İstanbul Med J 2023; 24(1): 65-70
DOI: 10.4274/imj.galenos.2023.44380

Investigation of the Prognostic Values of the Shock Index and Modified Shock Index in Predicting the Clinical Outcomes in Elderly Hospitalized Patients with Coronavirus Disease-2019

Serdar Yeşiltaş[1], Saadet Öztop[1], Mustafa Günay[1], İsmail Sümer[1], Sedat Akbaş[1], Sinan Yılmaz[1], Özge Pasin[2], Kazım Karaaslan[1]

[1]Bezmialem Vakıf University Faculty of Medicine, Department of Anesthesiology and Reanimation, İstanbul, Turkey
[2]Bezmialem Vakıf University Faculty of Medicine, Department of Biostatistics and Medical Informatics, İstanbul, Turkey

ABSTRACT

Introduction: Advanced age is an independent risk factor for increased mortality in coronavirus disease-2019 (COVID-19). However, the best method for estimating mortality in elderly patients with COVID-19 is still under debate. We performed this study to assess the shock index (SI) and the modified shock index (MSI) for the abovementioned problem.

Methods: A retrospective study was conducted including elderly cases (≥65 years) confirmed with COVID-19 who admitted to a tertiary university hospital between March-December 2020. The SI and MSI at the time of the emergency department visits were used to evaluate the intensive care unit admission, ventilator support, septic shock, and 30-day mortality in all patients. The receiver operating characteristic and area under the curve (AUC) were used to measure the overall ability of SI and MSI to predict clinical outcomes.

Results: We recruited 334 consecutive COVID-19 patients with a mean age of 75.2±7.3 and an almost equal gender distribution [170 males (50.9%)]. In deceased and surviving patients, the SI was 0.66±0.16 and 0.6±0.1 (p=0.014), while the MSI was 0.95±0.22 and 1.09±0.34 (p=0.003), respectively. In predicting mortality, the AUC of the SI and MSI were 0.590 [95% confidence interval (CI): 0.535 to 0.643] and 0.608 (95% CI: 0.553 to 0.660), respectively.

Conclusion: Increased SIs and MSIs are associated with 30-day mortality. SI and MSI can benefit the triage of elderly patients hospitalized for COVID-19. However, it was found that there is no single cut-off value of SI or MSI with optimum accuracy for predicting COVID-19-related clinical outcomes.

Keywords: COVID-19, modified shock index, mortality, shock index, septic shock

Introduction

Various risk factors for the clinical worsening of coronavirus disease-2019 (COVID-19) have been identified, including diabetes, hypertension, cardiovascular disease, and organ failure (1). Additionally, advanced age and male gender were defined as major non-modifiable risk factors associated with mortality (2-6). Older adults infected with COVID-19 have higher morbidity and mortality rates than younger ones. The mortality rate was higher in the elderly aged 64 years and over (6). Data from China and Italy show that the mortality rate for patients with COVID-19 is 2.3%, with more than 50% resulting in death in patients aged 50 years and older (7). In a study reported in Turkey, the overall mortality rate was 8.5%, while this rate was 14.5% in elderly patients (8).

The COVID-19 places a significant load on healthcare systems. Therefore, efforts are underway to develop simple, non-invasive, and reproducible early warning scores to predict the course of the disease to make appropriate triage at hospital admission, make different clinical decisions and encourage the correct use of medical equipment.

Shock index (SI) is a non-invasive, simple, and reproducible dynamic monitoring method. Allgöwer and Buri (9) introduced the SI in 1968 to measure the grade of hypovolemia in shocks due to hemorrhage and infections. The SI is a good predictor of mortality in different infectious conditions, exemplarily sepsis, and pneumonia (10-14). Additionally, the modified SI obtained by the ratio of the heart rate (HR) to the mean arterial pressure is a better indicator of prognosis than the SI in infectious diseases (15).

Address for Correspondence: Serdar Yeşiltaş MD, Bezmialem Vakıf University Faculty of Medicine, Department of Anesthesiology and Reanimation, İstanbul, Turkey
Phone: +90 542 363 26 30 **E-mail:** syesiltas@bezmialem.edu.tr **ORCID ID:** orcid.org/0000-0001-5811-0104

Received: 18.12.2022
Accepted: 27.01.2023

Cite this article as: Yeşiltaş S, Öztop S, Günay M, Sümer İ, Akbaş S, Yılmaz S, Pasin Ö, Karaaslan K. Investigation of the Prognostic Values of the Shock Index and Modified Shock Index in Predicting the Clinical Outcomes in Elderly Hospitalized Patients with Coronavirus Disease-2019. İstanbul Med J 2023; 24(1): 65-70.

Several studies have described the association between SI and MSI and the severity and mortality of COVID-19 (16-21). However, these reviews exclude a sub-analysis of the elderly patients, and it is still unclear whether SI and MSI have prognostic value in elderly patients. Accordingly, we investigated the ability of SI and MSI, to the prediction of 30-day mortality in elderly patients (aged above 65 years) hospitalized due to COVID-19. Secondary aims were to expect intensive care unit (ICU) hospitalization, ventilator support, and septic shock (SS) development.

Methods

This study was conducted at Bezmialem Vakıf University, a 600-bed tertiary medical center located northwest of Turkey. We retrospectively analyzed elderly patients (age above 65 years) hospitalized due to COVID-19 between March 11, 2020, and December 31, 2020. According to the World Health Organization guidelines, between March 11, 2020 and December 31, 2020, all hospitalized patients aged 65 and over who were diagnosed with COVID-19 confirmed by positive reverse transcriptase-polymerase chain reaction and died or were discharged during their follow-up were included in our study. All patients were admitted to the emergency department with COVID-19-related symptoms and a positive reverse transcription polymerase chain reaction (RT-PCR) test. A consent form was not considered due to the retrospective design. Our study was approved by the Bezmialem Vakıf University Non-Interventional Research Ethics Committee (approval number: 14/308, date: 25.08.2020). Patients were excluded in the following conditions: under 65 years of age, negative RT-PCR results, end-stage liver and kidney failure, lung cancer, cystic fibrosis, pulmonary tuberculosis, immunosuppressive therapy, history of transplantation, hospitalization 72 h before symptom onset, and unavailable data. Additionally, all patients with a critical clinical presentation (ICU admission, coma, endotracheal intubation, or receiving vasoactive drug therapy) at the time of hospital admission were also excluded from the study.

We obtained the patient's demographics, diagnoses, medical history, and laboratory and test results from the hospital's electronic health records. In addition, we evaluated comorbidities, vital signs (HR, non-invasive blood pressure, basal body temperature), laboratory results, ICU admission, ventilator support, SS development, altered mental status, length of hospital stay, and 30-day mortality. The date of nasopharyngeal swab collection was defined as the onset of infection. Altered mental status was accepted as the threshold for all patients with worsening compared with baseline mental status. Altered mental status is a general term used to describe various disorders of cognitive functioning ranging from slight confusion to coma and assessed via the Glasgow Coma scale. ICU admissions were used to describe patients who needed intensive care during their follow-up. Ventilator support refers to patients requiring invasive and non-invasive mechanical ventilation modalities due to respiratory failure. SS was used to describe patients with a lactate value greater than two mmol/L in the absence of hypovolemia and given vasopressors to maintain mean arterial pressure above 65 mmHg (22). Patients hospitalized for less than 30 days were called to determine their survival if they were not seen in the outpatient clinic.

Initial blood pressure values measured in the emergency department were used to calculate SI and MSI. The SI was calculated as the HR to systolic blood pressure (SBP), while MSI was calculated as the ratio of HR to mean arterial pressure. Since no single cut-off point is specified for SI and MSI in COVID-19 patients in the literature, we used the optimal cut-off values calculated according to the Youden index.

Statistical Analysis

The descriptive statistics of the qualitative variables in the study are given as numbers and percentages, and the descriptive statistics of the numerical variables are presented as mean, median, standard deviation, minimum, and maximum. The pearson chi-square test was used to compare the qualitative variables in terms of the distribution of the groups. The conformity of numerical variables to normal distribution was examined by the Shapiro-Wilk test. The Mann-Whitney U test was used for the mean comparisons of the groups consisting of two categories. To evaluate the SI and MSI for ICU admission, ventilator support, SS development, and 30-day mortality receiver operating characteristic (ROC) analysis was performed to obtain the area under the curve (AUC), sensitivity, and specificity. Optimal cut-off points were obtained according to the Youden index. The statistical significance level was taken as 0.05. The SPSS Version 26.0 (Statistical Package for Social Sciences Statistics for Windows, Armonk, NY: IBM Corp) and the MedCalc statistical software package were used for statistical analysis.

Results

This study was conducted with 334 patients aged 65 and over that were diagnosed with COVID-19. We recruited 334 consecutive COVID-19 patients with a mean age of 75.2±7.3 and an almost equal gender distribution [170 males (50.9%)]. Of the 334 patients included in the study, 115 (34.4%) were admitted to the ICU, 97 (29%) required ventilator support, 38 (11.4%) patients developed SS, and 83 (24.9%) patients died within 30 days. Patients who died were significantly older than surviving patients and were more likely to be male. Of the deceased and surviving patients, the SI was 0.7±0.3 and 0.6±0.1 ($p=0.044$), while the MSI was 1.1±0.4 and 0.9±0.2 ($p=0.022$), respectively. The patients' demographics, clinical features, and severity scores were compared in Table 1 regarding deceased and surviving cases.

We evaluated SI and MSI to predict 30-day mortality, ICU admission, ventilator support, and SS development. Therefore, ROC curves were obtained, and AUC values were calculated. Regarding 30-day mortality, the optimal cut-off values for SI and MSI were found to be 0.84 and 1.16, respectively. Optimal cut-off values were obtained according to the Youden index. The sensitivity, specificity, positive predictive, and negative predictive values obtained based on the optimal cut-off points of SI and MSI for clinical outcomes are summarized in Table 2.

Of the predicting mortality, the AUC of the SI and MSI were 0.590 (95% CI: 0.535 to 0.643) and 0.608 (95% CI: 0.553 to 0.660), respectively. The AUC and corresponding ROC curves of SI and MSI for 30-day mortality, ICU admission, ventilator support, and SS development are shown in Figure 1, 2.

Table 1. The baseline characteristics data of surviving and deceased patients

	All patients, (n=334) Mean ± SD or n, (%)	Survival, (n=251) Mean ± SD or n, (%)	Non-survival, (n=83) Mean ± SD or n, (%)	p-value
Age	75.19±7.30	74.33±7.05	77.80±7.46	**<0.001**
Gender				**0.027**
Female	164 (49.1%)	132 (52.6%)	32 (38.6%)	-
Male	170 (50.9%)	119 (47.4%)	51 (61.4%)	-
Comorbidity				
HT	217 (65%)	158 (62.9%)	59 (71.1%)	0.178
DM	125 (37.4%)	92 (36.7%)	33 (39.8%)	0.612
CAD	101 (30.2%)	72 (28.7%)	29 (34.9%)	0.282
CHF	95 (28.4%)	66 (26.3%)	29 (34.9%)	0.130
COPD	84 (25.0%)	66 (26.3%)	18 (21.7%)	0.402
CVA	32 (9.6%)	20 (8.0%)	12 (14.5%)	0.082

HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, n: Number, SD: Standard deviation, p<0.05

Table 2. Comparison of surviving and deceased patients in terms of vital signs and clinical outcomes within 30 days of hospitalization

	All patients, (n=334) Mean ± SD or n, (%)	Survival, (n=251) Mean ± SD or n, (%)	Non-survival, (n=83) Mean ± SD or n, (%)	p-value
Vital signs				
BBT	36.59±0.88	36.56±0.86	36.69±0.94	0.154
HR	90.85±18.76	90.51±17.78	91.88±21.55	0.724
SBP	137.81±27.31	140.38±24.65	130.01±33.08	**0.004**
DBP	72.70±15.00	74.62±14.10	66.88±16.19	**<0.001**
MBP	94.40±17.32	96.54±15.67	87.92±20.33	**<0.001**
AMS	38 (11.4%)	18 (7.2%)	20 (24.1%)	**<0.001**
Septic shock	38 (11.4%)	9 (3.6%)	29 (34.9%)	**<0.001**
ICU admission	115 (34.4%)	37 (14.7%)	78 (94%)	**<0.001**
Ventilator support	97 (29%)	25 (10%)	72 (86.7%)	**<0.001**
LOS	9.99±9.52	9.84±10.03	10.42±7.82	**0.300**
SI	0.68±0.19	0.66±0.16	0.74±0.25	**0.014**
MSI	0.99±0.26	0.95±0.22	1.09±0.34	**0.003**

BBT: Basal body temperature, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, AMS: Altered mental status, ICU: Intensive care unit, MV: Mechanical ventilation, LOS: Length of hospital stay, SI: Shock index, MSI: Modified shock index, n: Number, SD: Standard deviation, p<0.05

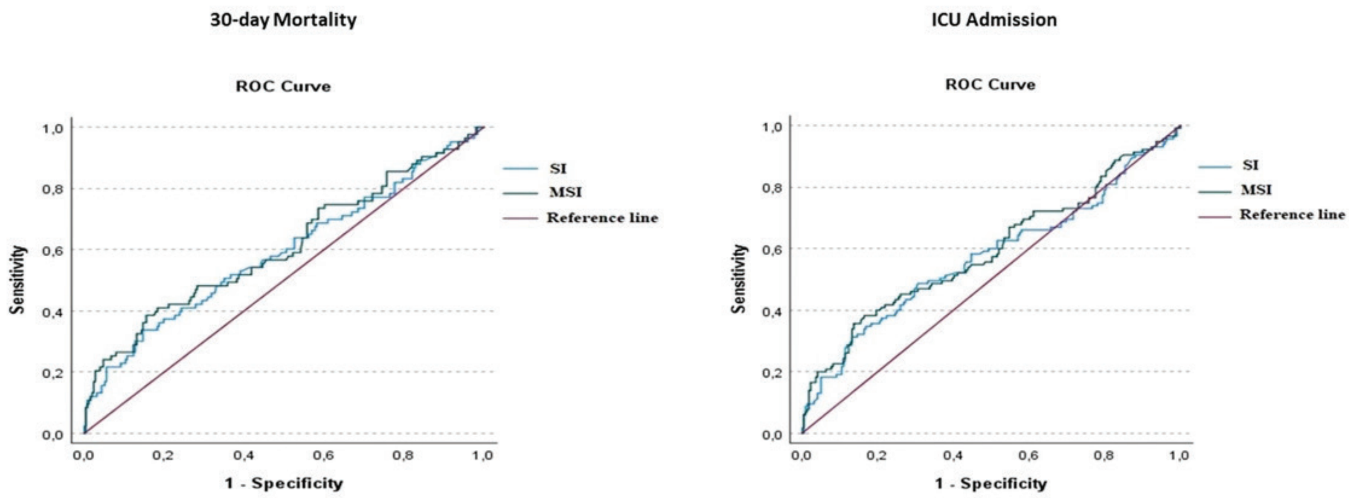
Discussion

This retrospective study evaluated the association between SI and MSI with critical clinical outcomes in elderly hospitalized patients with COVID-19. In our study, the SI and MSI were significantly higher in the group of deceased COVID-19 patients. Using SI and MSI, which are non-invasive, reproducible, and very simple to calculate, may be helpful in the triage of elderly COVID-19 patients. However, no single cut-off value of the SI and MSI with optimal accuracy for estimating critical clinical outcomes related to COVID-19 has been found.

COVID-19 has recently emerged as an essential cause of morbidity and mortality worldwide. As we mentioned, the clinical course is more severe in elderly patients. Early detection of patients who may be diagnosed with COVID-19 and need ICU is crucial. In this context, parameters that can help in clinical practice are still needed. Until today, only a few studies have analyzed the prognostic significance of SI and MSI in patients hospitalized due to COVID-19 (16-21). Studies on using SI and MSI as early warning scores in COVID-19 patients have not yielded consistent results.

In the study with 364 COVID-19 patients, Ak and Doğanay (16) determined the AUC as 0.755, sensitivity as 63.64%, and specificity as 87.4%, based on the SI cut-off value of 0.9 to estimate the 30-day mortality. They concluded that SI could be a valuable tool for estimating mortality and ICU requirements in adult patients with COVID-19.

van Rensen et al. (17) stated that SI obtained from the emergency department is unhelpful in detecting clinical deterioration and ICU admission in COVID-19. In the study by Jouffroy et al. (18), it was determined that SI in the prehospital setting was not associated with ICU admission and 30-day mortality in COVID-19.



30-day Mortality

Severity scores	AUC	CI 95%
SI	0.590	0.535 to 0.643
MSI	0.608	0.553 to 0.660

*SI/MSI p=0.19

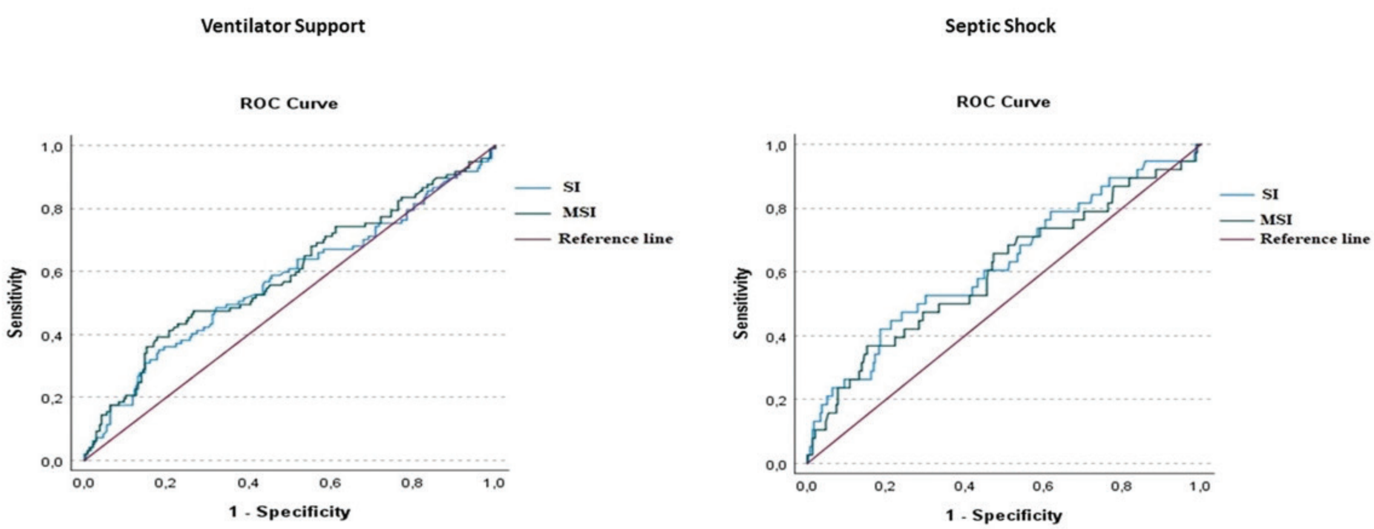
ICU Admission

Severity scores	AUC	CI 95%
SI	0.573	0.518 to 0.627
MSI	0.593	0.538 to 0.646

*SI/MSI p=0.12

Figure 1. Receiver operating characteristic curve for sensitivity, specificity, and area under the curve for 30-day mortality and intensive care unit admission estimated by shock index and modified shock index

ROC: Receiver operating characteristic, AUC: Area under the curve, ICU: Intensive care unit, SI: Shock index, MSI: Modified shock index, CI: Confidence interval



Ventilator Support

Severity scores	AUC	CI 95%
SI	0.569	0.514 to 0.622
MSI	0.591	0,536 to 0,644

*SI/MSI p=0.10

Septic Shock

Severity scores	AUC	CI 95%
SI	0.602	0.548 to 0.655
MSI	0.624	0.570 to 0.676

*SI/MSI p=0.25

Figure 2. Receiver operating characteristic curve for sensitivity, specificity, and area under the curve for ventilator support and septic shock estimated by shock index and modified shock index

ROC: Receiver operating characteristic, AUC: Area under the curve, ICU: Intensive care unit, SI: Shock index, MSI: Modified shock index, CI: Confidence interval

Aging is related to a high incidence of comorbidities and concomitant medication use. Blood pressure increases with age, and hypertension develops in almost 70% of the population over 70 (23,24). The use of antihypertensive drugs such as beta-blockers can decrease the HR rate and therefore mask the underlying shock (25). Some structural and functional changes in circulation occur with aging. So that even in the absence of these complicating factors, elderly patients may exhibit abnormal responses. Despite the high specificity, the low sensitivity of SI and MSI in our study may be explained by the deterioration of hemodynamic responses to physiological changes due to advanced age and high incidence of hypertension (65%).

HR and SBP are mainly vital signs that reflect the hemodynamic status and subsequent treatment effectiveness. However, HR and SBP can be within normal limits even in critical conditions. And it may cause delayed intervention and increased morbidity and mortality (26). Therefore, SI is a more sensitive indicator of hemodynamic decompensation. Moreover, bedside SI and vital sign evaluation may be beneficial in the clinical decision-making processes.

Study Limitations

As the main limitations, our study was retrospective, single-centered and had few participants. Since we used data from non-invasive blood pressure and HR measured at initial admission, we cannot guarantee that the measured values were obtained under optimal conditions. While the search for effective treatment regimens continued at the beginning of the coronavirus pandemic, patients were treated with different approaches as changes were made in the treatment algorithms. Our results may be biased, as this study needed to consider which treatment was effective and which was ineffective. However, new modifications are also needed to increase the sensitivity of SI and MSI in predicting COVID-19-related clinical deterioration. More extensive multicenter studies are required for this topic.

Conclusion

SI and MSI are valuable tools for predicting the disease behavior of hospitalized elderly coronavirus patients. Using SI and MSI, which are non-invasive, reproducible, and very simple to calculate, may be helpful in the triage of elderly COVID-19 patients.

Ethics Committee Approval: Our study was approved by the Bezmialem Vakıf University Non-Interventional Research Ethics Committee (approval number: 14/308, date: 25.08.2020).

Informed Consent: A consent form was not considered due to the retrospective design.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices - S.Y., İ.S., S.A.; Concept - S.Y., İ.S., S.A., K.K.; Design - S.Y., İ.S., S.A., S.Y., Ö.P., K.K.; Data Collection or Processing - S.Y., S.Ö., M.G., İ.S., S.Y., Ö.P.; Analysis or Interpretation - S.Y., S.Ö., M.G., S.A., S.Y., Ö.P., K.K.; Literature Search - S.Y., S.Ö., M.G., S.Y.; Writing - S.Y., Ö.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol 2021; 31: 1-10.
2. Cecconi M, Piovani D, Brunetta E, Aghemo A, Greco M, Ciccarelli M, et al. Early Predictors of Clinical Deterioration in a Cohort of 239 Patients Hospitalized for Covid-19 Infection in Lombardy, Italy. J Clin Med 2020; 9: 1548.
3. Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med 2020; 288: 469-76.
4. Ciceri F, Castagna A, Rovere-Querini P, De Cobelli F, Ruggeri A, Galli L, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol 2020; 217: 108509.
5. Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al; China Medical Treatment Expert Group for COVID-19. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. JAMA Intern Med 2020; 180: 1081-9.
6. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al; COVID-19 Lombardy ICU Network. 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.
7. Porcheddu R, Serra C, Kelvin D, Kelvin N, Rubino S. Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. J Infect Dev Ctries 2020; 14: 125-8.
8. Altunok ES, Alkan M, Kamat S, Demirok B, Satici C, Demirkol MA, et al. Clinical characteristics of adult patients hospitalized with laboratory-confirmed COVID-19 pneumonia. J Infect Chemother 2021; 27: 306-11.
9. Allgöwer M, Burri C. Shock-index. Ger Med Mon 1968; 13: 14-9.
10. Sankaran P, Kamath AV, Tariq SM, Ruffell H, Smith AC, Prentice P, et al. Are shock index and adjusted shock inde useful in predicting mortality and length of stay in community- acquired pneumonia? Eur J Intern Med 2011; 22: 282-5.
11. Cannon CM, Braxton CC, Kling-Smith M, Mahnken JD, Carlton E, Moncure M. Utility of the shock index in predicting mortality in traumatically injured patients. J Trauma 2009; 67: 1426-30.
12. Jaimes F, Farbiarz J, Alvarez D, Martínez C. Comparison between logistic regression and neural networks to predict death in patients with suspected sepsis in the emergency room. Crit Care 2005; 9: R150-6.
13. Otero R, Trujillo-Santos J, Cayuela A, Rodríguez C, Barron M, Martin JJ, et al; Registro Informatizado de la Enfermedad Tromboembólica (RIETE) Investigators. Haemodynamically unstable pulmonary embolism in the RIETE Registry: systolic blood pressure or shock index? Eur Respir J 2007; 30: 1111-6.
14. Rousseaux J, Grandbastien B, Dorkenoo A, Lampin ME, Leteurtre S, Leclerc F. Prognostic value of shock index in children with septic shock. Pediatr Emerg Care 2013; 29: 1055-9.
15. Jayaprakash N, Gajic O, Frank RD, Smischney N. Elevated modified shock index in early sepsis is associated with myocardial dysfunction and mortality. J Crit Care 2018; 43: 30-5.
16. Ak R, Doğanay F. Comparison of 4 different threshold values of shock index in predicting mortality of COVID-19 patients. Disaster Med Public Health Prep 2021; 1-15.

17. van Rensen IHT, Hensgens KRC, Lekx AW, van Osch FHM, Knarren LHH, van Kampen-van den Boogaart VEM, et al. Early detection of hospitalized patients with COVID-19 at high risk of clinical deterioration: Utility of emergency department shock index. Am J Emerg Med 2021; 49: 76-9.
18. Jouffroy R, Brami E, Scannavino M, Daniel Y, Bertho K, Abriat A, et al. Association between prehospital shock index and mortality among patients with COVID-19 disease. Am J Emerg Med 2022; 56: 133-6.
19. Doğanay F, Elkonca F, Seyhan AU, Yılmaz E, Batırel A, Ak R. Shock index as a predictor of mortality among the Covid-19 patients. Am J Emerg Med 2021; 40: 106-9.
20. Kurt E, Bahadirli S. The Usefulness of Shock Index and Modified Shock Index in Predicting the Outcome of COVID-19 Patients. Disaster Med Public Health Prep 2022; 16: 1558-63.
21. Avci M, Doganay F. Prognostic Performance of Shock Index, Diastolic Shock Index, Age Shock Index, and Modified Shock Index in COVID-19 Pneumonia. Disaster Med Public Health Prep 2022; 17: e189.
22. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315: 801-10.
23. Pedelty L, Gorelick PB. Management of hypertension and cerebrovascular disease in the elderly. Am J Med 2008; 121(8 Suppl): 23-31.
24. Wills AK, Lawlor DA, Matthews FE, Sayer AA, Bakra E, Ben-Shlomo Y, et al. Life course trajectories of systolic blood pressure using longitudinal data from eight UK cohorts. PLoS Med 2011; 8: e1000440.
25. Koch E, Lovett S, Nghiem T, Riggs RA, Rech MA. Shock index in the emergency department: utility and limitations. Open Access Emerg Med 2019; 11: 179-99.
26. Shoemaker WC. Relation of oxygen transport patterns to the pathophysiology and therapy of shock states. Intensive Care Med 1987; 13: 230-43.