), mean ± SD	ICU (-) n (%), mean ± SD	ICU (+) n (%), mean ± SD	*P value*
Number of patients	464 (100)	299 (64.4)	165 (35.6)	
Age, years	62.4 ± 16.7	55.8 ± 14.7	74.5 ± 13.0	< 0.001*
Gender				0.182**
Female	219 (47.2)	148 (49.5)	71 (43.0)	
Male	245 (52.8)	151 (50.5)	94 (57.0)	
Comorbidities				
Hypertension	200 (43.1)	111 (37.1)	89 (53.9)	< 0.001**
Diabetes	53 (11.4)	37 (12.4)	16 (9.7)	0.385**
Chronic renal failure	41 (8.8)	18 (6.0)	23 (13.9)	0.004**
Neurological diseases	46 (9.9)	8 (2.7)	38 (23.0)	< 0.001**
Ischemic heart disease	154 (33.2)	86 (28.8)	68 (41.2)	0.006**
COPD	174 (37.5)	74 (24.7)	100 (60.6)	< 0.001**
Cancer	83 (17.9)	31 (10.4)	52 (31.5)	< 0.001**
Number of comorbidities	1.6 ± 1.2	1.2 ± 1.1	2.3 ± 1.2	< 0.001***
Body temperature, °C	37.8 ± 1.1	37.6 ± 0.9	38.2 ± 1.1	< 0.001***
Systolic BP, mmHg	137.5 ± 33.3	137.1 ± 32.4	138.3 ± 35.0	0.621***
Diastolic BP, mmHg	85.6 ± 20.5	87.0 ± 20.4	83.1 ± 20.4	0.092***
Mean AP, mmHg	102.9 ± 24.2	103.7 ± 23.9	101.5 ± 24.7	0.466***
Saturation O_2	88.4 ± 7.6	92.6 ± 2.8	80.7 ± 7.5	< 0.001***
Pulse, beat/min	87.3 ± 21.8	79.2 ± 15.4	92.7 ± 23.4	< 0.001***
Respiratory rate, br/min	20.4 ± 5.9	17.0 ± 3.4	26.6 ± 4.3	< 0.001***
CRP, mg/dL	79.5 ± 75.6	34.2 ± 27.7	161.7 ± 65.0	< 0.001***
Shock index	0.68 ± 0.26	0.60 ± 0.17	0.81 ± 0.33	< 0.001***
Modified shock index	0.91 ± 0.35	0.79 ± 0.23	1.10 ± 0.44	< 0.001***
In-hospital mortality	73 (15.7)	4 (1.3)	69 (41.8)	< 0.001**

Notes: *Student's t-test, **Pearson's chi-square, ***Mann–Whitney U
AP = arterial pressure; BP = blood pressure; br = breath; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; and ICU = intensive care unit.

Table 2. Optimum cutoff points* for SI and mSI in predicting in-hospital mortality and ICU admissions

	Cutoff Point	Sens (%)	Spec (%)	PPV (%)	NPV (%)	AUC	Youden's Index
In-hospital mortality							
SI	0.72	71.2	69.6	30.4	92.8	0.719	0.408
mSI	1	74.0	72.4	33.3	93.7	0.739	0.464
ICU admissions							
SI	0.73	61.2	78.3	60.8	78.5	0.704	0.395
mSI	0.98	65.5	78.9	63.2	80.6	0.729	0.444

Notes: *Cutoff points with the highest Youden's index value were shown.
AUC = area under the curve; ICU = intensive care unit; mSI = modified shock index; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; SI = shock index; and Spec = specificity.

Table 3. Odds ratios of SI and mSI at optimal cutoff points

	Cutoff	OR	95% CI	*P*
In-hospital mortality				
SI	0.72	5.660	3.263 to 9.816	< 0.001
mSI	1	7.395	4.190 to 13.049	< 0.001
ICU admissions				
SI	0.73	5.681	3.745 to 8.618	< 0.001
mSI	0.98	7.098	4.642 to 10.852	< 0.001

Notes:
CI = confidence interval; ICU = intensive care unit; mSI = modified shock index; OR = odds ratio; and SI = shock index.

patients diagnosed and hospitalized with COVID-19. In this cohort, we concluded that both SI and mSI can be useful in predicting in-hospital mortality and ICU requirement.

Infections due to COVID-19 spread rapidly around the world, leading to a pandemic. The rapidly increasing case numbers and the high mortality/morbidity rate of the virus have caused widespread anxiety in the community. Descriptive data such as age and gender distributions of the cases will be useful in determining which populations the disease is more common in and risk groups, especially in cases where there are limited health care services.

In this study, we concluded that male gender is more associated with the ICU admission. There are articles in the literature

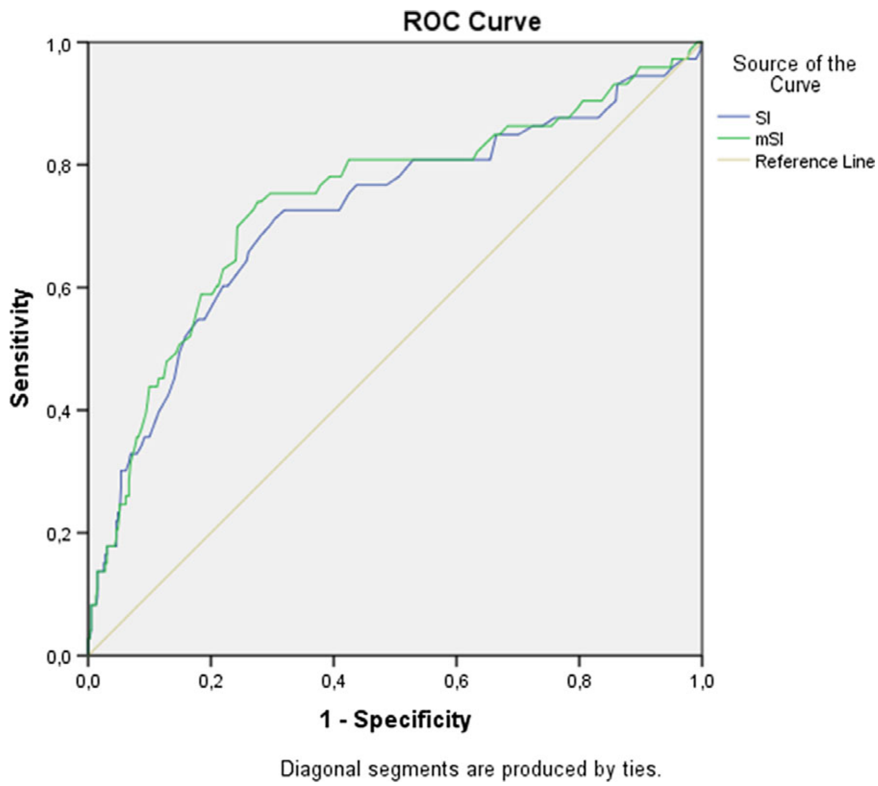

Figure 1. The ROC curves of SI and mSI for in-hospital mortality.

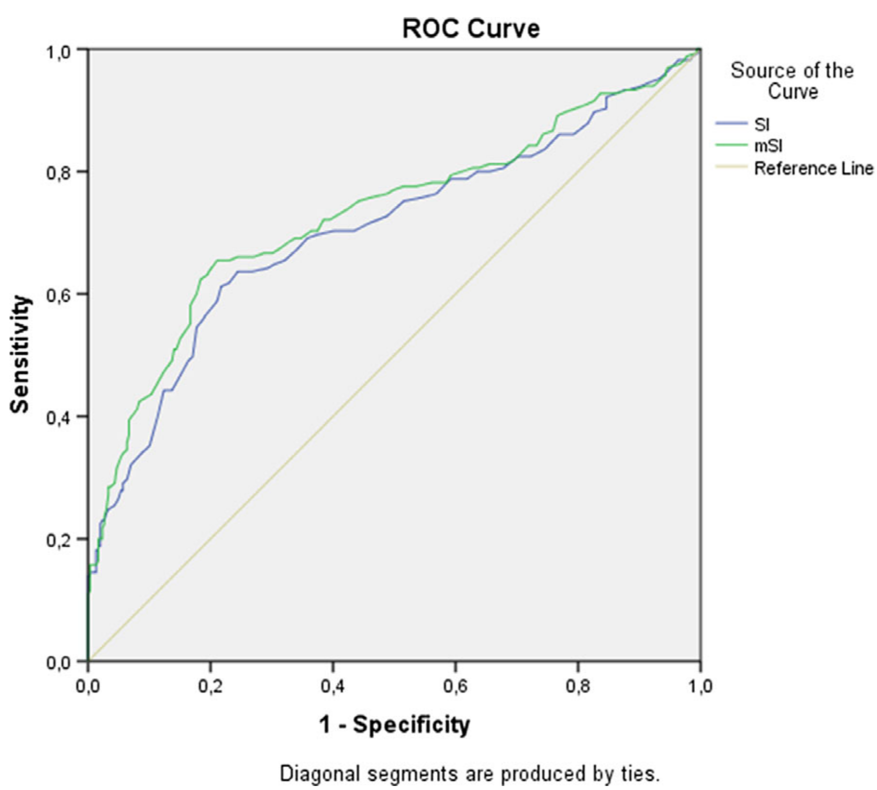

Figure 2. The ROC curves of SI and mSI for ICU admissions.

Table 4. The ROC analysis for in-hospital mortality and ICU admissions of SI and mSI

	AUC	SE	95% CI	*P*
In-hospital mortality				
SI	0.719	0.037	0.647 to 0.791	< 0.001
mSI	0.739	0.036	0.669 to 0.809	< 0.001
Comparison[a] SI-mSI	−0.020[b]		−0.033 to −0.007	0.003
ICU admissions				
SI	0.704	0.027	0.651 to 0.757	< 0.001
mSI	0.729	0.026	0.677 to 0.781	< 0.001
Comparison[a] SI-mSI	−0.025[b]		−0.034 to −0.016	< 0.001

Notes: [a]DeLong's test; [b]AUC difference.
AUC = area under the curve; CI = confidence interval; ICU = intensive care unit; mSI = modified shock index; ROC = receiver operating characteristics; SE = standard error; and SI = shock index.

reporting gender-related differences in terms of the prevalence and severity of the COVID-19 infection.[8,9] In studies conducted in China, it was reported that the disease is more common in males, since ACE2 expression is more dominant in Asian males and smoking is more common in males than in females.[10]

The in-hospital mortality rate observed in our study was high (15.7%). This may be due to the advanced age of the patient (mean age 62.4 ± 16.7 years) and the high rate of comorbidity. The relationship of advanced "age" with poor outcome due to COVID-19 has also been shown in previous studies.[11,12] This may be attributed to the inability to control viral replication due to age-related defects in T-cell and B-cell functions, excessive production of type-2 cytokines, and prolonged proinflammatory responses.[13]

Hypertension was in 43.1% of the patients in this study. There are studies in the literature examining the prognosis and comorbidity of COVID-19 patients. In a study of 5700 cases of COVID-19 hospitalized in New York, it was reported that hypertension was the most common comorbidity, followed by obesity and diabetes.[14] In another study linking hypertension and COVID-19, it was emphasized that the immune system is disrupted by hypertension and COVID-19, and this disorder is exacerbated when blood pressure is not properly controlled.[15] Therefore, blood pressure control seems very important in such patients.

Although SI is a non-invasive measurement, it is an important marker for the early evaluation of hemodynamics and tissue perfusion.[16] Although the term *shock index* was initially investigated in shock situations, it has been studied as a prognostic tool in other critical disease conditions, especially with those who are not in shock. The normal SI value is between 0.5 and 0.7. In addition to the trauma literature in which SI > 0.9 is defined as an early predictor of the need for hemorrhagic shock, mortality, and transfusion, SI has also been studied as the predictor of the hemodynamic instability, the morbidity, and the predictor of mortality (pneumonia, myocardial infarction, gastrointestinal bleeding, etc.).[17] The mSI is obtained by adding diastolic tension to the SI. Patients with an mSI higher than 1.3 are more likely to be admitted to the ICU and the death. Both indexes were found to be associated with the increased mortality risk, the injury severity, and the time of staying in the ICU.[18] In a study examining the relationship between COVID-19 and SI, it was emphasized that advanced age and increased SI are related to mortality.[19]

In this study, SI and mSI were found to be successful in predicting ICU requirement and in-hospital mortality in COVID-patients admitted to the ED and hospitalized. In the comparison of these 2 indexes, the predictive power of mSI is higher.

Limitations

As with any retrospective study, there are some limitations in this study. The sample size of this single center study was also relatively small. More studies with a larger sample size are essential to confirm these results.

Conclusion

SI and mSI are useful in predicting in-hospital mortality and ICU requirement in COVID-19 patients. In addition, another important result of the study is that the advanced age, male gender, and hypertension may be associated with a poor prognosis.

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