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Comparison of national early warning score 2 and quick sepsis-related organ failure assessment score in predicting severe coronavirus disease 2019: A validation study

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Abstract:

BACKGROUND AND AIM: Coronavirus disease 2019 (COVID-19) has imposed a heavy burden on the intensive care unit and health care systems worldwide. Therefore, early detection of high-risk patients in terms of poor prognosis is crucial. We aimed to compare the diagnostic yield of the two most reliable scoring systems (National Early Warning Score 2 [NEWS 2] and quick Sepsis-related Organ Failure Assessment [qSOFA]) when repeatedly performed during the COVID-19 course.

METHODS: The data of 403 COVID-19 patients admitted to our hospital between March 1, 2020, and November 30, 2020, were retrospectively reviewed. The demographic, comorbidity, and clinical data of the patients were recorded in the evaluation. NEWS2 and qSOFA score were retrospectively calculated at the time of admission, 24th hour, and 48th hour. We compared the effectiveness of qSOFA and NEWS2 for predicting the prognosis of COVID-19.

RESULTS: The mean NEWS2 at the time of admission, 24th hour, and 48th hour was significantly higher in patients with poor outcomes than in patients with good outcomes. The 48th-hour NEWS2 was found to be the most successful score in predicting the poor outcome (AUC: 0.854; 95% CI: 0.81–0.88; p<0.001). NEWS2 at 0th, 24th, and 48th hours were found to be superior to qSOFA scores at the same time points.

CONCLUSIONS: NEWS2 was superior to qSOFA in determining the need for intensive care support and/or mortality. A high NEWS2 at the 48th hour seems to be more valuable to predict worse outcomes.

Keywords:

COVID-19, early diagnosis, inpatients, Early Warning Score, Quick Sepsis-Related Organ Failure Assessment score

Our study was presented at the 43rd Annual Congress of the Turkish Respiratory Research Association on 02.10.2021 and was awarded the Remarkable Researcher Award.

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Introduction

Since December 2019, over 500 million people have been infected with the novel coronavirus, and more than 6 million people have died of coronavirus disease 2019 (COVID-19) globally.[1] As the disease may present with varying degrees of severity and offers a poorly predictable course, there is a need for reliable prognostic tools to determine which patient will develop respiratory insufficiency, multiple organ failure, and eventually die. Several individual prognostic factors were reported to be useful in predicting the disease course, but scoring systems would be more valuable and hence attractive as easy-to-use tools offering quantitative results.

There are several studies on the value of different scoring systems in COVID-19.[2–4] The results are remarkable, but they all give data on the scores applied at the time of admission. The disease course is highly unpredictable, scores vary over time, and initial assessment may not determine worse outcomes.[5] As literature lacks a comparative validation analysis on the value of repeated scores to predict the severity of COVID-19, we aimed to compare the diagnostic yield of the two most reliable scoring systems (National Early Warning Score 2 [NEWS 2] and quick Sepsis-related Organ Failure Assessment [qSOFA]) when repeatedly performed during COVID-19 course.

Materials and Methods

This retrospective methodological study was approved by the Ethical Committee of the tertiary care hospital where the study was conducted (16. Ethical Committee Meeting 1. Judgment [September 23, 2020]). Our study was performed in accordance with the ethical standards as laid down in the Helsinki Declaration of 1975, as revised in 2000.

The patients who had been diagnosed with COVID-19 and hospitalized in the inpatient services of a tertiary care hospital between March 1, 2020, and November 30, 2020, were involved. The diagnosis of COVID-19 was confirmed with polymerase chain reaction or antibody testing. Patients who were under the age of 18 years, whose state of consciousness could not be evaluated, who had insufficient data, and who had an additional infection were excluded from the study. Patients with symptoms and signs of any infectious disease other than COVID-19 and in whom the microbiological agent causing this disease could be isolated by cell culture, conventional, serological, or molecular tests were defined as patients with additional infection.

This was a retrospective methodological study. Medical records of the patients were collected through the hospital database. Demographic characteristics, comorbidities, vital signs, routine blood tests, hospitalization periods, treatment methods applied, and discharge status of the patients were recorded in the evaluation. The quantitative scores (qSOFA and NEWS2) were retrospectively calculated at the time of admission, 24th hour, and 48th hour, by clear instructions given in respective sources.[6,7] The patients who had insufficient data to calculate the scores were also excluded.

Poor outcome was defined as a composite result of the need for an intensive care unit or 28-day mortality. Patients who did not meet any of these were categorized as having a good outcome. The primary endpoint was to compare the two scoring systems to determine the poor outcome. The data on the need for intensive care unit, in-hospital mortality, and 28-day mortality were also given.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows® version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean±standard deviation (SD) for continuous variables and in number and frequency for categorical variables. Quantitative results of scoring systems were compared with receiver operating characteristic (ROC) curve analysis. The diagnostic performances of scores in predicting the poor outcome by means of sensitivity, specificity, positive and negative likelihood ratios, and area under the curve (AUC) values were given. A value of $p<0.05$ was considered statistically significant.

Results

A total of 617 patients were hospitalized during the study period. Among them, 403 patients were included in the study [Fig. 1]. Of those, 82 patients (20.3%) had a poor outcome. Based on current studies and guidelines, standard medical treatment was applied to all patients (favipiravir: 250 patients, hydroxychloroquine: 68 patients, hydroxychloroquine+favipiravir: 9 patients, and azithromycin+hydroxychloroquine: 76 patients). Prophylactic or therapeutic doses of low molecular weight

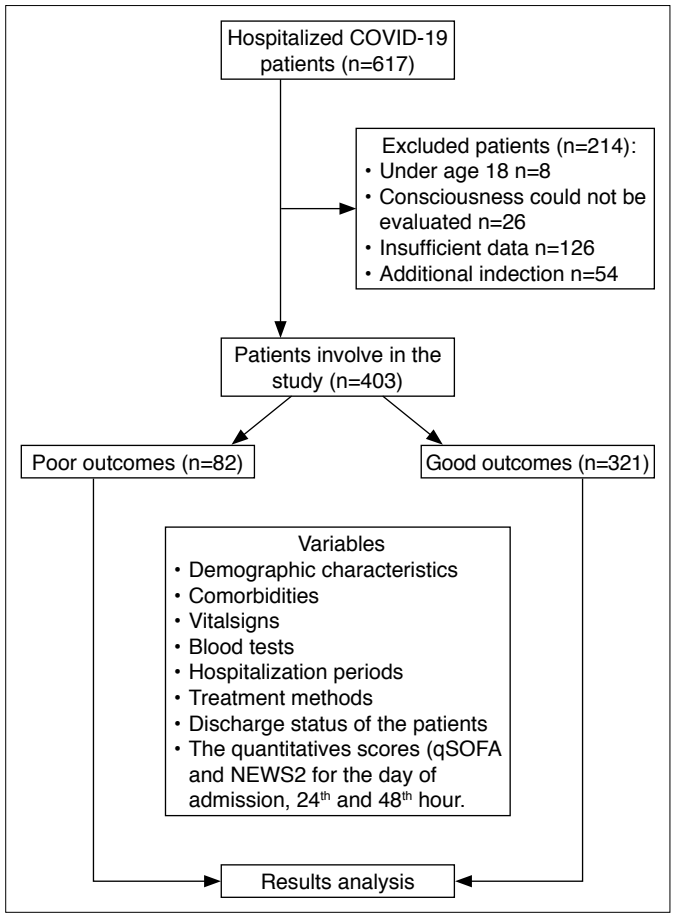

Figure 1: Patient selection flow chart
qSOFA: Quick Sepsis-related Organ Failure Assessment, NEWS2: National Early Warning Score 2

heparin were applied to all patients according to their d-dimer values. Oxygen support was started for patients with respiratory failure in room air (Table 1). In addition, all patients were given daily supportive care, and their diets were arranged to meet their energy needs. Several data on demographic features, comorbidities, and laboratory findings of the patients at the time of diagnosis are summarized in Table 1. The mean age of all patients was found to be 59.3±14.9 years. The mean age of poor outcome patients was significantly higher than that of good outcome patients (mean 66.6±14.6 years vs 57.5±14.5 years; p<0.001). Patients with poor outcomes were mostly males. Hypertension (HT) was the most common comorbid disease in both groups. HT, diabetes mellitus, malignancy, and heart failure were observed more frequently in patients with poor outcomes. The patients with poor outcome had admitted with higher respiration rates and lower oxygen saturation. In poor outcome patients, the need for oxygen support was found to be significantly higher than in the other group (p<0.001).

A statistically significant difference was found between the poor and good outcome patients by means of all laboratory parameters evaluated in our study. Cytopenia, higher C-reactive protein and d-dimer values, and hyperferritinemia were mostly seen in poor outcome patients. There was marked heterogeneity in treatment regimens between poor and good outcome groups (p<0.001). Patients with poor outcome had approximately 10 days longer to stay in the hospital than the good outcome patients. The mean duration of intensive care unit stay was 7 days in poor outcome patients. The in-hospital mortality rate of all patients was 11.2% while the 28-day mortality rate was 12.2%.

Intergroup comparisons of NEWS2 and qSOFA at the time of hospitalization, 24th, and 48th hours of admission are shown in Table 2. Average NEWS2 at the time of admission, 24th, and 48th hours was significantly higher in patients with poor outcome than in patients with good outcome. While NEWS2 was ≥5 in 51.2% of poor outcome patients at the time of admission, this rate was 66.2% at the 48th hour. The number of patients with NEWS2 of ≥5 was significantly higher in the poor outcome group at the time of admission and follow-up than in the other group (p<0.001). The qSOFA score was 0 in 65.9% of the patients in the poor outcome group during hospitalization, and the score was ≥2 in only 1 patient. When the qSOFA scores at the time of admission were compared, no significant difference was found between the groups (p=0.066), while after a 24-h and 48-h follow-up, the qSOFA score was found to be significantly higher in patients with poor outcome (p<0.001 and p<0.001, respectively).

Figure 2 shows the comparative ROC curves for the poor outcome. The diagnostic yield of the scores and the results of comparative analyses are given in Tables 3 and 4, respectively. The yield of NEWS2 was superior to qSOFA at the time of admission. The cutoff value of NEWS2 at the time of admission was found to be ≥4. The quick SOFA scores at admission and at the 24th hour failed to determine the poor outcome. The 24th-hour NEWS2 offered a similar yield with admission score, but was still superior to qSOFA at the same time point (p=0.278 and p<0.001, respectively).

The 48th-hour NEWS2 was found to be the most successful score in predicting the poor outcome. The cutoff value of the score was ≥5, sensitivity was 66.2%, specificity was 88.2% (AUC: 0.854; 95% CI: 0.81–0.88;

Table 1: Several demographic features of the cases with COVID-19 at the time of hospitalization

	All cases (n=403)		Poor outcome (n=82)		Good outcome (n=321)		p
	n	%	n	%	n	%	
Age (years) [mean±SD (min-max)]	59.3±14.9 (20–99)		66.6±14.6 (29–99)		57.5±14.5 (20–90)		**<0.001***
Sex							
Male	236		66		176		**0.003†**
Female	167		22		145		
Smoking (current or ex)	46	11.4	10	12.2	36	11.2	0.846†
Comorbidities							
Hypertension	147	36.5	39	47.6	108	33.6	**0.019†**
Diabetes mellitus	94	23.3	26	31.7	68	21.2	**0.044†**
Coronary artery disease	51	12.7	15	18.3	36	11.2	0.085†
COPD	46	11.4	12	14.6	34	10.6	0.304†
Malignancy	28	6.9	12	14.6	19	5.4	**0.002†**
CHF	14	3.5	6	7.3	8	2.5	**0.033†**
Cerebrovascular disease	5	1.2	2	2.4	3	0.9	0.269†
Other	90	22.3	22	26.8	68	21.2	0.273†
Long-term O_2 therapy	14	3.4	2	2.4	12	3.7	0.744†
Vital signs							
GCS of 15	401	99.5	80	97.6	321	100	**0.008†**
Fever (>38°C)	23	5.7	8	9.8	15	4.7	0.077†
Heart rate (beats/min)	88±11		90±10		87±11		0.065*
[mean±SD (min–max)]	(53–140)		(65–120)		(53–140)		
Systolic blood pressure (mmHg)	115±10		114±9		115±10		0.449*
[mean±SD (min–max)]	(80–166)		(90–140)		(80–166)		
Respiratory rate (breaths/min)	18±2		18±2		18±2		**0.015***
[mean±SD (min–max)]	(12–28)		(15–24)		(12–28)		
SpO_2 (%) (with O_2 if required)	94.8±2.5		93.2±2.9		95.0±2.3		**<0.001***
[mean±SD (min–max)]	(85–100)		(85–98)		(85–100)		
Need for O_2 supplementation	170	42.2	60	73.2	110	34.3	**<0.001†**
Blood tests							
Leukocyte (cells/mm^3)	7104±3443		8891±4227		6659±3068		**<0.001***
[mean±SD (min–max)]	(1000–24100)		(2700–24100)		(1000–23500)		
Lymphocyte (cells/mm^3)	1168±694		958±524		1221±721		**0.002***
[mean±SD (min–max)]	(100–8700)		(100–2600)		(100–8700)		
Neutrophil (cells/mm^3)	5271±3255		7157±4055		4800±2842		**<0.001***
[mean±SD (min–max)]	(500–22700)		(500–22700)		(700–19900)		
C-reactive protein (mg/L)	44.5		102.2		34.4		**<0.001****
[median (25–75 percentiles)]	(13.7–102.2)		(52.9–177.6)		(10.6–82.5)		
Troponin I (ng/mL)	5.30		15.2		4.7		**<0.001****
[median (25–75 percentiles)]	(3.00–12.10)		(5.1–27.3)		(3.0–8.9)		
Ferritin (mg/dL)	259		356		231		**<0.001****
[median (25–75 percentiles)]	(135–573)		(232–789)		(125–526)		
D-dimer (mg/dL)	842		1170		776		**<0.001****
[median (25–75 percentiles)]	(526–1439)		(711–2038)		(499–1255)		
Length of hospital stay	9.8±8.3		17.3±15.4		7.9±3.1		**<0.001***
[mean±SD (min–max)]	(1–122)		(2–122)		(1–22)		

*: Independent samples t-test, **: Mann-Whitney U test. †: Chi-squared test. COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, GCS: Glasgow Coma Scale, n/a: Not applicable, O_2: Oxygen, SpO_2: Oxygen saturation

p<0.001). Among qSOFA scores obtained at different time points, only the 48th-hour qSOFA score was found to be successful in predicting the poor outcome, but its yield was still behind the performance of 48th-hour NEWS2 (p<0.001).

Discussion

Many risk factors have been associated with the disease's severity in COVID-19. Among them, advanced age, male gender, smoking, comorbid diseases, and changes in lab-

Table 2: NEWS2 and qSOFA at admission, 24th and 48th hours

	All cases (n=403)		Poor outcome (n=82)		Good outcome (n=321)		p
	n	%	n	%	n	%	
Admission							
NEWS2 [mean±SD (min–max)]	2.9±1.9 (0–11)		4.4±2.1 (0–11)		2.5±1.6 (0–7)		<0.001*
NEWS2 ≥5 [n (%)]	81	20.1	42	51.2	39	12.1	<0.001†
qSOFA							0.066†
0	305	75.5	54	65.9	251	78.2	
1	95	23.6	27	32.9	68	21.2	
≥2	3	0.7	1	1.2	2	0.6	
24th hour			(n=81)				
NEWS2 [mean±SD (min–max)]	3.2±2.0 (0–12)		5.3±2.4 (0–12)		2.7±1.6 (0–8)		<0.001*
NEWS2 ≥5	93	23.1	52	64.1	41	12.8	<0.001†
qSOFA							<0.001†
0	307	76.2	54	66.6	253	78.8	
1	90	22.3	22	27.1	68	21.2	
≥2	5	1.2	5	6.1	0	0	
48th hour			(n=74)				
NEWS2 [mean±SD (min–max)]	3.2±2.0 (0–12)		5.6±2.3 (2–12)		2.7±1.5 (0–8)		<0.001*
NEWS2 ≥5	87	21.6	49	66.2	38	11.8	<0.001†
qSOFA							<0.001†
0	298	73.9	38	51.3	260	81.0	
1	93	23.1	34	45.9	59	18.4	
≥2	4	1.0	2	2.7	2	0.6	

*: Independent samples t-test, †: Chi-squared test. NEWS2: National Early Warning Score 2, qSOFA: Quick Sepsis-related Organ Failure Assessment

oratory parameters should be stated.[8–11] These were all consistent with our cases in this study. However, an individual marker may fail to predict the complex course of COVID-19 as some of the other deadly diseases. Therefore, several scoring systems have been developed and used to predict outcomes in critical illnesses. Among them, qSOFA and NEWS2 were compared in this study.

In the multicenter "Assessment of Clinical Criteria for Sepsis" study, the data of a huge number of patients between 2008 and 2013 were retrospectively analyzed, and qSOFA score was developed. Hospital mortality was found 3–14 times higher in patients who scored ≥2 from the scoring system than those who scored <2. The qSOFA score was found to be statistically superior to SOFA and Systemic Inflammatory Response Syndrome (SIRS) in predicting in-hospital mortality in patients other than those in the intensive care unit (ICU) (AUROC: 0.81; 95% CI: 0.80–0.82).[6] The Third International Sepsis and Septic Shock Definition Consensus guideline, published in 2016 recommended that qSOFA score be used in patients except for those in the ICU.[12] There were different results in studies about the efficiency of qSOFA in predicting the prognosis of COVID-19 disease. In the study by Heldt et al.,[13] qSOFA at the time of admission was not correlated with poor prognosis in COVID-19 and was not recommended for use. In another study, qSOFA at the time of admission was successful in predicting the prognosis of

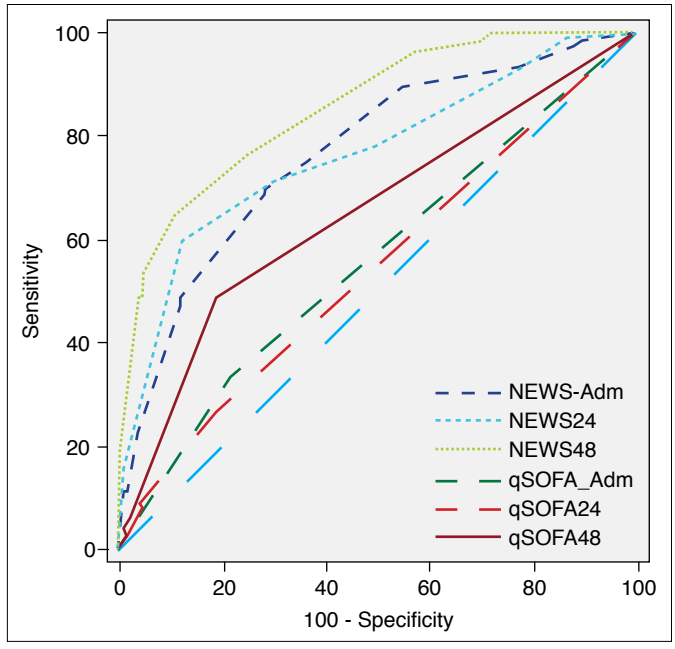

Figure 2: Receiver operating characteristic curves for poor outcome
NEWS: National Early Warning Score, Adm: Admission, qSOFA: Quick Sepsis-related Organ Failure Assessment

Table 3: Diagnostic performances of NEWS2 and qSOFA scores at specific time points

	Cutoff	Sensitivity (95% CI)	Specificity (95% CI)	+LR	–LR	AUC (95% CI)*	p
NEWS2-Adm	≥4	73.2 (62.2–82.4)	69.8 (64.4–74.8)	2.42	0.38	0.761 (0.716–0.802)	<0.001
NEWS2-24	≥5	64.2 (52.8–74.5)	87.2 (83.1–90.7)	5.03	0.41	0.804 (0.761–0.841)	<0.001
NEWS2-48	≥5	66.2 (54.3–76.8)	88.2 (84.1–91.5)	5.59	0.38	0.854 (0.816–0.888)	<0.001
qSOFA-Adm	≥1	34.1 (24.0–45.4)	78.2 (73.3–82.6)	1.57	0.84	0.562 (0.512–0.611)	0.087
qSOFA-24	≥2	33.3 (23.2–44.7)	78.8 (73.9–83.2)	1.57	0.85	0.567 (0.517–0.616)	0.065
qSOFA-48	≥1	48.6 (36.9–60.6)	81.0 (76.3–85.1)	2.56	0.63	0.649 (0.600–0.696)	<0.001

*: Receiver operating characteristic analysis. NEWS2: National Early Warning Score 2, qSOFA: Quick Sepsis-related Organ Failure Assessment, CI: Confidence interval, LR: Likelihood ratio, AUC: Area under the curve, Adm: Admission

Table 4: Comparison of the AUC values on the ROC curve*

	NEWS2-Adm	NEWS2-24	NEWS2-48	qSOFA-Adm	qSOFA-24	qSOFA-48
NEWS2-Adm		0.278	0.004	<0.001	<0.001	0.050
NEWS2-24	0.278		0.031	<0.001	<0.001	0.002
NEWS2-48	0.004	0.031		<0.001	<0.001	<0.001
qSOFA-Adm	<0.001	<0.001	<0.001		0.755	0.058
qSOFA-24	<0.001	<0.001	<0.001	0.755		0.020
qSOFA-48	0.050	0.002	<0.001	0.058	0.020	

*: p values were given by the receiver operating characteristic comparison. AUC: Area under the curve, ROC: Receiver operating characteristic, NEWS2: National Early Warning Score 2, Adm: Admission, qSOFA: Quick Sepsis-related Organ Failure Assessment

COVID-19.[14] Our study has differed from these studies in that the scores include not only the time of admission but also the measurements of the 24th and 48th hours. In our study, although the qSOFA at admission could not predict poor prognosis, qSOFA at 48 hours was successful in predicting poor outcomes. These results have demonstrated the importance of daily monitoring of the qSOFA in predicting the poor outcome of COVID-19.

NEWS2 was developed in 2012 and updated in 2017 by the multidisciplinary working group determined by the "Royal College of Physicians London (RCP London)" in the UK National Health Service (NHS) to provide standardization in the evaluation of acute diseases and determination of clinical response. It consists of seven parameters: respiration rate, oxygen saturation, blood pressure, pulse, temperature, state of consciousness, and oxygen support.[7] Many studies have supported the effectiveness of NEWS2. In a study from Scotland, NEWS2 successfully predicted 48-hour mortality and 30-day mortality and the need for ICU in both trauma and nontrauma patients.[15] The effectiveness of NEWS2 has also been demonstrated in studies on COVID-19. In the study by Gidari et al.[2] performed on 68 patients, the effectiveness of NEWS2 in determining the intensive care need in the early period was investigated, and it was observed that NEWS2 was positively correlated with ICU admission (AUC: 0.91; 95% CI: 0.70–0.97; p<0.001). In this study, when 5 points were used as the cutoff value, higher sensitivity was obtained, and when 7 points were used, higher specificity was obtained. In their study, Baker et al.[16] suggested using NEWS2 to predict worsening in COVID-19 patients. The data of our study showed that NEWS2 at admission was successful in predicting critical progress, as in the literature. In addition, our study has demonstrated that the diagnostic yield of NEWS2 increased gradually in the days after admission; therefore, it is important to follow NEWS2 not only at the time of admission but also daily.

NEWS2 was also found to be superior to qSOFA in determining both mortality and ICU need.[17,18] Regarding those data of different critical illnesses, investigators studied the yield of these scoring systems in COVID-19. In a study from Norway, a total of 66 COVID-19 patients were compared in terms of the effectiveness of scoring

systems. A NEWS2 of ≥6 at admission (AUC: 0.822; 95% CI: 0.690–0.953) was found to be superior to qSOFA score ≥2 (AUC: 0.624; 95% CI: 0.446–0.810; p<0.05) and other scoring systems in predicting in-hospital mortality.[4] Holten et al.[3] compared NEWS2, qSOFA, SIRS, Confusion, Urea >7 mM, Respiratory Rate ≥30 breaths/min, BP <90 mm Hg (Systolic) or <60 mm Hg (Diastolic), Age ≥65 Years (CURB-65) score and Pneumonia Severity Index (PSI) in determining severe COVID-19 patients in emergency services; NEWS2 (AUROC: 0.80; 95% CI: 0.72–0.88) was found to be superior to SIRS (AUROC: 0.70; 95% CI: 0.61–0.80) and qSOFA (AUROC: 0.70; 95% CI: 0.61–0.79) in determining severe COVID-19 patients in emergency services. However, it did not show a significant superiority over CURB-65 and PSI scores. In our study, NEWS2 at the time of admission was found to be superior to qSOFA in predicting the poor outcome. The presence of hypoxemia and the need for oxygen support treatment as a parameter in NEWS2, which are poor prognostic factors in COVID-19 patients, may explain the superiority of this score to the qSOFA score in a disease with lung involvement such as COVID-19. Another point to be addressed was the cutoff value determined in our study, which was ≥4. This indicates that a lower cutoff at the time of admission may decrease false negative results by NEWS2 in predicting worse outcomes of COVID-19.

The superiority of NEWS2 has been demonstrated, but the data in previous studies were all based on the scores at the time of admission. In our practice, we have seen varying courses of the disease with a hardly predictable follow-up. This aspect is shared by some other physicians.[5] We have calculated and compared NEWS2 and qSOFA at the 24th and 48th hours of hospitalization in our study. The 48th-hour NEWS2 was found to be superior to qSOFA and NEWS2 at all other time points in predicting the poor outcome. The 48th-hour qSOFA was also useful. These results underline the need for daily assessments with a reliable prediction rule to properly find a deteriorating patient.

Our study is remarkable with its high number of cases and unmatched data on daily assessments with scoring systems. However, there are still some limitations to be addressed. First, this was a retrospective analysis depending on medical records. Second, the comparison was carried out in hospitalized patients. The data on initially nonhospitalized patients who had readmitted and experienced severe disease were absent. Finally, a few other possible tools were not calculated and compared with NEWS2 and qSOFA.

NEWS2 was superior to qSOFA in determining the need for intensive care support and/or mortality. Repeated daily measures of the scores should be recommended, especially with the use of NEWS2. A high NEWS2 at the 48th hour seems to be more valuable to predict worse outcomes.

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Conflicts of interest

There are no conflicts of interest.

Ethics Committee Approval

The study was approved by the University of Health Sciences, Dr. Suat Seren Chest Disease and Thoracic Surgery Training and Research Hospital Clinical Research Ethics Committee (No: 13, Date: 14/09/2020).

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Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept – İ.O.A., B.K., M.O.G.; Design – İ.O.A., B.K., M.O.G.; Supervision – İ.O.A., B.K., M.O.G.; Funding – İ.O.A., B.K., M.O.G.; Materials – İ.O.A., M.O.G.; Data collection &/or processing – İ.O.A., M.O.G.; Analysis and/or interpretation – İ.O.A., M.O.G.; Literature search – İ.O.A., B.K., M.O.G.; Writing – İ.O.A., M.O.G.; Critical review – İ.O.A., B.K., M.O.G.

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