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Comparison of the ability of the shock index, modified shock index and age shock index to predict mortality in geriatric patients with COVID-19 pneumonia

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ABSTRACT

Introduction: A prognostic measure is urgently needed to predict the severity and mortality of the disease at an early stage in elderly patients with COVID-19 pneumonia. We aimed determine the shock, modified shock and age shock indexes in the early prediction of mortality in advanced-age patients with COVID 19 pneumonia.

Material and Method: The study included patients over 65 years of age with COVID-19 pneumonia confirmed with a positive RT-PCR test. All three indexes were calculated for all the included patients. The ROC analysis was used to determine the predictive values of the indexes in determining mortality.

Results: After evaluating the inclusion and exclusion criteria, the study was completed with a total of 134 patients. It was found that the shock index and age shock index did not statistically significantly differ in predicting mortality (p=0.23 and p=0.06, respectively). In the ROC analysis of the modified shock index in predicting mortality, the area under the curve was 0.658 (95% CI 0.572-0.738) and the Youden index was 0.35 (p=0.02). Cases with higher modified shock index values were found to be 86 times more likely to result in mortality than those with lower values.

Conclusion: The modified shock index is a fast, simple and effective method that can be used to predict mortality during triage in the emergency department in patients aged over 65 with COVID-19 pneumonia confirmed by RT-PCR and tomography.

Keywords: Age shock index, Coronavirus, COVID-19, modified shock index, pneumonia, shock index

INTRODUCTION

The COVID-19 pandemic, which started in December 2019 and still continues its effect across the world, remaining a serious global health problem. Advanced age alone is a risk factor for mortality in patients with COVID-19 pneumonia in elderly patients, COVID-19 pneumonia can quickly lead to acute respiratory distress syndrome and other serious complications (1). Acute respiratory distress syndrome (ARDS) that is unresponsive to treatment can lead to multi-organ failure and death. Therefore, early diagnosis and timely treatment are vital in critically ill patients. In this sense, a prognostic measure is urgently needed to predict the severity and mortality of the disease at an early stage in elderly patients with COVID-19 pneumonia. A simple, inexpensive, fast predictive method that can be evaluated especially at the time of initial presentation to hospital can contribute to reducing mortality. Thus, the clinician can take more aggressive approaches while evaluating treatment protocols and prevent mortality.

The shock index (SI) is a rate that can be easily calculated based on blood pressure and pulse measurements. It basically consists of heart rate/systolic blood pressure value (2). Although it was first used to determine the degree of hypovolemia in cases of hemorrhagic and septic shock, today it is also used as an assessment scale in all types of systemic conditions in which tissue perfusion is impaired (3-6). SI has been found to have a particularly strong association with the left ventricular stroke volume and cardiac output (2). SI has also been reported as an independent risk factor of six-week mortality related to community-acquired pneumonia (7).

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The modified shock index (MSI) is found by dividing the pulse by the mean arterial pressure, and the age shock index (ASI) is obtained by multiplying age and SI. These two derivations were produced considering the theoretical contribution of diastolic blood pressure and age to SI; however, MSI has been suggested to be a better marker than SI in some studies conducted in the emergency department (ED) (8,9). In patients with sepsis, a strong relationship has been observed between myocardial dysfunction and mortality (10). This situation is expected and can be explained by the mean arterial pressure having proven itself as a better marker than systolic or diastolic blood pressure value in terms of organ perfusion while evaluating fluid resuscitation and vasopressor requirement in critically ill patients (11,12).

We did not find any published studies concerning the predictive ability of SI, MSI and ASI for mortality in geriatric patients with COVID-19 pneumonia. Therefore, in the current study

our primary aim was to compare the ability of these three indexes to predict mortality in the geriatric patient population with COVID-19 infection. We considered that taking advantage of these indexes, which can be easily measured at the bedside without any wait, can contribute to treatment strategies and mortality prevention in this disease presenting with high mortality at advanced ages. Our secondary aim was to evaluate the superiority of these indexes over each other and explore the relationship of blood test results, vital signs and comorbidities at the time of presentation with mortality.

MATERIALS AND METHODS

This study was approved by Haydarpaşa Numune Education and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2021, Decision No: 2021/KK/78). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was planned retrospectively and observationally. Patients who presented to ED due to COVID 19 pneumonia and hospitalized between March 15, 2020 and February 1, 2021 were included in the study. The institutional review board approved the analysis and issued a waiver of consent.

All patients over the age of 65 who were admitted to the ED with COVID-19 complaints, who had oropharyngeal/nasopharyngeal swabs, and who hospitalized between March 1, 2020 and February 1, 2021 were included in the study. Patients whose reverse transcriptase polymerase chainr eaction (RT-PCR) test results were negative and whose ASI, SI and MSI could not be calculated were excluded from the study.

Data were collected from electronic medical hospital records. 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 ASI-SI-MSI. ASI defined as age multiplied by SI. SI was calculated as the ratio of HR to SBP (SI=HR/SBP). MAP was calculated as follows: MAP=[SBP+(2×DBP)]/3. The MSI was calculated as the ratio HR to MAP (MSI= HR/MAP). The formulas were calculated using the vital findings at the time of first admission to the ED.

The primary outcome was in-hospital mortality. The secondary outcome was the superiority of the these indexes to each other and their relationship with comorbidities and blood test results.

Statistical analyses were performed using SPSS v. 19.0 for Windows and Med Calc software packages. Descriptive criteria were presented as mean and standard deviation, median and minimum-maximum values, and percentage distribution. The compliance of the data with normal distribution was checked using the Kolmogorov-Smirnov test. The receiver operating characteristic (ROC) analysis was used to determine the predictive values of the three indexes in mortality. The method described by Delong et al. was used to compare the ROC curves of the indexes. $p < 0.05$ was taken as the level of significance.

RESULTS

After performed the inclusion and exclusion criteria, the study was completed with 134 patients. The demographic data, vital signs, blood test results and index values of the patients are summarized in Table 1. The patients that were survivors (survivors group) and those that died (non-survivors group) were compared in relation to various data. As a result of the statistical analysis, the mean age, body temperature, pulse, neutrophil count, D-dimer, ferritin, SI, MSI and ASI were statistically significantly higher in the non-survivors group than in the survivors group, and the mean saturation and lymphocyte levels of the former were statistically significantly lower compared to the latter (**Table 1**).

The groups were compared with the chi-square test in terms of comorbidity distributions. As a result of the analysis, no statistically significant difference was found between the groups in comorbidity distributions (**Table 2**). In the ROC analysis for mortality prediction, the area under the curve (AUC) was 0.581 [95% confidence interval (CI): 0.493-0.666) and the Youden index was 0.23 for SI. In the same analysis for ASI, AUC was calculated as 0.623 (95% CI: 0.535-0.705) and the

Youden index as 0.26. Accordingly, SI and ASI did not have statistically significant value in predicting mortality (p=0.23 and p=0.06, respectively). In contrast, the ROC analysis for MSI in the prediction of mortality showed that the AUC value was 0.658 (95% CI: 0.572-0.738) and the Youden index was 0.35 (**Figure 1**). Thus, MSI was a statistically significant parameter in mortality prediction (p=0.02). When the cut-off value of MSI in determining mortality was taken as 1.07, it had 55.6% sensitivity, 79.4% specificity, 38.9 positive predictive value, and 86.7 negative predictive value (**Table 3**).

Table 2. Comparison of comorbidities between the discharged and mortality groups

	Survivors n (%)	Non-survivors n (%)	p value*
Diabetes mellitus	51 (47.7)	12 (44.4)	.77
Hypertension	82 (76.6)	19 (70.4)	.50
Coronary artery disease	22 (20.6)	3 (11.1)	.26
Asthma	5 (4.7)	3 (11.1)	.21
COPD	22 (20.6)	4 (14.8)	.50
Chronic heart failure	8 (7.5)	3 (11.1)	.54
Chronic kidney failure	12 (11.2)	5 (18.5)	.31
Other	25 (23.4)	11 (40.7)	.07

*Chi-square test, COPD: Chronic obstructive pulmonary disease

Table 1. Demographic characteristics, clinical and shock index results of the discharged and mortality groups

	Total Mean ± SD Median(min-max) n (%)	Survivors Mean ± SD Median (min-max) n (%)	Non-survivors Mean ± SD Median (min-max) n (%)	p value
Age,years	75.1 (7.4) 74 (65–97)	74.2 (7.1) 73 (65-97)	78.3 (7.7) 77 (67-97)	.01[a]
Gender Male Female		58 (76.3) 49 (84.5)	18 (23.7) 9 (15.5)	.24[b]
Body Temperature, °C	37.0 (0.9) 36.7 (35–40.5)	36.6 (3.3) 36.6 (35.0-39.5)	37.4 (1.2) 36.8 (36.0-40.5)	.03[a]
Pulse, beat/min	84.9 (16.7) 84 (54–120)	84.5 (13.5) 82.5 (54-120)	92.5 (15.5) 90 (60-120)	.006[a]
Systolic blood pressure, mmHg	128.9 (20.2) 130 (80–170)	129.1 (22.3) 130.0 (80– 170)	124.7 (23.5) 126.0 (80-168)	.29[a]
Diastolic blood pressure, mmHg	73.6 (14.2) 70 (40 -114)	74.1 (14.1) 70.0 (49-114)	71.5 (14.9) 70.0 (40-100)	.72[a]
Saturation O_2	93.8 (4.6) 95.5 (77-100)	97.8 (3.7) 96.0 (80-100)	89.9 (5.8) 90.0 (77-98)	.001[a]
Leukocyte count	8.7 (4.8) 8.4 (0.5–29.0)	8.3 (4.5) 7.1 (1.6-29.0)	10.2 (5.5) 9.4 (0.5-21.3)	.08[a]
Neutrophil count	5.9 (4.5) 5.2 (0.01–24.6)	6.2 (4.3) 5.1 (1.0-24.6)	8.5 (5.0) 8.1 (0.01-19.9)	.02[a]
Lymphocyte count	1.5 (0.9) 1.3 (0.2–6.3)	1.5 (0.8) 1.3 (0.2-4.8)	1.3 (1.5) 0.9 (0.2-6.3)	.01[a]
Hemoglobin	11.9 (2.5) 12.3 (1.1–17.1)	12.0 (2.7) 12.3 (1.1-17.1)	11.5 (2.0) 11.9 (6.3-14.5)	.11[a]
Platelet*1000	215.7 (82.9) 196.5 (44–628)	222.9 (84.8) 201.0 (81-628)	187.3 (69.4) 181 (44-337)	.05[a]
D-dimer	1694.0 (1840.4) 1040.0 (140–9989)	1406.9 (1380.9) 940.0 (140-7965)	2832.1 (2807.2) 1480.0 (240-9989)	.004[a]
Ferritin	426.7 (734.8) 201.5 (9–5842)	394.5 (762.1) 186.0 (18-5842)	539.2 (614.1) 360.0 (9-3173)	.004[a]
Mean arterial pressure	87.0 (5.9) 87.3 (67.7–100.7)	87.9 (5.2) 87.7 (76.0 -100.1)	83.7 (7.3) 84.7 (64.7-98.0)	.194[a]
Shock index	0.73 (0.7) 0.67 (0.1–8.0)	0.73 (0.72) 0.66 (0.1-8.0)	0.74 (0.27) 0.73 (0.13-1.46)	.01[a]
Modified shock index	0.97 (0.21) 0.98 (0.15–1.73)	0.96 (0.17) 0.97 (0.17-1.29)	1.07 (0.31) 1.08 (0.15-1.73)	.01[a]
Age shock index	54.3 (46.9) 49.2 (8.2–124.4)	48.6 (10.9) 48.7 (8.2-79.2)	57.9 (22.6) 52.5 (10.8-124.4)	.04[a]

[a]Mann-Whitney U test, [b]Chi-square test
SD, standard deviation

Table 3. ROC analysis results of the modified shock index in predicting mortality

Cut-off value	AUC (95% CI)	Youden index	P value	Sensitivity	Specificity	PPV	NPV
>1.07	0.658 (0.572-0.738)	0.35	.02	55.6%	79.4%	38.9	86.7

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value

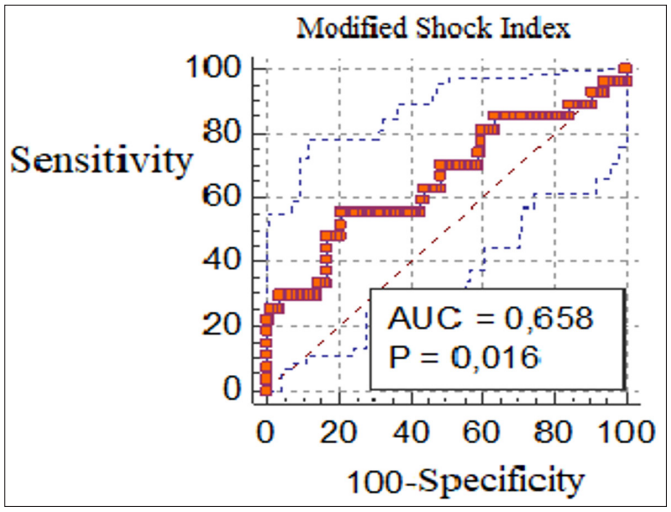

Figure. Receiver operating characteristic curve of the modified shock index

The effect of MSI on the mortality of the patients was examined using the logistic regression analysis after correcting the data according to patient age and body temperature levels which were included in the multivariate model after being determined as significant in the univariate analysis (**Table 4**). The statistical analysis showed that the cases with higher MSI values were 86 times more likely to result in mortality than those with lower MSI values.

DISCUSSION

This is the first study in the literature to compare SI, MSI and ASI in terms of their ability to predict mortality in geriatric patients with COVID-19 pneumonia. In addition to the efficacy of these indexes in mortality prediction, we also aimed to determine their superiority over each other, if any. According to our results, MSI was a simple, fast and effective predictor of mortality in advanced-age patients with COVID-19 pneumonia and it was superior to SI and ASI in this respect.

The main target in the pathogenesis of COVID-19 infection is the respiratory system with severe pneumonia (13). Severe pneumonia caused by human coronaviruses results in acute lung damage and ARDS by triggering a cytokine storm as a result of the uncontrolled excess production of cytokines 14. Increased cytokine release causes dysfunction in all tissues and organs due to the pressure created by inflammation. Vital parameters are almost always the easiest available tools to assess systemic response. Any trauma, infection, tissue and organ disorder that creates stress in the body are objectively reflected by vital parameters in the fastest way. Thus, SI, ASI, and MSI have been derived from these parameters to allow the clinician to predict the severity of the disease. Some studies have determined that SI can be used in many systemic conditions, including sepsis, trauma, pulmonary embolism, and pneumonia (7, 15-17).

In studies evaluating all age groups, it has been reported that advanced age is a single risk factor in COVID-19 pneumonia (18). In our study, when age was evaluated alone, a statistically significant difference was found between the non-survivors and survivor groups. In this sense, while ASI is expected to be an effective parameter, it did not show any statistically significant difference between the non-survivors and survivors' groups in the ROC analysis. This unexpected result can be explained by COVID-19 leading to the development of myocarditis, which is an inflammatory disease of the heart presenting with myocardial damage without an ischemic cause (19).

It has been shown that ACE2 expression, which is the main target cell in COVID-19, is particularly high in the lung, heart, ileum, kidney, and bladder (20). While no decrease in ventricular functions is generally observed in cardiac damage due to COVID-19, patients have uncomplicated lymphocytic myocarditis accompanied by normal cardiac functions (21). In more severe cases, patients may present with jugular venous fullness, peripheral edema, and right upper quadrant pain accompanied by signs of right heart failure (21). The right ventricle is considered to have high compliance and low-resistance pulmonary circulation and is suited to adapt to changes in volume rather than pressure (22).

Since the time it was introduced, SI has been used as a more significant parameter in cases of hemorrhagic shock; i.e., presence of a rapid volume change (3). Systemic infection and myocarditis due to COVID-19 more often cause right ventricular hypertrophy and acute insufficiency symptoms, which have higher adaptability to volume changes (23). In this regard, while the systolic pressure and pulse values of patients may be affected later, this pathophysiological point of view supports the results of our study.

Table 4. Logistic regression analysis of the effect of MSI on mortality

	B	SE	Wald	SD	P	Exp (B)	95% CI Lower	95% CI Upper
Age	0.09	0.034	6.70	1	0.01	1.09	1.02	1.17
Body temperature	0.683	0.249	7.52	1	0.006	1.98	1.21	3.22
MSI	4.46	1.52	8.57	1	0.003	86.146	4.36	1701.6
Constant	-37.9	10.53	12.98	1	0	0		
Nagelkerke R2=0.283 Omnibus chi-square=25.89 p=0.001 Hosmer and Lemeshov=0.16								

MSI, modified shock index; SE, standard error; SD, standard deviation; CI, confidence interval

When calculating MSI, the pulse value is divided by the mean arterial pressure. The mean arterial pressure is a stronger value than other vital parameters and used to evaluate the contraction force of the heart and vasopressor requirement of patients. In our study, a striking finding was that the cases with higher MSI were 86 times more likely to result in mortality than those with lower MSI values.

In our study, the number of patients was limited due to the selection criteria including RT-PCR positivity and a specific age group being examined. This limitation can be avoided by conducting further studies in multiple centers with a prospective and long-term design.

According to the ROC analysis conducted in the current study, SI and ASI were not effective parameters in the prediction of mortality in geriatric patients with COVID-19 pneumonia. Although these two indexes were previously reported to be effective methods in the evaluation of sepsis and other pneumonia cases, our results did not show similar efficacy in COVID-19 pneumonia (24).

CONCLUSION

MSI is a fast, simple and effective method that can be used to predict mortality during triage in the ED in geriatric patients with COVID-19 pneumonia confirmed by RT-PCR.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Haydarpaşa Numune Education and Research Hospital Clinical Researches Ethics Committee (Date: 01.03.2021, Decision No: 2021/KK/78).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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