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Original Article

Comparison of Early Mortality Prediction Methods for COVID-19 Patients Admitted to the Intensive Care Unit

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Keywords: COVID-19; intensive care unit; scoring systems.

ABSTRACT

Objective: To compare the effectiveness of shock index (SI), modified shock index (MSI), Rapid Emergency Medicine Score (REMS), quick Sepsis-Related Organ Failure Assessment (qSOFA), and Acute Physiology and Chronic Health Evaluation (APACHE II) scoring systems in the early prediction of 30-day mortality in critically ill COVID-19 patients admitted to the intensive care unit.

Methods: This study was conducted as a single-center, retrospective, observational cohort study and included patients admitted to the intensive care unit due to COVID-19 infection during the 12-month period between March 2020 and February 2021. The receiver operating characteristic curves of the scoring systems were constructed to predict 30-day mortality, and their area under curve (AUC) values were calculated. A p-value of 0.05 or less was accepted as statistically significant.

Results: The study was completed with a total of 634 intensive care patients. Mortality occurred in 75.7% (n=480) of the patients. The AUC values of the SI, MSI, REMS, qSOFA, and APACHE II scores in predicting 30-day mortality were found to be 0.59, 061, 0.72, 0.59, and 0.63, respectively. The most effective scoring was determined as REMS.

Conclusion: According to our results, REMS is a scoring system that can be used to predict 30-day mortality in COVID-19 patients admitted to the intensive care unit.

INTRODUCTION

COVID-19, which was declared a pandemic in March 2020, continues to have an impact across the world and remains a global health problem. The disease course shows different levels of severity in individuals. While some patients with COVID-19 recover from the disease at home, it can cause acute respiratory distress syndrome (ARDS) in other cases.[1] When evaluated quantitatively, critical disease is observed in 5% and serious disease in 15% of all COVID-19 patients.[2] In addition, 6%–20% of all COVID-19 patients require hospitalization, and mortality occurs in 11%–28% of hospitalized patients.[3] ARDS is the most serious complication that develops in these patients. Patients who have developed ARDS due to COVID-19 often require invasive mechanical ventilation, and their mortality rate is similar to those with ARDS secondary to other conditions.[4]

The early identification of critical COVID-19 patients ensures that they receive specific treatments promptly. This can reduce mortality rates, especially among those who develop ARDS. Furthermore, some specific drugs (steroids or anti-interleukin-6) have been found to be effective in patients with severe ARDS and elevated inflammatory markers.[5] Predicting which patient will have a worse prognosis can also help use resources more efficiently. Based on this information, patients whose conditions are likely to deteriorate can be hospitalized early, closely followed up and monitored, and given aggressive treatment, if necessary, under the guidance of the available medical sources.

Epidemiological studies investigating mortality in COVID-19 have revealed that the advanced age group is at a higher risk.[1,6] Therefore, we consider that the use of simple, inexpensive, and fast prediction methods that can be applied at the time of first admission to the hospital can contribute to the fight against the pandemic. Also, the pandemic has caused changes in the mortality rates of many critical diseases.[7] The prognosis can also be affected by the use of different scoring systems and markers. Discussing how well they work can make a difference in COVID-19 as in many other diseases.[8–10]

The shock index (SI) is a ratio that can be simply calculated in all cases where blood pressure and pulse can be measured. It basically consists of the pulse/systolic arterial pressure value.[11] Although it was first used to determine the degree of hypovolemia in patients with hemorrhagic and septic shock, it is also used as an assessment scale in all systemic conditions where tissue perfusion is impaired. The modified shock index (MSI), obtained by dividing the pulse by the mean arterial pressure, was developed considering the theoretical contribution of diastolic blood pressure to SI.[11] In some studies conducted in the emergency department, MSI was found to be a better predictor than SI for mortality. It has also been reported to be strongly associated with myocardial dysfunction and mortality in patients with sepsis.[1,2] This finding can be explained by the mean arterial pressure having been proven as a better predictor of organ perfusion than systolic or diastolic blood pressure when evaluating fluid resuscitation and vasopressor needs in critically ill patients.[1–3] Another scoring system, the Rapid Emergency Medicine Score (REMS), has been shown to be effective in predicting in-hospital and out-of-hospital mortality.[12,13] In the literature, it has been discussed in relation to many conditions from trauma to internal medicine emergencies.[14,15] However, REMS has been previously investigated in terms of its predictive ability for prehospital mortality in COVID 19. This predictive power has not been compared with other scores in critically ill patients.[16] The quick Sepsis-Related Organ Failure Assessment (qSOFA) is a rapid and simple scoring used to predict in-hospital mortality, and it is frequently used in patients with sepsis. Although the current sepsis guideline prioritizes other scoring systems, qSOFA has an established place in clinical practice across the world.[17] Finally, the Acute Physiology and Chronic Health Evaluation II (APACHE II) has been accepted as the most effective scoring system in the prediction of mortality and the most frequently used scoring system in intensive care units. Although this scoring system consists of too many parameters, which is considered a limitation, we included it in our study for comparative purposes.

In this study, our primary aim was to compare the mortality prediction abilities of SI, MSI, qSOFA, REMS, and APACHE II scores calculated at the time of first admission to the hospital in patients treated in the intensive care unit due to COVID-19 infection. We consider that utilizing these indices, which can be calculated quickly at admission, can contribute to treatment strategies in this disease that progresses with high mortality in intensive care patients. Our secondary aim was to explore the superiority of these indices over one another, evaluate blood tests at admission, and determine the relationship between vital signs and mortality.

MATERIALS AND METHODS

Design and setting

This research was planned as a single-center, retrospective, and observational study. The necessary permission was obtained from the institutional review board (date: March 29, 2021, number: 2021/514/198/32). The study included patients who presented to our hospital over the 12-month period between March 2020 and February 2021 and admitted to the intensive care unit primarily due to COVID-19 infection. The center where the study was conducted was a tertiary healthcare institution with 110 intensive care beds. This center allocated an intensive care unit with 70 beds to patients diagnosed with COVID-19 infection during the pandemic.

Participants

All patients with COVID-19 infection who were admitted to the intensive care unit after the presentation to the hospital and confirmed to have COVID-19 according to the reverse transcription-polymerase chain reaction test were evaluated in terms of eligibility for the study. The inclusion criteria were being aged over 18 years, receiving treatment in the intensive care unit, and COVID-19 infection being the primary reason for admission to the intensive care unit. Patients whose data could not be accessed from the hospital automation system and those who had been transferred to another hospital during their intensive care follow-up were excluded from the study.

Data collection

In our hospital, a special triage form is routinely created for each patient referred to the emergency department or the COVID-19 outpatient clinic. These forms are then transferred electronically to the hospital automation system and archive system. We obtained the data of patients from these systems and recorded them in a data form we prepared for the study. The first measured blood pressure, pulse, fever, respiratory rate per minute, and oxygen saturation values of the patients in the emergency department were transferred to this data form. In addition, the results of the first blood tests performed at arrival were recorded in this form. These tests included leukocyte, hemoglobin, hematocrit, neutrophil, lymphocyte, platelet, alanine amino transferase, aspartate amino transferase (AST), urea, creatinine, lactate dehydrogenase (LDH), procalcitonin, ferritin, d-dimer, C-reactive protein, pH, partial pressure of oxygen (pO_2), partial pressure of carbon dioxide (pCO_2), bicarbonate, base excess (BE), and lactate values. The patients' SI, MSI, REMS, qSOFA, and APACHE II scores were calculated using these values. Then, the mortality prediction abilities of these scores were compared.

Statistical analysis

IBM SPSS Statistics for Windows, Version 26.0 (Armonk, New York) and MedCalc Statistical Software, Version 19.0.6 (Armonk, New York) (MedCalc Software bvba, Ostend, Belgium, 2019) were used for statistical analyses. The normality analysis of the values was determined by creating histograms and performing the Kolmogorov–Smirnov test and the Shapiro–Wilk test. Variables with a normal distribution were compared with the Mann–Whitney U test in terms of mortality. The receiver operating characteristic (ROC) curves of the scoring systems were drawn to predict 30-day mortality, and the area under curve (AUC) values were calculated. The optimal cutoff values were determined for each scoring system using Youden's index. According to this value, the sensitivity, specificity, positive and negative predictive values, and effectiveness of the scores were calculated. A p-value of 0.05 or less was accepted as statistically significant.

RESULTS

During the 12-month study period, a total of 729 patients were included in the initial evaluation. The study was completed with 634 intensive patients due to 52 patients having a negative RT-PCR test and 43 not having COVID-19 as the primary reason for admission to the intensive care unit (ischemic cerebrovascular disease in 17, sepsis in 14, and multitrauma in 12).

It was determined that 62.30% (n=395) of the patients were males and 37.70% (n=239) were females. Of the patients who died, 63.3% (n=304) were male and 36.7% (n=176) were female patients. The survivor group had a significantly longer hospital stay than the nonsurvivor group (9.6±12.3 vs 7.6±8.5) ($p<0.05$). When examined in terms of the presence of comorbid diseases, it was determined that 89.6% of the nonsurvivor patients had at least one comorbidity. In this regard, statistically, the presence of comorbidities was strongly associated with mortality (p=0.006). When the survivor and nonsurvivor groups were compared, especially age, length of hospital day, platelet, AST, urea, creatinine, LDH, PCT, CRP, pO_2 and BE values, systolic and diastolic blood pressures at admission, pulse, minute respiratory rate, and oxygen saturation were strongly associated with mortality ($p<0.05$). The demographic data of the groups and laboratory parameters are given in more detail in Table 1.

The mean SI of the survivor group was determined as 0.8±0.3 and that of the nonsurvivor group as 0.9±0.3 (p=0.004). The mean MSI was 1.1±0.4 in the survivor group and 1.2±0.5 in the nonsurvivor group (p=0.001). The mean REMS scores of the survivor and nonsurvivor groups were 10.5±2.9 and 12.9±2.9, respectively (p=0.001). The mean

Table 1. Comparison of demographic and laboratory characteristics between the survivor and nonsurvivor groups

	Survivor group		Nonsurvivor group		p
	Mean	SD	Mean	SD	
Age[a]	67.9	14.9	72.9	13.1	0.001
LOHS (days)[b]	9.6	12.3	7.6	8.5	0.03
WBC[b]	11.9	6.4	12.7	10.9	0.99
Hemoglobin[a]	11.7	2.4	11.7	2.3	0.87
Hematocrit[a]	35.5	7.4	35.6	6.8	0.96
Neutrophil[b]	9.4	5.5	9.5	6.2	0.85
Lymphocyte[b]	0.9	0.8	1.2	2.4	0.63
Platelet[b]	268.3	112.1	223.6	100.0	0.003
ALT[b]	62.1	134.4	60.4	160.6	0.57
AST[b]	88.8	290.3	88.3	200.1	0.01
Urea[b]	64.9	48.4	96.6	83.1	0.001
Creatinine[b]	1.5	1.9	1.8	1.7	0.002
LDH[b]	460.8	330.6	661.7	1614.3	0.02
PCT[b]	3.9	12.7	8.4	70.2	0.001
Ferritin[b]	698.4	596.8	764.7	610.3	0.36
D-dimer[b]	2919.6	386.6	4072.8	5485.7	0.07
CRP[b]	102.8	81.1	150.9	109.2	0.001
pH[a]	7.40	0.11	7.34	0.12	0.06
pO_2[b]	78.8	48.9	67.5	39.2	0.03
pCO_2[a]	41.8	12.3	43.7	14.4	0.24
HCO_3[a]	24.0	4.9	22.9	6.1	0.12
BE[b]	-0.2	5.2	-2.5	11.8	0.02
Lactate[b]	2.5	1.5	3.3	2.8	0.06
SBP[a]	125.3	26.7	119.1	26.9	0.01
DBP[a]	72.6	13.7	69.1	14.9	0.01
Pulse[a]	93.5	18.9	98.5	22.1	0.01
Body temperature[a]	36.7	0.5	36.8	2.3	0.63
Respiratory rate[a]	28.2	7.8	30.6	7.6	0.001
Saturation[a]	92.1	7.1	87.3	9.8	0.001
Shock index[a]	0.8	0.3	0.9	0.3	0.004
Modified shock index[a]	1.1	0.4	1.2	0.5	0.001
REMS[a]	10.5	2.9	12.9	2.9	0.001
qSOFA score[a]	2.1	0.6	2.3	0.6	0.001
APACHE II score[a]	27.6	8.7	31.2	8.3	0.001

[a]Student's t-test. [b]Mann–Whitney U test. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; PCT: Procalcitonin; pO_2: Partial pressure of oxygen; pCO_2: Partial pressure of carbon dioxide; HCO_3: Bicarbonate; BE: Base excess; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; REMS: Rapid Emergency Medicine Score; qSOFA: Quick Sepsis-Related Organ Failure Assessment; APACHE II: Acute Physiology and Chronic Health Evaluation II; SD: Standard deviation.

Table 2. Predictive values of the scoring systems for mortality

	AUC	Cutoff	Sensitivity	Specificity	+LR	−LR	PPV	NPV	Youden's index (nonsurvivor)
Shock index	0.59 (0.56–0.64)	>0.76	58.2	60.4	1.47	0.69	82.0	31.7	0.19
Modified shock index	0.61 (0.57–0.64)	>1.24	37.5	81.2	1.99	0.77	85.3	29.2	0.19
APACHE II	0.63 (0.59–0.67)	>29	61.7	62.9	1.67	0.6	83.9	34.5	0.25
REMS	0.72 (0.68–0.76)	>12	56.3	77.1	2.5	0.6	88.4	36.2	0.33
qSOFA	0.59 (0.55–0.63)	>2	35.8	77.3	1.58	0.83	83.1	27.9	0.13

Receiver operating characteristic analysis. AUC: Area under the curve; LR: Likelihood ratio; PPV: Positive predictive value; NPV: Negative predictive value; APACHE II: Acute Physiology and Chronic Health Evaluation II; REMS: Rapid Emergency Medicine Score; qSOFA: Quick Sepsis-Related Organ Failure Assessment.

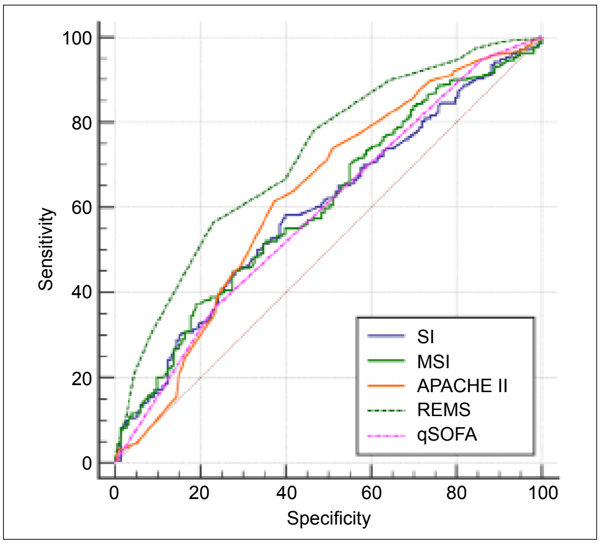

Figure 1. Graphical comparison of the area under the curve values of the scoring systems.

qSOFA score was 2.1±0.6 in the survivor group and 2.3±0.6 in the nonsurvivor group (p=0.001). Finally, in terms of APACHE II, a scoring system frequently used in intensive care units, the survivor group had a mean score of 27.6±8.7 and the nonsurvivor group had a mean score of 31.2±8.3.

Using the ROC analysis, we calculated the AUC values of the scoring system in the prediction of 30-day mortality (Table 2, Fig. 1). The AUC values of SI, MSI, REMS, qSOFA, and APACHE II scores were 0.59, 0.61, 0.72, 0.59, and 0.63, respectively (Table 2). REMS was found to be statistically significantly more effective than the remaining scoring system in the early prediction of mortality in COVID-19 patients admitted to the intensive care unit.

DISCUSSION

In this study, we investigated the effectiveness of SI, MSI, qSOFA, REMS, and APACHE II scoring systems in the prediction of early mortality in COVID-19 patients admitted to the intensive care unit. According to our results, REMS is an effective scoring system that can be used for this purpose.

The early prediction of mortality due to COVID-19 remains a controversial issue. The early identification of critically ill patients with easy-to-access parameters can allow the clinicians to apply more aggressive treatment approaches when necessary. Identifying cases that are likely to have a fatal course of COVID-19 can also provide the clinicians with foresight for the treatment plan, preparation, and advanced treatment approaches, such as higher-dose steroids or anti-interleukin-6 drugs.[5]

SI and MSI are parameters that can be measured using the pulse and systolic blood pressure values of the patients at their first presentation.[11] These scoring systems have been investigated in terms of their ability to predict mortality due to COVID-19, but different results have been reported. In a study evaluating geriatric patients with COVID-19, SI and MSI were found to be effective in the prediction of mortality (p<0.01).[11] However, in the same study, MSI, which was found to have a higher predictive ability, had a low AUC value (0.658) at a cutoff value of 1.07.[11] Consistent with the literature, we obtained low AUC values from SI and MSI (0.59 and 0.61, respectively) in the prediction of mortality in critically ill COVID-19 patients.

qSOFA is a scoring system used to identify patients with a poor prognosis in inpatient and emergency departments.[18,19] In a study conducted in China in the early period of the pandemic, it was reported that patients with a lower qSOFA score had a lower rate of mortality.[20] Another study published later reported that qSOFA could not be used to predict mortality risk in critically ill patients.[21] In the current study, there was a significant difference between the qSOFA scores of the survivor and nonsurvivor groups (p=0.001). However, when the AUC value was examined, qSOFA had a disappointing result, presenting a value of 0.59. This is in line with the current results in the literature.

REMS has been investigated in many different clinical settings, both in-hospital and prehospital.[16,22] This score consists of the mean arterial pressure, pulse, respiratory rate, oxygen saturation, Glasgow Coma Scale score, and patient age. The score ranges from 0 to 26 points.[23] In a study including a total of 13 830 patients, the mean REMS being ≥8 was found to be strongly associated with in-hospital mortality (AUC=0.79).[16] In our study, REMS was found to be strongly associated with mortality, with a higher AUC

(0.72) value than the remaining scoring systems. Although the variables included in this score appear to be many, they are already included in the initial evaluation of each patient. Therefore, this score can be used to predict mortality in critically ill COVID-19 patients admitted to the intensive care unit under all socioeconomic conditions. In our study, REMS even had a higher AUC value than APACHE II, which is considered to be the most effective scoring system in the prediction of mortality in intensive care units.

The retrospective nature of the study, its single-center design, and the comorbid diseases of the patients not being equated with an index can be regarded as limitations. In further prospective studies, the collection of data at presentation and the evaluation of pulmonary function tests and neuroprognosis, as well as the long-term mortality status, can provide more useful data.

CONCLUSION

The COVID-19 pandemic continues with varying intensity in different parts of the world. The early prediction of mortality in COVID-19 patients admitted to the intensive care unit can contribute to reducing mortality rates in this patient population. According to the results of our study, REMS is a simple, inexpensive, and effective scoring method in the early prediction of mortality in critically ill COVID-19 patients.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Date: 29.03.2021, Decision No: 2021/514/198/32).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: U.D.H., J.S.K., K.T.S.; Design: U.D.H., J.S.K.; Supervision: K.T.S., G.A.; Fundings: H.A.İ., E.Y., G.A.; Materials: E.Y., H.A.İ; Data: E.Y., G.A.; Analysis: H.A, K.T.S.; Literature search: U.D.H., J.S.K.; Writing: U.D.H., J.S.K.; Critical revision: H.A., K.T.S, G.A.

Conflict of Interest

None declared.

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Yoğun Bakım Ünitesinde Takip Edilen COVID-19 Hastalarında Erken Dönemde Mortalite Prediksiyon Yöntemlerinin Kıyaslanması

Amaç: Bu çalışmanın amacı yoğun bakımda yatan kritik hastada 30 günlük mortalitenin erken prediksiyonunda şok indeks, modifiye şok indeks, Rapid Emergency Medicine Score (REMS), quick Sepsis Related Organ Failure Assessment (qSOFA) ve The Acute Physiology and Chronic Health Evaluation (APACHE II) skorlama sistemlerinin etkinliğini kıyaslamaktır.

Gereç ve Yöntem: Bu çalışma tek merkezli, geriye dönük, gözlemsel kohort çalışması olarak yapıldı. Mart 2020–Mart 2021 arasındaki 12 aylık dönemde COVID-19 enfeksiyonu sebebi ile yoğun bakıma alınan hastaları kapsamaktadır. Otuz günlük mortaliteyi öngörmede skorlama sistemlerinin receiver operating characteristic (ROC) eğrileri çizilmiş ve area under curve (AUC) değerleri hesaplanmıştır. İstatistiksel anlamlılık olarak p değeri 0.05 veya daha altı kabul edilmiştir.

Bulgular: Çalışma toplamda 634 yoğun bakım hastası ile tamamlandı. Hastaların %75.7 (n=480) inde mortalite ile görüldü. Değerlendirmeye alınan shockindex, modified shock index, REMS, qSOFAand APACHE 2 skorlarının 30 günlük mortaliteyi tahmin etmede AUC değerleri sırasıyla 0.59, 061, 0.72, 0.59 ve 0.63 saptandı. Buna göre en etkin skorlama REMS olarak tespit edildi.

Sonuç: Çalışmamıza göre REMS skorlama sistemi COVID-19 enfeksiyonu geçiren yoğun bakım hastasında 30 günlük mortalteyi predikte etmede kullanılabilecek bir skorlamadır.

Anahtar Sözcükler: COVID-19; skorlama sistemleri; yoğun bakım ünitesi.