ORIGINAL ARTICLE

The Performance of Risk Scoring Systems Used for Severe COVID-19 Cases in The Emergency Department

Acil Serviste Ciddi COVID-19 Vakalarında Kullanılan Risk Puanlama Sistemlerinin Performansı

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ABSTRACT
Introduction: *The aim of this study is to evaluate the performance of CURB-65, Quick Sequential Organ Failure Assessment (qSOFA), and National Early Warning Score 2 (NEWS 2) scores in predicting mortality in COVID-19 patients in emergency department.*
Method: *A total of 502 patients diagnosed with severe COVID-19 in the emergency department of a pandemic hospital were analyzed retrospectively. Demographic, clinical and laboratory data of the patients were obtained from the hospital registry system. The CURB-65, qSOFA, and NEWS2 scores of each patient were calculated separately. These patients were divided into two groups as those who survivor and those who non-survivor. All parameters and calculated risk scores were statistically compared between these two groups.*
Results: *While 281 out of 502 patients survivor, 221 non-survivor. When the CURB-65, NEWS2, qSOFA scores were compared between the two patient groups, a significant difference was found (p<0.001 for all). NEWS2 had the highest values with a sensitivity of % 92.3 and an NPV of % 90.2 when it was ≥8 (AUC: 0.861, p<0.001).*
Conclusion: *Because the NEWS2 score is superior to CURB-65 and qSOFA for predicting mortality, it can be used in the triage of severe COVID-19 patients, predicting prognosis and improving outcomes.*
ÖZET
Amaç: *Acil serviste COVID-19 hastalarında mortaliteyi öngörmede CURB-65, Quick Sequential Organ Failure Assessment (qSOFA) ve Ulusal Erken Uyarı Skoru 2 (NEWS 2) puanlarının performansını değerlendirmektir.*
Yöntem: *Bir pandemi hastanesinin acil servisinde ciddi COVID-19 tanısı alan toplam 502 hasta geriye dönük olarak incelendi. Hastaların demografik, klinik ve laboratuvar verilerine hastane kayıt sisteminden ulaşıldı. Her hastanın CURB-65, qSOFA ve NEWS2 skorları ayrı ayrı hesaplandı. Bütün hastalar hayatta kalanlar ve ölenler olarak iki gruba ayrıldı. Tüm parametreler ve hesaplanan risk skorları bu iki grup arasında istatistiksel olarak karşılaştırıldı.*
Bulgular: *502 hastanın 281'i hayatta kalırken, 221'i öldü. CURB-65, NEWS2, qSOFA skorları iki hasta grubu arasında karşılaştırıldığında, anlamlı fark bulundu (p<0,001). NEWS2 ≥8 iken, %92.3 hassasiyet ve %90.2 NPV ile en yüksek değerlere sahipti (AUC: 0.861, p<0.001).*
Sonuç: *NEWS2 skoru mortaliteyi tahmin etmede CURB-65 ve qSOFA'dan daha üstün bulunduğundan, ciddi COVID-19 hastalarının triyajında, prognozu tahmin etmede ve sonuçları iyileştirmede kullanılabilir.*

INTRODUCTION

The new type of coronavirus disease (COVID-19) caused by SARS-CoV-2, spread rapidly in a short time and was declared a worldwide pandemic by the World Health Organization. While the mortality rate is 7% in those younger than 60 years of age, it rises to 55% in those over 60 years of age (1). Therefore, early diagnosis, initiation of treatment and making the decision for hospitalization are important for the prognosis. To date, many prognostic models have been proposed to predict severe pneumonia, sepsis and death (2). Since the beginning of the pandemic, emergency services have played an important role as first line of management. Hence, the effort towards a simplified prognostic risk score model that will facilitate triage, especially in emergency room settings, is still ongoing. Prognostic scores can improve the clinical decision making in COVID-19 and this practice has been supported by international guidelines (3).

The CURB-65 score, which consists of 5 parameters, is a scoring system used for guidance in the treatment of community-acquired pneumonia (CAP). CURB-65 was confirmed to estimate the clinical outcomes in viral pneumonia. Mortality has recently been determined to increase in COVID-19 patients over 65 years of age, indicating the prognostic value of CURB-65 (4).

The National Early Warning Score 2 (NEWS 2) is a scoring

system based on routine physiological measurements and studies conducted with emergency service population indicating that the prediction value of NEWS 2 for mortality and the hospitalization at intensive care unit (ICU) are high (AUC: 0.768, 0.857, respectively) (3,5).

The Sequential Organ Failure Assessment (SOFA) score has been reported to be related to an increased mortality rate in COVID-19 patients. The Quick Sequential Organ Failure Assessment (qSOFA) score that consists of 3 clinical parameters was first developed for assessment of septic patients, it has also recently been reported to be effective for estimation of mortality in non-sepsis patients (6).

These scoring systems can help predict the prognosis and mortality rates of critically ill patients, especially in situations such as pandemics (7). This study was evaluated the performance of the mentioned risk scores in predicting mortality in COVID-19 patients in emergency department (ED).

MATERIAL AND METHOD
Study design
A total of 502 patients who had been diagnosed with severe COVID-19 in the ED and hospitalized in the ICU of a pandemic hospital between 01.04.2020 and 01.02.2021 who fulfilled the inclusion criteria, were retrospectively analyzed. The pandemic hospital where the cases were collected is a training and research hospital with a daily emergency service admission of 1000-1500 people and a 900-bed capacity. Between these dates, a total of 750 patients were examined retrospectively, but 248 patients were excluded from the study according to exclusion criteria. These patients were divided into two groups as those who survivor and those who non-survivor. All parameters and calculated risk scores were statistically compared between these two groups. The study was approved by the Necmettin Erbakan University Faculty of Medicine Local Ethics Committee (date: 19/03/2021 and number: 2021/3166) and conducted in accordance with the ethical principles of the Declaration of Helsinki.

Study population
The following criteria were considered for the diagnosis of severe COVID-19 pneumonia: 1- Presence of fever and respiratory tract infection findings and/or 2- Respiratory rate>30/min and/or 3-Severe respiratory distress (dyspnea, tachypnea, use of extra respiratory muscles) and/or 4-Oxygen saturation at room temperature of <90% (PaO2/FiO2≤300 in patients receiving oxygen) and/or 5-Presence of the characteristic thorax computed tomography (CT) findings of COVID-19 pneumonia (bilateral lobular, peripheral, widespread patchy ground glass opacities) (4,8). Patients whose thorax spiral tomography (CT) report was approved by a radiologist or a pulmonologist, and in whom real-time reverse transcriptase polymerase chain reaction (RT-PCR) tests was found to be positive, were included in the study.

Exclusion criteria
Patients younger than 18 years, pregnant women, those with chronic obstructive pulmonary disease, cancers, immunosuppressive patients, those who had been exposed to trauma, those whose information could not be accessed from the electronic registry system and whose

unconfirmed diagnosis of SARS-CoV-2 infection, were excluded from the study.

Data collection
Age, gender, Glasgow Coma Scale (GCS) score, systolic blood pressure, fever, pulse, respiratory rate, saturation, need for nasal O2 support, urea, lymphocyte, ferritin, procalcitonin, D-dimer values, PCR results, thorax CT report, need for mechanical ventilation (non-invasive/invasive/high-flow nasal cannula oxygen) and the clinical outcomes (discharge/ in-hospital mortality) were obtained retrospectively from the patient epicrisis forms. The CURB-65 score, which consists of the parameters of confusion, urea, respiratory rate, systolic blood pressure and age, is scored from 0 to 5. While a score of 0-1 indicates low mortality, a score of ≥2 is associated with higher mortality (4). In the qSOFA score, 1 point is assigned to each of the respiratory rate, GCS score and systolic blood pressure parameters. A qSOFA score of ≥2 indicates high in-hospital mortality (9). The NEWS2 score uses fever, pulse, systolic blood pressure, respiratory rate, level of consciousness, saturation, and supportive oxygen parameters. Each parameter is given a score between 0 and 3. NEWS is divided into three categories: low risk (0-4), medium risk (5-6) and high risk (≥ 7) (10). The CURB-65, qSOFA and the NEWS2 scores of each patient were calculated separately at the admission of emergency service.

Statistical Analysis
A descriptive analysis was performed. The categorical data were given as ratios and numbers. They were compared using the chi-square test. The distribution of numerical data was examined using the visual and analytical methods. There were no normally distributed variables and non-normally distributed variables were given as median and interquartile range (IQR). The differences between survivors and non-survivors were compared using the Mann– Whitney U test for non-normally distributed variables. The diagnostic decision-making properties of NEWS2, CURB-65 and qSOFA in predicting mortality were analyzed by the Receiver Operating Characteristics (ROC) curve analysis. In the presence of significant breakpoints, the sensitivity, specificity, positive predictive (PPV) and the negative predictive values (NPV) of these limits were calculated. In the assessment of the area under the curve, cases with a Type-1 error level below 5% were interpreted as the diagnostic value of the test being statistically significant. Cases with a p value of < 0.05 were considered statistically significant. Statistical analysis was calculated using the IBM SPSS 22 program.

RESULTS
The comparison of the demographic, clinical and laboratory results of the two patient groups (1. Survivor patients, 2. Non-survivor patients) has been presented in Table 1. While 281 out of 502 patients survivor, 221 non-survivor. The mortality rate was 44%. The mean age of all patients was 73 (IQR 18) years and 260 (51.8%) were male. There was a significant difference between the groups with regard to age and gender (p<0.05). The mean duration of hospital stay was 10 days (IQR 9) and no significant difference was found between the groups (p=0.089). While age, clinical and laboratory

Table 1: Comparison of demographic, clinical and laboratory findings of survivor and non-survivor patients

Variable	All patients (n=502)		Survivor patients (n=281)		Non survivor patient (n=221)		p-Value
	Value	Min - Max	Value	Min - Max	Value	Min - Max	
Age. median (IQR). years	73 (18)	20 – 105	72 (21)	21 – 105	75 (16)	20 – 93	0.020*
Male. n(%)	260(51.8)		128(45.5)		132(59.7)		0.002*
Female. n(%)	242(48.2)		153(54.5)		89 (40.3)		
GCS. median (IQR)	12 (4)	6 – 15	14 (3)	8 – 15	10 (4)	6 – 15	<0.001*
Urea. median (IQR). mg/dL	53.5 (51)	13 – 343	47 (44)	13 – 273	66 (68)	17 – 343	<0.001*
Respiratory rate. median (IQR)	18 (16)	10 – 38	12 (4)	10 – 36	28 (6)	12 – 38	<0.001*
Saturation. median (IQR)	80 (12)	35 – 97	85 (8)	35 – 97	77 (12)	50 – 95	<0.001*
Fever. median (IQR).°C	36.8 (1.6)	35 – 41	36.4 (0.5)	35 –38.5	37.8 (0.7)	36 – 41	<0.001*
Heart rate. median (IQR)	85 (45)	60 – 150	75 (20)	60 – 130	120 (30)	60 – 150	<0.001*
SBP. median (IQR). mmHg	100 (30)	10 – 185	120 (30)	80 – 185	95 (15)	10 – 170	<0.001*
Receiving O2 support. n(%)	300(59.8)	35 – 97	107(35.7)	35 – 97	193(64.3)	50 – 95	<0.001*
Lymphocyte count. median (IQR). 103/mL	0.74(0.55)	0.96 –43	0.82(0.54)	0.96 –32	0.60(0.54)	2.8 – 43	<0.001*
Ferritin. median (IQR). µg/L	320 (573)	8 – 2800	247 (529)	8 – 1800	398.5(615)	20 –2800	<0.001*
D-dimer. median (IQR). µg/mL	1.2 (6.8)	0.1–45507	0.9 (3.6)	0.1 – 2983	2 (8.6)	0.1- 45507	0.003*
PRC. median (IQR). µg/mL	0.2 (0.7)	0 – 105	0.2 (0.4)	0 – 100	0.4 (1.4)	0 – 105	<0.001*
MV support. n(%)	252 (50.2)		58 (23)		194 (77)		<0.001*
Consolidation in CT. n(%)	440 (87.6)		232 (52.7)		208 (47.3)		<0.001*
Length of stay in hospital. median (IQR). day	10 (9)	1 – 57	10 (9)	1 – 53	10 (10)	1 – 57	0.089
CURB-65. median (IQR)	2 (2)	0 – 5	1 (1)	0 – 3	3 (2)	0 – 5	<0.001*
NEWS2. median (IQR)	9 (4)	3 – 19	7 (3)	3 – 16	11 (5)	3 – 19	<0.001*
qSOFA. median (IQR)	1 (1)	0 – 3	1 (1)	0 – 3	2 (2)	0 – 3	<0.001*

†GCS: glaskow coma scale. SBP: systolic blood pressure. PRC: procalcitonin. MV: mechanical ventilation. CT: Computed tomography.

findings other than saturation, systolic blood pressure and lymphocytes, CURB-65, NEWS2 and qSOFA scores of the non-survivor were higher (p<0.05), also their nasal O2 and mechanical ventilation requirements were higher (p<0.001). When these three risk scores were compared between the patient groups, a significant difference was found (p<0.001).

The ROC analysis of the CURB-65, NEWS2, and qSOFA scores in predicting mortality has been demonstrated in Figure 1. The AUC values of these scores in prediction of mortality have been displayed in Table 2, and NEWS2 had the highest AUC value compared to other scores. But

Table 2: Area under the receiver operating characteristics curve (AUROC) for the scoring system in predicting severe COVID-19 mortality.

Scores	AUC	95% confidence interval	p-Value
NEWS2	0.861	0.828 – 0.894	<0.001*
CURB-65	0.833	0.797 – 0.869	<0.001*
qSOFA	0.761	0.719 – 0.803	<0.001*

qSOFA had the lowest AUC value in other scores (AUC: 0.861, 0.833, 0.761, respectively).

The sensitivity, specificity, PPV and NPV values in estimating mortality according to the cut-off values of the scores have been demonstrated in Table 3. When compared with CURB-65 and qSOFA, NEWS2 had the highest values with a sensitivity of 92.3% and an NPV of 90.2% when it was ≥8. When compared with NEWS2 and qSOFA, CURB-65 had the highest values with a specificity of 97.9% and an PPV of 95.4% when it was ≥3.

DISCUSSION

Advanced age, comorbidity and the male gender are risk factors for the development of severe COVID-19 (11). Cheng P et al. stated that most patients with COVID-19 pneumonia were male, elderly and had comorbid diseases. They also stated that the need for non-invasive and invasive ventilator support, mortality and hospital stay of these patients were 49.1%, 37.7%, 30% and 35 days, respectively (12). In our study, most of the patients who non-survivor were elderly and male, and the need for nasal O2 support and mechanical ventilation was higher than those who survivor. The fact that all patient groups

Table 3: Diagnostic performance of score systems in predicting mortality.

|	Score (n)	Death (n)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CURB65	<2 (177)	28	87.3	53	59.4	84.2
	≥2 (325)	193				
	<3 (372)	97	56.1	97.9	95.4	73.9
	≥3 (130)	124				
NEWS2	<8 (174)	17	92.3	55.9	62.2	90.2
	≥8 (328)	204				
	<9 (242)	35	84.2	73.7	71.5	85.5
	≥9 (260)	186				
qSOFA	<2 (315)	88	60.2	80.8	71.1	72.1
	≥2 (187)	133				

in our study consisted of those hospitalized in ICU can be explained as the reason for the higher mortality rate and shorter hospital stay.

Early diagnosis and treatment of severe COVID-19 patients can prevent ICU admissions and even death. Therefore, emergency physicians must distinguish those with high mortality risk. With early warning scoring systems, decisions can be made to provide advanced care conditions for patients to be admitted to the ICU (13). Therefore, studies are ongoing to develop a scoring system that can predict the prognosis in patients with COVID-19 (14). The scoring systems used thus far in sepsis and pneumonia have also been evaluated for COVID-19, but it has not yet been determined whether or not these scores can also be used in COVID-19 patients (15). Community-acquired pneumonia guidelines have recommended that patients with a CURB-65 score of 0 and 1 should be treated as outpatient, those with a score of 2 should be hospitalized and those with a score of 3 or above should be evaluated for admission to the ICU (16). Guo J et al. reported that the cut-off value of CURB-65 ≥2 value could serve to predict the rapid progression of COVID-19 and

death4. Satıcı C. et al. also found 73% sensitivity and 85% specificity when CURB-65 was ≥ 2, in predicting the 30-day mortality (17). Shi Y. et al. also reported that NPV was 97% in inpatients and 88% in critically ill patients when CURB65 was ≥22. Bradley P. et al. stated that low CURB-65 scores did not support early COVID-19 discharge, and that only high scores could predict poor outcomes (18). According to the results of our study, AUC value for CURB-65 score was 0,833. Sensitivity was found to be 87.3%, PPV 59.4% and NPV 84.2% when cut-off value was ≥2. While high NPV found in our study enabled to better discriminate patients with low mortality and may prevent these patients to be unnecessarily hospitalized in ICU. So, as mentioned by Bradley et al., CURB-65 score seems to be able to be used only when cut-off value is ≥2 in triage of severe COVID-19 patients.

Due to its simple, rapid, and acceptable accuracy, the qSOFA score used for septic patients can be used in the ED or during hospitalization in cases where SOFA parameters cannot be obtained (7). Seymour CW et al. associated a qSOFA score of 2 or higher with increased hospital mortality9. However, in several studies, it was stated that qSOFA did not have an appropriate predictive power for the severity of the disease and mortality in COVID-19 (19,20). Jang JG et al. attributed the inability of SIRS and the qSOFA scores to predict poor outcomes in COVID-19 patients whose oxygen saturations were usually low to 'silent hypoxemia' (21). Consistent with the literature, the qSOFA score in our study showed the lowest performance in predicting mortality among other risk scoring systems (AUC 0.76). Despite the advantage of being a simple and fast-calculated score, when used alone, qSOFA may insufficient in predicting the mortality in this group of patients, most of whom are hypoxic.

Many studies have shown that the measurement of NEWS2 at the time of admission to the ED can predict important clinical outcomes such as severe sepsis, ICU admission, duration of hospital stay and mortality (22,23). Respiratory failure, which usually develops without circulatory failure, is a distinctive feature in COVID 19 patients (24). Sun Q et al. reported that the need for oxygen support was an independent risk factor for severe COVID pneumonia (25). The reason for the high predictive value of NEWS2 in COVID-19 has been associated with respiratory failure,
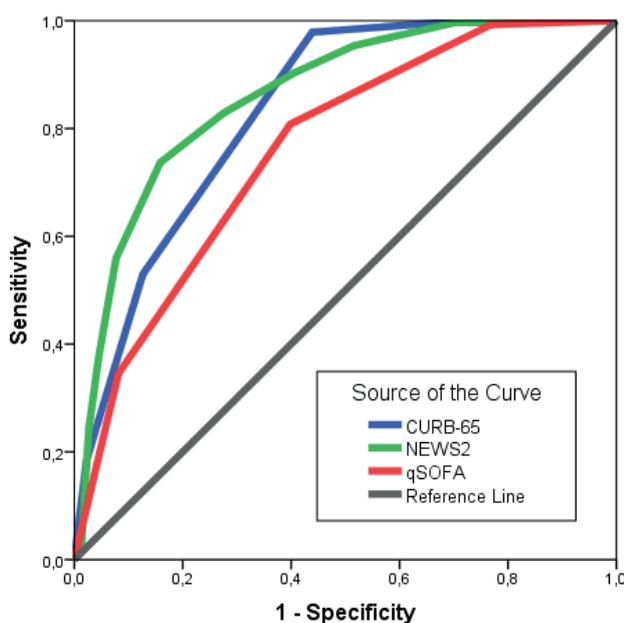
Figure 1: Roc analysis of scores in predicting mortality.

hypoxia and oxygen need (21). Myrstad et al. showed that when the NEWS2 score on admission was ≥6, its power in predicting severe disease and mortality was higher than other risk scores (26). Covino et al. emphasized that NEWS scores could be used to identify COVID-19 patients who could be followed in the non-ICU setting due to their high NPV (27). According to the results of our study, the NEWS2 score showed a higher AUC value (0.861) compared to CURB-65 and qSOFA, and reached the highest sensitivity and NPV values when NEWS was ≥8. The reasons for the superiority of NEWS2 to the other two scores for prediction of prognosis may be defined as follows: 1-Saturation, the need for oxygen support, fever and pulse parameters are also included. 2- Due to its high NPV, NEWS2 may exhibit a better performance in prediction of the patients who do not need hospitalization in ICU or who have a low mortality risk, particularly in emergency service.

LIMITATION
Our study had some limitations. First, our study was single-centered, retrospective and observational, and the validity of the data recorded through the hospital electronic registry system was not externally verified. Therefore, it should be confirmed by larger and multi-center studies. Second, we did not determine the risk factors such as smoking, alcohol consumption, immobilization, obesity and liver function tests that could determine the time of onset of symptoms, admission to the ED and mortality. Third, most of the patients had been transferred from another center to our hospital (as it is a pandemic hospital). Information regarding the initial presentation of these patients to the other hospitals could not be accessed.

CONCLUSION
The NEWS2 score can be used in the triage of severe COVID-19 patients, as its predictive value for mortality is superior to that of CURB-65 and qSOFA. We suggest that it can predict the prognosis and improve the results. With more comprehensive, prospective studies carried out in the future, new models can be created to develop a specific prognostic score for COVID-19.

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