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Predicting Mechanical Ventilation, Intensive Care Unit Admission, and Mortality in COVID-19 Patients: Comparison of Seven Different Scoring Systems

COVİD-19 Hastalarında Mekanik Ventilasyon, Yoğun Bakım Ünitesine Yatış ve Mortalite Tahmini: Yedi Farklı Skorlama Sisteminin Karşılaştırılması

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ABSTRACT *Objective:* In this study, we investigated whether scoring systems determine COVID-19 severity.
Materials and Methods: COVID-19 patients hospitalized between 01.09.2020 and 31.04.2021 were retrospectively assessed. The National Early Warning Score (NEWS), Modified Early Warning Score (MEWS), Rapid Emergency Medicine Score (REMS), Quick Sequential Organ Failure Assessment Score (q-SOFA), CURB-65, MuLBSTA, and ISARIC 4C scores on admission day were calculated. Scoring systems' ability to predict mechanical ventilation (MV) need, intensive care unit (ICU) admission, and 30-day mortality were assessed.
Results: A total of 292 patients were included; 137 (46.9%) were female, and the mean age was 62.5±15.4 years. 69 (23.6%) patients required ICU admission, 45 (15.4%) needed MV, and 49 (16.8%) died within 30 days. No relationship was found between qSOFA and MV need (p=0.167), but a statistically significant relationship was found between other scoring systems and MV need, ICU admission, and 30-day mortality (p<0.05). ISARIC-4C (optimal cut-off >5.5) and NEWS (optimal cut-off >3.5) had the highest area under the curve in ROC curve analyses, whereas qSOFA had the lowest.
Conclusion: The severity of COVID-19 could be estimated by using these scoring systems, especially ISARIC-4C and NEWS, at the first admission. Thus, mortality and morbidity would be reduced by making the necessary interventions earlier.
Keywords: COVID-19, ISARIC-4C, mortality, NEWS, scoring systems

ÖZ *Amaç:* Çalışmada skorlama sistemlerinin COVID-19 şiddetini belirleyip belirlemediğini araştırdık.
Gereç ve Yöntem: 01.09.2020-31.04.2021 tarihleri arasında yatan COVID-19 hastaları retrospektif olarak incelendi. Başvuru günündeki National Early Warning Skoru (NEWS), Modifiye Early Warning Skoru (MEWS), Rapid Emergency Medicine Skoru (REMS), quick sequential organ failure assessment skoru (q-SOFA), CURB-65, MuLBSTA ve ISARIC 4C skorları hesaplandı. Skorlama sistemlerinin mekanik ventilasyon (MV) ihtiyacını, yoğun bakım (YB) yatışını ve 30 günlük mortaliteyi öngörme kapasitesi incelendi.
Bulgular: Toplam 292 hasta dahil edildi, 137'si (%46.9) kadındı, yaş ortalaması 62.5±15.4 yıldı. Hastaların 69'unun (%23.6) YB yatışı gerekti, 45 (%15.4) hastada MV'a ihtiyaç duyuldu ve 49 (%16.8) hasta 30 gün içinde öldü. qSOFA ile MV ihtiyacı arasında bir ilişki bulunmadı (p=0.167) ancak diğer tüm skorlama sistemleri ile MV ihtiyacı, YB yatış ve 30 günlük mortalite arasında istatistiksel olarak anlamlı bir ilişki bulundu (p<0.05). ROC eğrisi analizlerinde eğri altında kalan alanı en yüksek olanlar ISARIC-4C (optimal cut-off >5.5) ve NEWS (optimal cut-off>3.5) iken en düşük qSOFA idi.
Sonuç: İlk başvurularında ISARIC-4C ve NEWS başta olmak üzere mevcut skorlama sistemleri kullanılarak COVID-19'un şiddeti tahmin edilebilecektir. Böylece gerekli müdahalelerin daha erken yapılarak mortalite ve morbiditenin azaltılabilecektir.
Anahtar Kelimeler: COVID-19, ISARIC-4C, Mortalite, NEWS, Skorlama sistemleri

Introduction

The Coronavirus Disease 2019 (COVID-19) has been diagnosed in over 750 million people, and more than 6.8 million people have died due to this disease to date (1). The disease can be asymptomatic or mild with a flu-like syndrome. However, in some cases, it progresses more severely, and pneumonia and acute respiratory distress syndrome (ARDS) can be seen (2). In severe cases, the patient may require mechanical ventilation, admission to the intensive care unit (ICU), and even die. Many studies have examined the correlation between the severity of COVID-19 and markers such as blood type (3), blood inflammation and coagulation biomarkers, and viral load (4). In addition, it is reported that various scoring systems can predict worsening and mortality in COVID-19 patients (5-13, 15-21). We aimed to investigate whether the scoring systems that can be easily calculated during the emergency admissions of COVID-19 patients determine the requirement for mechanical ventilation, ICU admission, and mortality that may occur in the follow-up of the patients.

Materials and Methods

The research is a single-center, retrospective descriptive study. Patients aged 18 years and over and hospitalized in the infectious diseases clinic and pulmonary diseases clinic with a diagnosis of COVID-19 confirmed by positive Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) between 01.09.2020 and 31.04.2021 in a secondary care hospital were included in our study. The patients' epidemiological data, chronic diseases, clinical signs, laboratory values detected at the emergency admission, and outcomes were evaluated retrospectively from the patient files. National Early Warning Score (NEWS), Modified Early Warning Score (MEWS), Rapid Emergency Medicine Score (REMS), quick sequential organ failure assessment score (q-SOFA), CURB-65, MuLBSTA and ISARIC 4C scores were calculated using MDCalc online calculator (https://www.mdcalc.com) at admissions to the hospital (Table 1). The primary endpoint of the study was 30-day mortality. Secondary endpoints were the need for mechanical ventilation and ICU admission.

Statistical Analysis

The statistics of the study were made with the IBM Statistical Package for the Social Sciences (SPSS) Version 22.0 (Armonk, NY: IBM Corp) program. Analytical tests (Kolmogorov-Smirnov / Shapiro-Wilk) were used to check variables for normal distribution. Descriptive analyses were presented using means (±standard deviation) for the normally distributed variables and medians (minimum-maximum) for the non-normally distributed. The Mann-Whitney U test was used to evaluate the association between scoring systems and the endpoints of the study since none of the scoring systems were normally distributed. The capacity

Table 1. Scoring systems evaluated in the study and the parameters they contain

Scoring System	Parameters
NEWS*	Respiratory rate, Oxygen saturation, Any supplemental oxygen Temperature, Systolic blood pressure, Heart rate, AVPU†
MEWS*	Systolic blood pressure, Heart rate, Respiratory rate, Temperature, AVPU†
REMS*	Age, Mean arterial pressure, Heart rate, Respiratory rate Peripheral oxygen saturation, Glasgow coma scale
qSOFA*	Glasgow coma scale, Respiratory rate, Systolic blood pressure
CURB-65	Confusion, BUN, Respiratory rate, Systolic or diastolic blood pressure, Age
MuLBSTA	Multilobe infiltrate, Absolute lymphocyte count, Bacterial coinfection Smoking history, History of hyper-tension, Age
ISARIC-4C	Age, Male sex, Number of comorbidities‡, Respiratory rate Peripheral oxygen saturation on room air, Glasgow coma scale Urea, C-reactive protein

*NEWS: National Early Warning Score, MEWS: Modified Early Warning Score, REMS: Rapid Emergency Medicine Score, q-SOFA: Quick sequential organ failure assessment score.
†AVPU; A:Alert, V: Response to voice, P: Response to pain, U: Unresponsive
‡Comorbidities include chronic cardiac disease, chronic respiratory disease (excluding asthma), chronic renal disease (estimated glomerular filtration rate ≤30), mild to severe liver disease, dementia, chronic neurological conditions, connective tissue disease, diabetes mellitus (diet, tablet, or insulin controlled), HIV or AIDS, and malignancy

of scoring systems in predicting the need for mechanical ventilation, ICU admission, and 30-day mortality were analyzed using receiver operating characteristic (ROC) curve analysis. Significant cut-off values were dedicated, and the sensitivity and specificity values were presented. A power analysis was conducted with a power of 95%, a margin of error of 0.05, and an effect size of 0.8, using the G*Power 3.1.9.2 program. The analysis revealed that a minimum sample size of 108 and 22 participants for groups was required to achieve adequate statistical power. A p-value of less than 0.05 was considered statistically significant.

Ethics

Ethics committee approval of the study was received from the ethics committee of Recep Tayyip Erdoğan University on 19/08/2021 with decision number 2021/149. The principles of the Helsinki Declaration were followed in the study.

Results

The data of 445 patients followed up due to COVID-19 within the specified date range were analyzed, and 153 of them did not meet the research criteria due to missing data. Thus, 292 patients were included in the study. The mean age was 62.5 ±15.4 years, and 137 patients (46.9%) were female.

During the follow-up of the patients, 69 (23.6%) required ICU admission, 45 (15.4%) needed mechanical ventilation, and 49 (16.8%) died within 30 days. The median values of the scoring systems and the distribution of these values according to the outcomes are shown in Table 2. While no statistically significant relationship was found between qSOFA and the need for mechanical ventilation (p=0.167), a statistically significant relationship was found between all scoring systems except this one and the need for mechanical ventilation, ICU admission, and 30-day mortality (Table 2). When the ROC curve was examined for the outcomes, ISARIC-4C (0.919, 0.974, and 0.918, respectively) and NEWS (0.785, 0.735, and 0.759, respectively) scores were found to have the highest area under the curve (AUC), while qSOFA (0.543, 0.556, and 0.580, respectively) have the lowest (Figure 1, Table 3). The optimal cut-off values determined for outcomes were found to be >5.5 in the ISARIC-4C score and >3.5 in the NEWS score. The percentages of sensitivity and specificity according to the determined optimal cut-off values are shown in Table 3.

Discussion

COVID-19 can be presented with a wide spectrum from asymptomatic to severe disease which may result in death. It is important to be able to predict how the prognosis will progress at the first admission of patients. In our study, the performance of scoring systems, which can be easily calculated during the first admission of COVID-19 patients, to determine the requirement for mechanical ventilation, ICU admission, and 30-day mortality was examined. Especially in patients with ISARIC-4C score >5.5 and NEWS score >3.5, COVID-19 disease was found to be more severe, while CURB-65 and MuLBSTA scores had the lowest performance.

During the course of COVID-19, the need for mechanical ventilation with endotracheal intubation may develop due to ARDS (5). Similar to our study, in determining the

Table 2. Distribution of median (minimum-maximum) values of the scoring systems according to the need for mechanical ventilation, intensive care unit admission, and 30-day mortality

	All Patients	Mechanical Ventilation		p*	Intensive Care Unit Admission		p*	30-Day Mortality		p*
		No	Yes		No	Yes		No	Yes	
NEWS†	3 [0 – 11]	2 [0 – 10]	5 [1 – 11]	<0.001	2 [0 – 10]	4 [0 – 11]	<0.001	2 [0 – 9]	5 [1 – 11]	<0.001
MEWS†	1 [0 – 5]	1 [0 – 4]	2 [1 – 5]	<0.001	1 [0 – 4]	2 [1 – 5]	<0.001	1 [0 – 4]	2 [1 – 5]	<0.001
REMS†	5 [0 – 14]	4 [0 – 10]	6 [0 – 14]	<0.001	4 [0 – 10]	6 [0 – 14]	<0.001	4 [0 – 11]	6 [1 – 14]	<0.001
qSOFA†	1 [1 – 3]	1 [1 – 2]	1 [1 – 3]	0.167	1 [1 – 2]	1 [1 – 3]	0.033	1 [1 – 2]	1 [1 – 3]	0.008
CURB-65	1 [0 – 5]	1 [0 – 4]	1 [0 – 5]	0.002	1 [0 – 4]	1 [0 – 5]	<0.001	1 [0 – 3]	2 [0 – 5]	<0.001
MuLBSTA	9 [0 – 16]	9 [0 – 16]	9 [0 – 16]	0.009	9 [0 – 16]	9 [0 – 16]	<0.001	9 [0 – 16]	9 [7 – 16]	<0.001
ISARIC-4C	3 [0 – 17]	2 [0 – 16]	10 [4 – 17]	<0.001	2 [0 -11]	10 [4 – 17]	<0.001	2 [0 – 16]	10 [2 – 17]	<0.001

*Data with a p-value below 0.05 were considered statistically significant.
†NEWS: National Early Warning Score, MEWS: Modified Early Warning Score, REMS: Rapid Emergency Medicine Score, q-SOFA: Quick sequential organ failure assessment score

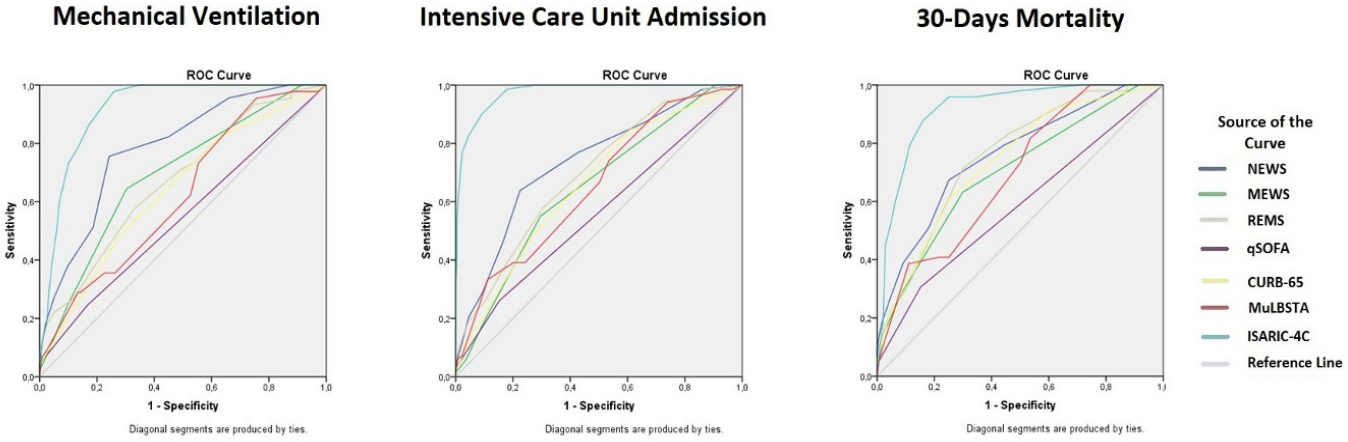

Figure 1. ROC curves of the scoring systems according to the need for mechanical ventilation, intensive care unit admission, and 30-day mortality

*NEWS: National Early Warning Score, MEWS: Modified Early Warning Score, REMS: Rapid Emergency Medicine Score, q-SOFA: Quick sequential organ failure assessment score

requirement for mechanical ventilation in COVID-19 patients, Ocho et al. (6) reported that ISARIC-4C (AUC=0.85) was better than CURB-65 (AUC=0.82) and qSOFA (AUC=0.67), and in another study (7), NEWS (AUC=0,69) was better than qSOFA (AUC=0,61). Kuroda et al. (8) found that the ISARIC-4C predicts the composite outcome of the need for mechanical ventilation and mortality better than REMS in COVID-19 patients. Chang et al. (9) reported that the detection of NEWS>7 at the first admission to the hospital can determine the need for mechanical ventilation with 72.3% sensitivity and 92.5% specificity. However, it has been reported that the MuLBSTA score (AUC=0.836) is better than CURB-65 and qSOFA in determining the need for mechanical ventilation (10). In our study, ISARIC-4C (AUC=0.919, 95% CI 0.887 – 0.951) and NEWS (AUC=0.785 95% CI 0.716 – 0.854) were the best performing scores in line with the literature in demonstrating the requirement for mechanical ventilation of COVID-19 patients while qSOFA and MuLBSTA performed poorly.

Severe COVID-19 patients may need to be admitted to the ICU for close monitoring and supportive treatment. Studies are reporting that especially the NEWS score is good at predicting ICU admission (11,12). In a study that compares scoring systems in COVID-19 patients, the NEWS score (AUC=0.73) showed the best performance for predicting ICU admission, but good results were not obtained in the qSOFA, CURB-65, and REMS scores (11). In another study, early warning scores were evaluated and it was reported that the NEWS score (AUC=0.783) was more successful in predicting ICU hospitalization within 7 days compared to MEWS, REMS, and qSOFA scores (12). However, unlike our study, it was reported that CURB-65 (AUC=0.898) was better than ISARIC-4C (AUC=0.797) (13) and MuLBSTA was better than CURB-65 and qSOFA (10) in predicting ICU admission. In our study, the most successful scores in predicting ICU admission were ISARIC-4C (AUC=0.974, 95% CI 0.959 – 0.989), NEWS (AUC= 0.735 95% CI 0.667 – 0.803) and REMS (AUC=0.694, 95% CI 0.626 – 0.763) while qSOFA did not show the expected performance.

COVID-19 may have a severe course and be mortal due to reasons such as pneumonia, sepsis, ARDS, and pulmonary thromboembolism (2,14). It is crucial to identify these patients in the early period for the chance to prevent mortality. Similar to our findings, previous research has shown that the ISARIC-4C and NEWS scores are reliable indicators of mortality in COVID-19 patients (7,8,15-18). However, studies are reporting that REMS is better than the qSOFA, NEWS, MEWS, and CURB-65 scores (11,12), and CURB-65 is better than the ISARIC-4C (13) in the prediction of mortality. Moreover, MEWS, CURB-65, and qSOFA scores have also been reported to be successful in predicting mortality (19,20). Kalani et al. (21) reported that MuLBSTA (AUC=0.832) and CURB-65 (AUC=0.809) scores performed well in predicting 30-day mortality. In our study, ISARIC-4C (AUC=0.918 95% CI 0.881 – 0.955), NEWS (AUC=0.759 95% CI 0.684 – 0.833), and REMS (AUC= 0,756 95% CI 0.688 – 0.825) scores were found to be reliable predictors of 30-day mortality, but the qSOFA did not show promising results.

Table 3. The median values of the areas under the ROC curve (AUC) of the scoring systems according to the need for mechanical ventilation, intensive care admission, and 30-day mortality, and sensitivity, and specificity results according to the optimal cut-off values

	Mechanical Ventilation					Intensive Care Unit Admission					30-Day Mortality				
	AUC (95% CI)*	p†	Cut-off	Sensitivity (%)	Specificity (%)	AUC (95% CI)*	p†	Cut-off	Sensitivity (%)	Specificity (%)	AUC (95% CI)*	p†	Cut-off	Sensitivity (%)	Specificity (%)
NEWS‡	.785 (.716 - .854)	<0.001	3.5	75.6	75.7	.735 (.667 - .803)	<0.001	3.5	63.8	77.6	.759 (.684 - .833)	<0.001	3.5	67.3	74.9
MEWS‡	.692 (.610 - .775)	<0.001	1.5	64.4	69.6	.649 (.577 - .721)	<0.001	1.5	55.1	70.4	.701 (.619 - .783)	<0.001	1.5	63.3	70
REMS‡	.670 (.585 - .756)	<0.001	5.5	57.8	66.8	.694 (.626 - .763)	<0.001	5.5	58	69.5	.756 (.688 - .825)	<0.001	5.5	71.4	70
qSOFA‡	.543 (.447 - .638)	0.360		NA		.556 (.476 - .637)	0.157		NA		.580 (.487 - .673)	0.077		NA	
CURB-65	.639 (.552 - .727)	0.003	1.5	48.9	71.7	.657 (.585 - .729)	<0.001	1.5	47.8	73.5	.739 (.665 - .813)	<0.001	1.5	61.2	74.5
MuLBSTA	.620 (.535 - .705)	0.010	8.5	62.2	47.4	.653 (.581 - .725)	<0.001	8.5	66.7	49.8	.694 (.620 - .769)	<0.001	8.5	73.5	49.8
ISARIC-4C	.919 (.887 - .951)	<0.001	5.5	86.7	82.6	.974 (.959 - .989)	<0.001	5.5	89.9	91.0	.918 (.881 - .955)	<0.001	5.5	87.8	84

*AUC: Area under the ROC curve, CI: Confidence interval.
†Data with a p-value below 0.05 were considered statistically significant.
‡NEWS: National Early Warning Score, MEWS: Modified Early Warning Score, REMS: Rapid Emergency Medicine Score, q-SOFA: Quick sequential organ failure assessment score.

Our research has limitations. First of all, it is a retrospective study. Secondly, other factors that may cause the need for mechanical ventilation, ICU admission, and mortality such as co-infections were not investigated.

Conclusion

Especially ISARIC-4C and NEWS scores showed high performance in predicting the requirement for mechanical ventilation, ICU admission, and 30-day mortality, but good results were not obtained in qSOFA. With the early use of these scoring systems in COVID-19 patients, it will be possible to distinguish patients with a risk of clinical worsening. In this way, it was thought that necessary interventions could be made earlier and a decrease in mortality rate could be achieved.

Ethics

Ethics Committee Approval: Ethics committee approval of the study was received from the ethics committee of Recep Tayyip Erdoğan University on 19/08/2021 with decision number 2021/149. The principles of the Helsinki Declaration were followed in the study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.İ., S.M.Ç., K.A., G.Ç.O., S.K., Ö.Y., Design: T.İ., Ö.Y., Data Collection and Process: T.İ., S.M.Ç., K.A., G.Ç.O., S.K., A.Ö., A.T., Analysis or Interpretation: T.İ., S.M.Ç., A.Ö., A.T., Ö.Y., Literature Search: T.İ., K.A., G.Ç.O., S.K., A.Ö., A.T., Writing: T.İ.

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