DOI: 10.4274/mjima.galenos.2021.2021.60
 Mediterr J Infect Microb Antimicrob 2021;10:60
 Erişim: <http://dx.doi.org/10.4274/mjima.galenos.2021.2021.60>

Evaluating the Mortality Rates of COVID-19 Patients in the Intensive Care Unit Using the Rapid Emergency Medicine Score, Acute Physiology and Chronic Health Assessment-II, Charlson Comorbidity Index and Sequential Organ Failure Assessment Scoring Models

Yoğun Bakımda Yatan COVID-19 Hastalarında Hızlı Acil Tıp Skoru, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II, Charlson Komorbidite İndeksi ve Sıralı Organ Yetmezliği Değerlendirmesi Skorlama Modelleri Kullanılarak Mortalitenin Değerlendirilmesi

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Abstract

Introduction: Four scoring models, including the Rapid Emergency Medicine Score (REMS), Charlson Comorbidity Index (CCI), Acute Physiology and Chronic Health Assessment-II (APACHE-II), and Sequential Organ Failure Assessment (SOFA), were examined. The effectiveness of these scores in mortality prediction of intensive care unit (ICU)-admitted Coronavirus disease-2019 (COVID-19) patients was investigated.

Materials and Methods: The present retrospective analysis was conducted in a single center among patients with confirmed or suspected COVID-19 diagnosis who were admitted to emergency department and then ICU between March and December 2020. The REMS, APACHE-II, CCI, and SOFA were used to evaluate the mortality associated factors.

Results: The sample included 411 patients above 18 years of age, with a median age of 71 (interquartile range: 60-80), and made up of 61.6% males. High creatinine, potassium, fraction of inspired oxygen and white blood cell levels as well as low hematocrit levels, pH, mean arterial pressure, and systolic and diastolic blood pressure accounted for a poor prognosis. Statistically significant differences were determined between laboratory values and physiological findings ($p<0.05$). Comorbidity was found in 368 (89.5%) patients while malignancy and dementia were significantly associated to mortality ($p<0.001$ and 0.019 , respectively). The scoring systems are clearly among the important indicators of in-hospital mortality ($p<0.001$). Additionally, the receiver operating curve analysis did not reveal significant differences in the scoring systems when considered in terms of discriminative power ($p>0.05$).

Conclusion: The results revealed the effectiveness of REMS, CCI, APACHE-II, and SOFA in the prediction of critical COVID-19 patients' in-hospital mortality; but none of the scoring systems prevailed over others. Therefore, the REMS, APACHE-II, CCI, and SOFA scoring models can guide not only emergency physicians but also all clinicians who contribute to the management of critical COVID-19 cases.

Keywords: Coronavirus disease-2019 (COVID-19), mortality, prognosis, emergency service, intensive care units

Cite this article as: Songür Kodik M, Öztürk E, Uz İ, Özçete E, İnci Ö, Ersel M. Evaluating the Mortality Rates of COVID-19 Patients in the Intensive Care Unit Using the Rapid Emergency Medicine Score, Acute Physiology and Chronic Health Assessment-II, Charlson Comorbidity Index and Sequential Organ Failure Assessment Scoring Models. Mediterr J Infect Microb Antimicrob. 2021;10:60.

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Received/Geliş Tarihi: 29.03.2021 Accepted/Kabul Tarihi: 15.09.2021 ORCID ID: orcid.org/0000-0003-4565-3374

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 Mediterranean Journal of Infection, Microbes and Antimicrobials published by Galenos Yayınevi.

Published: 17 September 2021

Öz

Giriş: Çalışmamız, yoğun bakım ünitesinde (YBÜ) yatan Koronavirüs hastalığı-2019 (COVID-19) hastalarının mortalitesini öngörmeye dört puanlama modelinin etkinliğini incelemeyi amaçladı. Bu bağlamda kullanılan modeller şunlardır: Hızlı Acil Tıp Skoru (REMS), Charlson Komorbidite İndeksi (CCI), Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) ve Sıralı Organ Yetmezliği Değerlendirmesi (SOFA).

Gereç ve Yöntem: Hastanemizde YBÜ'de yatan kesin veya olası COVID-19 hastaları dikkate alınarak, tek merkezli ve retrospektif bir analiz yapıldı. Çalışmamıza 11.03.2020-31.12.2020 tarihleri arasında acil servise başvuran ve buradan direkt YBÜ'ye transfer olan COVID-19 hastaları dahil edildi.

Bulgular: Çalışma için 18 yaş üstü 411 hasta uygun bulundu. Hastaların medyan yaşı 71 (çeyrekler arası aralık: 60-80) ve %61,6'sı erkekti. Kötü prognoz ve mortalite; yüksek kreatinin seviyeleri, artmış potasyum seviyeleri, artmış solunan havanın oksijen oranı seviyeleri ve artmış beyaz kan hücreleri seviyeleri ile ilişkilendirilirken, düşük hematokrit seviyeleri, azalmış pH, düşük ortalama arter basıncı ve düşük sistolik ve diyastolik kan basıncı ile ilişkililiydi. Ayrıca 368 (%89,5) hastada komorbidite görüldü ve malignite ve demans istatistiksel olarak ölümle ilişkili bulundu (sırasıyla $p<0,001$ ve $0,019$). Puanlama sistemlerinin dördü de (REMS, CCI, APACHE-II ve SOFA) istatistiksel olarak hastane içi mortalitenin bir göstergesiydi ($p<0,001$). Ancak puanlama sistemlerinin ayırt edici gücünü karşılaştırmak için ROC analizi kullanıldığında istatistiksel olarak önemli bir fark tespit edilmemiştir ($p>0,05$).

Sonuç: REMS, CCI, APACHE-II ve SOFA'nın kritik olan COVID-19 hastalarında hastane içi mortaliteyi belirlemede etkili olduğunu incelendi; ancak birbirleri arasında kayda değer bir üstünlük olmadığı gözlemlendi. Sonuçlarımız REMS, CCI, APACHE-II ve SOFA'nın kritik olan COVID-19 hastalarında hastane içi mortaliteyi belirlemede etkili olduğunu; ancak hiçbir skorlama sisteminin diğerlerine göre daha üstün olmadığını göstermektedir.

Anahtar Kelimeler: Koronavirüs hastalığı-2019 (COVID-19), ölüm oranı, prognoz, acil servis, yoğun bakım üniteleri

Introduction

Coronavirus disease-2019 (COVID-19) leads to severe acute respiratory syndrome coronavirus 2. The disease was first detected in Wuhan, China. It spread abruptly and became a pandemic with devastating consequences globally. Poor prognosis is observed in all age groups with triggering diseases, especially hypertension and diabetes^[1]. Having weaker resistance to the disease, middle-aged and older people are hospitalized at higher rates in intensive care units (ICUs) with higher rates of fatality^[2]. Estimating the risk factors associated with mortality rates during admission to emergency department (ED) is of great importance in terms of evaluating COVID-19 treatment options and the course of the disease^[3].

The development of easy-to-apply scoring systems that have high effectiveness in the assessment of the COVID-19 severity and prognosis pose a challenge to health workers. The Rapid Emergency Medicine Score (REMS) is a system often used for emergency patients^[4]. It is recommended for the estimations of the mortality of ED-admitted nonsurgical patients^[5]. The Sequential Organ Failure Assessment (SOFA), which was not initially proposed for use in mortality prediction, later emerged as a score to predict mortality and morbidity in critical patients^[6]. It measures various parameters to delineate the severity of multiorgan dysfunctions^[7]. Recent studies have shown that the use of SOFA at admission can help to classify patients who suffer from COVID-19 in terms of in-hospital mortality^[6,7].

The Charlson Comorbidity Index (CCI) and Acute Physiology and Chronic Health Assessment-II (APACHE-II) are scoring systems employed in the prediction of additional diseases and mortality in different disease groups^[8,9]. Charlson Comorbidity Index is a common and practical method and is used in the determination

of ten-year mortality risk in patients with comorbidities^[8]. Various studies have been conducted to determine its advantages and interpret its correlation with poor results in patients who suffer from COVID-19^[10-12]. A study in COVID-19 patients has associated an increase of 16% in the risk of death with each increment in the CCI score and a CCI score above 0 with increased mortality rates^[12]. Lastly, regarded as a measure of disease severity, the APACHE-II scoring system is predominantly used in ICU-admitted patients. In addition, it has been linked to mortality in clinical settings and in patients suffering from severe conditions^[13]. The results of a study evaluating vital signs such as respiratory rate, oxygen saturation, white blood cell, neutrophil count, inflammation markers such as C-reactive protein, and APACHE-II scores in COVID-19 patients have revealed that the indications added to its discriminating effectiveness along with it being successful in the prediction of the severity of the patient outcome^[14].

The application of such scoring systems for ED-admitted COVID-19 patients, a hot discussion topic recently, may allow the prompt and truthful assessment of the risk of mortality. Therefore, in this study, the four scores were used in the suspected/confirmed COVID-19 cases transferred to ICU upon admission to ED. In the present study, we evaluated the factors affecting in-hospital mortality by comparing the scores to each other.

Materials and Methods

Study Design

Adopting the retrospective evaluation methodology, the study was conducted using the facilities of a single center and carried out in Ege University, Emergency Medicine Clinics. It is a tertiary

healthcare center in İzmir, Turkey with an annual average of 190,000 patient admissions. The study was reported in line with the Strobe Guidelines^[15]. The Ege University Local Ethics Committee approved the protocol with issue no. 21-1.1T/71, dated 21.01.2021.

Setting

The study included patients admitted to ED, with suspected or diagnosed COVID-19 infection, and were transferred to ICU between March 11, 2020 and December 21, 2020. The final study sample was made up of 411 patients aged over 18 years. The determination of the diagnostic criteria, case classification, and treatments was carried out in keeping with the "COVID-19 General Information, Epidemiology and Diagnosis" report published by the Turkish Ministry of Health^[16].

Data Collection

The data were obtained from the digital archive that was issued with the clinical code for COVID-19 in Turkey, U07.3 ICD (International Statistical Classification of Diseases and Related Health Problems)^[17]. The data on demographics, clinical features, comorbidities, laboratory data, and results were extracted from medical records and used to calculate REMS, SOFA, CCI, and APACHE-II scores.

Variables

The scores on the SOFA, REMS, CCI, and APACHE-II scoring models were the main variables of the study. Three models include Glasgow Coma Scale (GCS) as a parameter, except for the CCI. Thus, the variables were as follows:

GCS: It is a functional method for assessing patients' state of consciousness with respect to their responsiveness to certain visual-oral/motor stimuli. In this method, the total score varies between 3 and 15. A score of 3 to 8 indicates a major injury, a score of 9 to 12 indicates moderate injuries, and a score of 13 to 15 indicates minor injuries^[18].

REMS: It is used to estimate in-hospital mortality in nonsurgical ED-admitted patients. Among the variables of the model are heart and respiratory rate, blood pressure, GCS, saturation level, and age. The maximum score on this scale is 26, with higher scores indicating more severe conditions^[4].

SOFA: It is useful in identifying conditions such as, a functional disorder/failure occurring in an organ. Fraction of inspired oxygen, partial pressure of oxygen in arterial blood (PaO_2), GCS, creatinine and urine volume, bilirubin, and platelets were used to evaluate. The SOFA scores range between 0 and 24, with higher scores indicating worse conditions^[19].

CCI: This index is grounded upon a scoring system for use in the evaluation of the long-term prognosis and survival rate in patients with associated disorders such as heart, liver, and

lung diseases. The maximum obtainable score is 37 with higher scores indicating higher mortality during the first year of hospitalization^[8].

APACHE-II: It is applied within the first 24 hours of ICU admission. It estimates mortality using patient findings, laboratory values, acute and chronic diseases. The scores range between 0 and 71, with higher scores indicating a higher mortality risk^[9,13].

Statistical Analysis

Statistical Package for Social Sciences for Windows, version 25.0 (Chicago, IL, USA) and MedCalc program (MedCalc Software, Belgium) were used in analyses. The results were reported as medians, interquartile ranges (IQR), frequencies, and percentages depending on whether the variables were numerical or categorical. The Shapiro-Wilk test was adopted to examine the conformity of the variables to the normality assumption. The results revealed that the data did not follow parametric assumptions. Hence, the Mann-Whitney U test and chi-square test were used to examine group differences for the numerical and categorical variables, respectively. The receiver operating curve (ROC) analysis and the DeLong method^[20] were used to examine the area under the curve (AUC). In addition, the Cox regression analysis was performed. A p-value below 0.05 was considered statistically significant. The factors influencing mortality of COVID-19 patients were evaluated using the four scoring models.

Results

Firstly, the medical records of 786 ED- and ICU-admitted patients between March 11, 2020 and December 31, 2020, were selected. The undiagnosed COVID-19, files with inadequate data, deceased cases, or cases not admitted into the ICU from the ED were excluded from the sample. Finally, 411 patients were included in the study, with 122 patients being confirmed COVID-19 cases, 247 suspected/possible COVID-19 cases, and 42 probable COVID-19 cases (Figure 1). The final sample had a median age of 71 (IQR: 60-80), with 61.6% males.

First, the categorical variables were analyzed, revealing that 368 (89.5%) patients had comorbidities. Diabetes mellitus was the most common comorbidity with a frequency of 156 (37.9%) patients. Table 1 shows the comparison of categorical variables with respect to survival rate. Mortality was significantly associated with malignancy and dementia (p-values <0.001 and 0.019, respectively). In addition, 144 patients required continuous positive airway pressure/mechanical ventilation (CPAP/MV) and 116 of these patients were deceased. Fewer patients (n=65) needed inotropic therapy, but 57 of these patients were as well deceased. Both CPAP/MV and inotropic treatment yielded statistically significant results in terms of mortality rates (p<0.001).

Figure 1. Case exclusion and study population disposition flow chart

ED: Emergency department, ICU: Intensive care unit, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction, CT: Computed tomography

The comparison of the categorical variables revealed that the deceased patients had significantly higher rates of malignancy and dementia and more frequently needed inotropic treatment and CPP/MV (Table 1).

The analysis of numerical variables revealed significant differences between the four scores in terms of survival (Table 2). The physiological findings (MAP, systolic BP, diastolic BP, etc.) during admissions to both the ED and ICU were statistically significantly different between the nonsurvivor group and survivor group. Age was related to mortality ($p < 0.001$). Furthermore, results of the laboratory tests (including pH, creatinine, WBC, K, and hematocrit) were significantly different in terms of survival.

Figure 2 shows the findings of the ROC analysis, which was employed in the determination of the discriminating power of the four scoring systems. The sensitivity results of the scores were not significantly different from each other (Table 3) as the differences in the AUC were insignificant including p -values above 0.05.

The potential factors influencing mortality were investigated in a multivariate model via the Cox regression analysis. The factors that were preliminarily found to be significant in the univariate analyses were used as independent variables, including age, heart rate, and potassium level (Table 4).

Figure 2. Results of the receiver operating curve analysis used to determine the discriminatory power of the four scoring systems: REMS, CCI, SOFA, and APACHE-II

REMS: Rapid Emergency Medicine Score, CCI: Charlson Comorbidity Index, APACHE: Acute Physiology and Chronic Health Assessment, SOFA: Sequential Organ Failure Assessment

Table 1. Comparison of the categorical variables in terms of survival

		Survival				χ^2	p
		Survived		Died			
		n	%	n	%		
Comorbidity		132	85.7	236	91.8	3.843	0.050
DM		52	33.8	104	40.5	1.836	0.175
CHF		25	16.2	47	18.3	0.281	0.596
COPD		17	11.0	36	14.0	0.756	0.385
CAD		44	28.6	67	26.1	0.306	0.580
Malignancy		11	7.1	59	23.0	17.043	<0.001
CVA/TIA		11	7.1	32	12.5	2.897	0.089
Hemiplegia		8	5.2	23	8.9	1.947	0.163
Chronic renal failure		21	13.6	27	10.5	0.915	0.339
Dementia		7	4.5	29	11.3	5.471	0.019
Gastrointestinal bleeding		1	0.6	5	1.9	1.125	0.289
Cirrhosis		2	1.3	5	1.9	0.241	0.624
Myocardial ischemia		2	1.3	3	1.2	0.014*	1.000
Rheumatologic diseases		3	1.9	5	1.9	0.000	0.999
Lymphoma		3	1.9	5	1.9	0.000	0.999
Leukemia		1	0.6	3	1.2	0.268	0.605
AIDS		1	0.6	0	0.0	1.673*	0.375
CPAP/MV		28	18.2	116	45.1	30.738	<0.001
PCR outcome	Certain	43	27.9	79	30.7	0.366	0.545
	Uncertain	111	72.1	178	69.3		
Inotrope dose	Not needed	146	94.8	200	77.8	20.983	<0.001
	0.1	2	1.3	10	3.9		
	>0.1	6	3.9	47	18.3		

χ^2 : Chi-square value, *Fisher's exact test value. *Statistically significant values ($p < 0.05$) are shown in bold.

DM: Diabetes mellitus, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CVA/TIA: Cerebrovascular accident/transient ischemic attack, AIDS: Acquired immunodeficiency syndrome, PCR: Polymerase chain reaction, CPAP/MV: Continuous positive airway pressure/mechanical ventilation

Discussion

Administrative and clinical challenges have arisen in healthcare systems globally with the onset of the COVID-19 pandemic. Due to the crisis in medical resources after its onset, the evaluation of high-risk patients beforehand for adequate monitoring and treatment has become more important^[7]. A scoring system may be useful in assessing the status and mortality of COVID-19 patients, especially for emergency physicians, but the effectiveness of such systems is still an ongoing investigation. Correspondingly, the study focused on the evaluating four scoring systems, namely, REMS, APACHE-2, CCI, and SOFA.

The SOFA is used for regular and continuous assessment of organ dysfunction during hospitalization. The results of various studies have associated high SOFA scores to high in-hospital mortality among COVID-19 patients^[2,6]. In this study, the high

SOFA scores were significant indicators of mortality as well ($p < 0.001$). The GCS, MAP, creatinine, and fraction of inspired oxygen variables were significantly different in survivors and nonsurvivors ($p < 0.05$). Similarly, in a study to predict mortality in ventilated patients, all SOFA measures differed significantly between the nonsurvivor and survivor groups, except for the GCS. In the same study, the median value and IQR were found to be 6 and 4–8, respectively^[7]. Equally, our sample had a median of 5 and an IQR of 3–8. Therefore, the SOFA value can also be used to assess the probability of mortality in critical COVID-19 patients.

The APACHE-II and REMS were developed to identify high-risk patients in addition to their use for the regulation of patient management in ED^[21]. The REMS was proposed as an alternative scoring system for the estimation of one-month mortality in a study with 392 ED-admitted COVID-19 patients^[22].

Table 2. Comparison of numerical variables in terms of survival

	Survival						Z/t	p
	Survived			Died				
	Median	IQR		Median	IQR			
REMS	7	5	9	8	6	11	5.101	<0.001
CCI	4	2	5	5	4	7	5.806	<0.001
SOFA	3	2	5	5	3	8	7.169	<0.001
APACHE-II	12	7	16	16	12	21	6.859	<0.001
Heart rate at the time of admission to ED (bpm)	100	85	116	102	88	120	0.984	0.325
Systolic BP at the time of admission to ED (mmHg)	138	120	157	131	111	149	2.711	0.007
Diastolic BP at the time of admission to ED (mmHg)	82	70	96	76	65	87	2.758	0.006
MAP at the time of admission to ED (mmHg)	99	88	112	95	82	107	2.790	0.005
SpO ₂ at the time of admission to ED (%)	95	90	97	93	85	97	2.923	0.003
Respiratory rate at the time of admission to ED (bpm)	20	20	24	20	20	24	0.931	0.352
Fever at the time of admission to ED (°C)	36.60	36.10	37.50	36.50	36.10	37.50	0.337	0.736
Glasgow Coma Score	15	15	15	15	11	15	5.334	<0.001
Age (years)	67	56	76	73	65	82	4.782	<0.001
Heart rate at the time of admission to ICU (bpm)	90	78	101	97	84	115	3.481	<0.001
Systolic BP at the time of admission to ICU (mmHg)	139	120	157	123	106	142	5.349	<0.001
Diastolic BP at the time of admission to ICU (mmHg)	75	65	87	70	60	80	3.349	0.001
MAP at the time of admission to ICU (mmHg)	97	85	106	89	76	99	4.726	<0.001
SpO ₂ at the time of admission to ICU (%)	96	94	98	95	92	98	1.477	0.140
Respiratory rate at the time of admission to ICU (bpm)	22	19	26	22	18	26	0.678	0.498
Fever at the time of admission to ICU (°C)	36.30	36.00	36.70	36.20	36.00	36.60	1.439	0.150
Bilirubin (mg/dL)	0.51	0.32	0.74	0.54	0.34	0.91	1.523	0.128
Creatinine (mg/dL)	1.02	0.74	1.63	1.29	0.90	2.15	2.642	0.008
Na (mmol/L)	138	135	141	138	134	141	0.265	0.791
K (mmol/L)	4.10	3.60	4.50	4.20	3.80	4.80	2.227	0.026
WBC (×10 ³ /μL)	10.8	7.4	14.8	12.9	8.6	18.1	2.868	0.004
HTC (%)	36.8	32.0	40.6	34.8	30.0	39.4	2.143	0.032
PLT (×10 ³ /μL)	227.0	170.0	291.0	219.0	148.0	301.0	0.586	0.558
pH	7.42	7.36	7.46	7.39	7.29	7.44	2.958	0.003
Calculated FiO ₂ (%)	37.00	29.00	41.00	41.00	37.00	60.00	6.149	<0.001
PaO ₂ (mmHg)	85.5	68.8	112.0	88.9	64.9	124.0	0.432	0.666
PaCO ₂ (mmHg)	34.8	30.5	40.9	34.5	29.4	40.7	0.557	0.578

*Statistically significant values (p<0.05) are shown in bold.

IQR: Interquartile range, ED: Emergency department, ICU: Intensive care unit, Z: Mann-Whitney U test value, t: Independent samples t-test value, MAP: Mean arterial pressure, SpO₂: Oxygen saturation, REMS: Rapid Emergency Medicine Score, CCI: Charlson Comorbidity Index, SOFA: Sequential Organ Failure Assessment, APACHE-II: Acute Physiology and Chronic Health Assessment-II, WBC: White blood cell, PLT: Platelets, Na: Sodium, K: Potassium, PaCO₂: Partial pressure of carbon dioxide, PaO₂: Oxygen partial pressure, FiO₂: Fraction of inspired oxygen, HTC: Hematocrit

Table 3. Pairwise comparison of receiver operating curve curves

	Difference between areas under the curves	SE ^a	95% CI	Z	p
APACHE-SOFA	0.00798	0.0235	-0.0381 to 0.0541	0.339	0.7345
APACHE-CCI	0.0255	0.0314	-0.0360 to 0.0871	0.813	0.4163
APACHE-REMS	0.0429	0.0313	-0.0185 to 0.104	1.370	0.1706
SOFA-CCI	0.0176	0.0369	-0.0547 to 0.0898	0.476	0.6337
SOFA-REMS	0.0349	0.0344	-0.0325 to 0.102	1.015	0.3102
CCI-REMS	0.0173	0.0350	-0.0513 to 0.0860	0.495	0.6208

SE: Standard error^[20], 1988, CI: Confidence interval, REMS: Rapid Emergency Medicine Score, CCI: Charlson Comorbidity Index, SOFA: Sequential Organ Failure Assessment, APACHE-II: Acute Physiology and Chronic Health Assessment-II

Table 4. Cox regression analysis results of a multivariate model investigating factors influencing mortality

	B	Wald	p	Exp(B)	95.0% CI for Exp(B)	
					Lower	Upper
Age	0.023	19.281	<0.001	1.023	1.013	1.034
ICU heart rate	0.01	11.839	0.001	1.01	1.004	1.016
ICU systolic BP	-0.014	2.679	0.102	0.986	0.97	1.003
ICU diastolic BP	0.005	0.088	0.767	1.005	0.974	1.036
ICU MAP	-0.004	0.037	0.847	0.996	0.951	1.042
Creatinine	-0.013	0.095	0.758	0.987	0.911	1.07
K	0.218	6.025	0.014	1.243	1.045	1.48
WBC	0.01	9.745	0.002	1.01	1.004	1.016
HTC	-0.021	4.618	0.032	0.979	0.961	0.998
pH	-0.801	1.472	0.225	0.449	0.123	1.637
Calculated FiO ₂	0.015	13.355	<0.001	1.015	1.007	1.023
Malignancy	0.601	13.804	<0.001	1.825	1.329	2.506
Dementia	0.513	5.83	0.016	1.67	1.101	2.533
CPAP/MV	0.458	7.907	0.005	1.581	1.149	2.176

*Statistically significant values (p<0.05) are shown in bold.

CI: Confidence interval, ICU: Intensive care unit, BP: Blood pressure, MAP: Mean arterial pressure, K: Potassium, WBC: White blood cell, HTC: Hematocrit, CPAP/MV: Continuous positive airway pressure/mechanical ventilation, FiO₂: Fraction of inspired oxygen

Hu et al.^[21] found the AUC of REMS to be 0.841 in the estimation of in-hospital mortality. The researchers found a solid association between the REMS criteria and age, respiratory rate and a link between GCS and mortality. Considering previous findings, the REMS was also examined in the present study. The nonsurvivor group had higher REMS scores (p<0.001); age and GCS parameters also differed significantly between the groups.

With a complex predictive score, APACHE-II is among the best predictors of mortality in ED patients, despite being less practical compared to REMS for having variables that are difficult to pinpoint during early admission^[23]. Zou et al.^[24] stated that an APACHE-II score equal to or greater than 17 is alarming. Researchers delineated that this score can guide physicians during the clinical decision-making process. The results of this study are consistent with theirs as we predicted a median value of 16 in nonsurviving COVID-19 patients and linked higher

scores to higher mortality (p<0.001). Olsson and Lind^[25] have noted that the effectiveness of REMS and APACHE-II are similar in terms of the determination of mortality in nonsurgical ED patients. A different study comparing the APACHE-II and SOFA scores revealed APACHE-II as a better mortality predictor^[24]. Comparing the three scores, namely, APACHE-II, SOFA, and REMS scores, no difference was found in terms of mortality estimation. Clinical findings have revealed that COVID-19 patients may have additional diseases associated with severe outcomes. In a sample of 178 hospitalized patients in the USA, 89.3% of the patients were found to have comorbidities^[26]. In the present study, the rate of comorbidities was reported to be 89.5%. Another study from China has revealed that the cancer patients were severely affected by COVID-19^[27]. A study performed among 18,650 cancer patients with COVID-19 has revealed a higher risk of dying in patients who suffer from

both diseases in addition to the higher rates of dementia and mortality^[28-30]. Our results also disclosed a statistically significant relationship between increased mortality and dementia and malignancy. Other studies have linked hypertension, chronic obstructive pulmonary disease (COPD), and diabetes with increased morbidity^[1,31].

Comorbidities are seen as important factors in estimating the mortality risk in COVID-19 patients. Hence, the CCI, a scoring system that considers additional diseases, was examined in our study. Various studies have shown that the use of CCI in risk stratification in COVID-19 patients may be advantageous and poor outcome is generally linked to relatively higher CCI scores^[10-12]. In the present study, a significant correlation was found between mortality and higher scores. The CCI scores of the nonsurvivor group with a median CCI value of 5 were found to be close to those of a study with 383 COVID-19 patients^[11]. This study stands out as the first comparison of the CCI to SOFA, REMS, and APACHE-II in COVID-19 patients. The CCI and other scoring systems did not significantly differ in how well they can predict mortality in ICU-admitted COVID-19 patients. Future studies should focus on comparing the effectiveness and accuracy of different models.

Study Limitations

First, being a single-center retrospective investigation, the sample size is limited. Thus, multi-center studies that include larger sample sizes are needed to validate the scoring systems prospectively. Second, the widely applied COVID-19 medications were limited in terms of their availability at the beginning of the outbreak, thus possibly worsening patient outcomes. Another limitation of the study is the delayed, polymerase chain reaction (PCR) results (6-8 h), leading to symptom- and computed tomography (CT)-based admissions without referring to PCR results. Thus, some patients were admitted to the COVID-19 ICU for having the symptoms despite having negative PCR results and/or CT scans.

Conclusion

The number of studies examining the mortality scoring systems in terms of their effectiveness in admissions to the ED and follow-ups in ICU during the COVID-19 outbreak is limited. We found that the four scoring systems were significant indicators of mortality in ICU-admitted patients, with none surpassing the others. Our results revealed that prognostic scoring models could serve as guides for emergency doctors for the prompt assessment of patients' conditions and prioritization of high-risk groups. This study compared the REMS scoring system, which is an easy-to-apply mortality indicator for use on arrival, and CCI scoring systems, another mortality indicator for use on arrival, to the SOFA and APACHE-II scoring systems, which

are applied after ICU admission, as indicators of mortality. In comparison with other scoring systems, the REMS is easily applicable and can be used on arrival to ED, without the need for any additional investigation. On the other hand, CCI, SOFA, and APACHE-II require further examination. In the present study, we compared the on-arrival scoring systems that are indicators of long-term mortality to other scoring systems in terms of their effectiveness in COVID-19 patients. However, our analyses revealed no significant differences between the scoring systems. Thus, we believe that the REMS is recommendable for use in the prediction of mortality on arrival to ED and before admission to ICU for COVID-19 patients and the four scoring models can guide not only emergency physicians but also all clinicians who contribute to the management of critical COVID-19 cases.

Ethics

Ethics Committee Approval: The Ege University Local Ethics Committee approved the protocol with issue no. 21-1.1T/71, dated 21.01.2021.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.S.K., Design: M.S.K., M.E., Data Collection or Processing: E.Ö., İ.U., En.Ö., Analysis or Interpretation: İ.U., En.Ö., Ö.İ., Literature Search: M.S.K., E.Ö., Writing: M.S.K., E.Ö., İ.U., En.Ö., Ö.İ., M.E.

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

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

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