JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Prognostic factors for COVID-19 patients

Uğur Önal[1], Özge Aydın Güçlü[2], Halis Akalın[1], Nilüfer Aylin Acet Öztürk[2], Cihan Semet[1], Ezgi Demirdöğen[2], Aslı Görek Dilektaşlı[2], İmran Sağlık[3], Esra Kazak[1], Güven Özkaya[4], Funda Coşkun[2], Dane Ediger[2], Yasemin Heper[1], Ahmet Ursavaş[2], Emel Yılmaz[1], Esra Uzaslan[2], Mehmet Karadağ[2]

[1] Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Uludag University, Bursa, Turkey
[2] Department of Pulmonary Diseases, Faculty of Medicine, Uludag University, Bursa, Turkey
[3] Department of Microbiology, Faculty of Medicine, Uludag University, Bursa, Turkey
[4] Department of Biostatistics, Faculty of Medicine, Uludag University, Bursa, Turkey

Abstract

Introduction: Determining prognostic factors in patients with coronavirus disease (COVID-19) can have great impact on treatment planning and follow-up strategies. Herein, we aimed to evaluate prognostic factors and clinical scores for confirmed COVID-19 patients in a tertiary-care hospital in the Bursa region of Turkey.

Methodology: Patients who had been diagnosed with COVID-19 microbiologically and/or radiologically between March and October 2020 in a tertiary-care university hospital were enrolled retrospectively. Adult patients (≥ 18 years) with a clinical spectrum of moderate, severe, or critical illness were included. The dependent variable was 30-day mortality and logistic regression analysis was used to evaluate any variables with a significant *p* value (< 0.05) in univariate analysis.

Results: A total of 257 patients were included in the study. The mortality rate (30-day) was 14.4%. In logistic regression analysis, higher scores on sequential organ failure assessment (SOFA) ($p < 0.001$, odds ratio (OR) = 1.86, 95% CI = 1.42-2.45) and CURB-65 pneumonia severity criteria ($p = 0.001$, OR = 2.60, 95% CI = 1.47-4.57) were found to be significant in predicting mortality at admission. In deceased patients, there were also significant differences between the baseline, day-3, day-7, and day-14 results of D-dimer ($p = 0.01$), ferritin ($p = 0.042$), leukocyte ($p = 0.019$), and neutrophil ($p = 0.007$) counts.

Conclusions: In our study of COVID-19 patients, we found that high SOFA and CURB-65 scores on admission were associated with increased mortality. In addition, D-dimer, ferritin, leukocyte and neutrophil counts significantly increased after admission in patients who died.

Key words: COVID-19; prognostic factors; SOFA; CURB-65.

J Infect Dev Ctries 2022; 16(3):409-417. doi:10.3855/jidc.15845

(Received 22 September 2021 – Accepted 14 January 2022)

Introduction

The first pneumonia cases of unknown origin were identified in Wuhan, the capital city of Hubei province, in early December 2019 and the pathogen was identified as a novel betacoronavirus, labeled Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1,2]. The World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak to be a global pandemic on March 11, 2020 [3].

As the pandemic progressed, several factors such as advanced age, male gender and the presence of comorbidities were recognized as increasing the risk for poor outcomes in patients with COVID-19. Many laboratory parameters such as lymphocyte count, C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin and D-dimer, which are mostly related to the inflammatory state, were also identified as poor prognostic factors [4]. In a prognostic approach, clinical score systems have also been investigated in order to identify patients with COVID-19 who are at high risk for mortality and intensive care unit admission [5]. Clearly, the high mortality and morbidity rates in COVID-19 patients are driving factors in identifying essential prognostic tools to predict risk of deterioration and mortality, allowing clinicians to adjust their approach to monitoring and therapy.

Herein, we aimed to evaluate prognostic factors and clinical scores (sequential organ failure assessment (SOFA) score, quick SOFA (qSOFA), modified early warning score (MEWS), CURB-65, Glasgow coma scale (GCS), and the Charlson comorbidity index (CCI) of confirmed COVID-19 patients in a tertiary-care hospital in the Bursa region of Turkey.

Methodology

Patients who had polymerase chain reaction (PCR) positivity and/or typical radiological findings for COVID-19 at the Bursa Uludag University Hospital, between 10th March 2020 and 10th October 2020, were enrolled to this study retrospectively. The patients were evaluated on admission (Day 0) and subsequently on days 3, 7, 14 and 30. All patients were treated according to the national COVID-19 treatment guidelines for adult patients published by the Turkish Ministry of Health during that period [6].

Demographic, clinical and laboratory findings of COVID-19 patients on days 0, 3, 7, 14 and 30 were included in the case assessment forms.

Inclusion criteria were:

- Age ≥ 18 years (adult patients)
- Meeting criteria for the clinical spectrum of SARS-CoV-2 infection according to National Institutes of Health (NIH) COVID-19 Treatment Guidelines [7];
- Positive PCR result and/or presence of typical radiological findings for COVID-19 on computed tomography (CT), defined as round ground-glass opacities with peripheral, bilateral/multilobar or multifocal distribution [8].

Exclusion criteria were:

- Atypical and/or undetermined radiological findings in cases with negative PCR result for COVID-19.

Ethics

Ethical committee approval was granted by the Uludag University with protocol number 2020-22/11. Permission was also given by the Republic of Turkey, Ministry of Health.

Microbiological analysis

COVID-19 RT-qPCR (Bio-speedy, Bioeksen, TR) detection kits were used for the diagnosis of COVID-19, using the gold standard method: real-time reverse transcriptase PCR [8].

Criteria for clinical scoring systems

The SOFA score was calculated using the following parameters (on a scale of 0-4 points per parameter): GCS (Eye opening response: 1-4 points; verbal response: 1-5 points; motor response: 1-6 points); PaO2/FiO2 with respiratory support; serum thrombocytes; bilirubin; creatinine with urine output; mean arterial pressure and the use of vasopressor agents [9].

qSOFA score was based on respiratory rate ≥ 22 breaths/min; systolic blood pressure ≤ 100 mmHg; and altered mental state (1 point for the presence of each criteria) [9].

MEWS was calculated using the parameters of respiratory rate, heart rate, systolic blood pressure, temperature, and level of consciousness (0-3 points per parameter) [10].

CURB-65 score was based on the following: confusion; serum urea > 7 mmol/L or blood urea nitrogen ≥ 20 mg/dL; respiratory rate ≥ 30 minutes; systolic blood pressure < 90 mmHg or diastolic blood pressure ≤ 60 mmHg; and age ≥ 65 years (1 point for the presence of each criteria) [11].

CCI was assessed as 1 point for the presence of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer, mild liver disease, diabetes without chronic complications; 2 points for the presence of hemiplegia, moderate/severe renal failure, diabetes with chronic complications and any malignancy including leukemia and lymphoma; 3 points for the presence of moderate/severe liver disease; and 6 points for the presence of metastatic solid tumour, or AIDS. 1 point was also added for each decade over 50 years of age [12].

Statistical analysis

SPSS 25.0 program (Statistical package for the social sciences) was used for the statistical analysis. Comparison of categorical values between the two groups was performed using the Chi-square test. Independent sample t-test was performed for the normally distributed numerical values of the independent groups, whereas Mann-Whitney U test was performed on ordinal or continuous values which were distributed non-normally. Receiver operating characteristic (ROC) analysis was used to show the significance of the clinical score systems regarding the prediction of 30-day mortality of COVID-19 patients using MedCalc program. Friedman tests were performed in order to identify a significant change in the laboratory parameters at different time periods and subgroup analysis of the deceased COVID-19 patients' laboratory parameters on day 0, 3, 7, and 14 was performed via Friedman's two-way analysis by ranks.

Univariate and multivariate analyses were performed in order to determine significant prognostic factors that affected the 30-day mortality of our COVID-19 patients. Univariate and binary logistic regression analyses were performed using the forward

method. Mortality was the dependent variable and variables with a $p < 0.05$ in univariate analysis were considered covariates and were included into logistic regression analysis. A p value of less than 0.05 was considered significant.

Results

General characteristics

A total of 257 patients (45.5% female) fulfilled the study inclusion criteria. Healthcare personnel composed 5.1% of the patients. Mean age was 56.04 ± 1.05 years. Mean neutrophil, lymphocyte, thrombocyte, ferritin, D-dimer, lactate dehydrogenase (LDH), procalcitonin, and C-reactive protein (CRP) levels at admission were 6126 ± 405/mm^3, 1613 ± 87/mm^3, 215857 ± 6675/mm^3, 741.56 ± 157.38 ug/L, 1.56 ± 0.17 mg/L, 349 ± 23.51 U/L, 1.02 ± 0.31 ug/L and 68.85 ± 4.8 mg/L, respectively. The most common comorbidities were recorded as: hypertension (35.4%), diabetes mellitus (22.5%), and malignancy (10.5%). The most common symptoms on admission were cough (49.5%), fever (42%), and dyspnea (38.9%). In addition, mean neutrophil-to-lymphocyte ratio (NLR) and thrombocyte-to-lymphocyte ratio (TLR) on admission were recorded as 5.92 ± 0.55 and 185.45 ± 10.26, respectively. Mean duration from onset of symptoms to hospital admission and hospital stay of the patients were 4.4 ± 0.2 and 9.3 ± 0.3 days, respectively.

Mean clinical scores on admission were as follows – MEWS: 1.51 ± 0.08; SOFA: 1.53 ± 0.13; GCS: 14.85 ± 0.06; CCI: 1.04 ± 0.92; qSOFA: 0.38 ± 0.03; CURB-65: 0.71 ± 0.05.

Table 1. Univariate analysis of prognostic factors for 30-day mortality.

Variables	Patients with 30-day mortality		*p* value	Odds Ratio	95% CI
	Yes	No			
Age (years)	66.51 ± 2.74	54.28 ± 1.09	< 0.001	1.049	1.024-1.075
Gender					
Male	23	117	0.312	0.691	-
Female	14	103			
Hypertension					
Yes	17	74	0.150	1.677	-
No	20	146			
Diabetes mellitus					
Yes	11	47	0.263	1.557	-
No	26	173			
Chronic obstructive pulmonary disease					
Yes	3	9	0.293	2.069	-
No	34	211			
Chronic renal failure					
Yes	5	8	0.018	4.141	1.275-13.442
No	32	212			
Malignancy					
Yes	9	18	0.005	3.607	1.478-8.805
No	28	202			
Pregnancy					
Yes	1	1	0.205	6.083	-
No	36	219			
Organ transplantation					
Yes	2	6	0.395	2.038	-
No	35	214			
Cerebrovascular disease					
Yes	4	2	0.004	13.212	2.327-75.004
No	33	218			
Asthma					
Yes	1	9	0.688	0.651	-
No	36	211			
Number of comorbidities > 2					
Yes	20	41	< 0.001	5.136	2.475-10.660
No	17	179			
Dyspnea					
Yes	20	80	0.044	2.059	1.020-4.156
No	17	140			

Table 1 (continued). Univariate analysis of prognostic factors for 30-day mortality.

Variables	Patients with 30-day mortality		*p* value	Odds Ratio	95% CI
	Yes	*No*			
Cough					
Yes	11	116	0.012	0.379	0.179-0.805
No	26	104			
NIH-Severe Illness					
Yes	21	60	< 0.001	5.530	2.461-12.426
No	16	160			
NIH-Critical Illness					
Yes	6	2	< 0.001	47.400	8.461-265.556
No	31	218			
Hearth rate (/min)	93.81 ± 3.32	89.90 ± 1.02	0.172	1.015	-
Pulse Oxygen (%)	90.19 ± 1.07	94.31 ± 0.44	0.010	0.925	0.872-0.982
Respiratory Rate (/min)	21.38 ± 0.53	18.56 ± 0.30	0.002	1.147	1.051-1.252
Modified Early Warning System (MEWS)	2.49 ± 0.26	1.35 ± 0.07	< 0.001	1.823	1.403-2.370
Systolic Blood Pressure (mmHg)	121.08 ± 5.43	128.65 ± 1.22	0.047	0.983	-
Diastolic Blood Pressure (mmHg)	72.16 ± 2.17	78.88 ± 0.81	0.003	0.956	0.928-0.985
qSOFA	0.95 ± 0.13	0.28 ± 0.03	< 0.001	4.676	2.590-8.439
Glasgow Coma Score	14.49 ± 0.24	14.91 ± 0.05	0.044	0.752	0.570-0.992
Troponin I (ng/L)	141.41 ± 44.33	50.76 ± 32.74	0.340	1.000	-
SOFA	4.41 ± 0.5	1.05 ± 0.09	< 0.001	1.978	1.601-2.445
Charlson Comorbidity Index	2.43 ± 0.33	0.81 ± 0.08	< 0.001	1.817	1.435-2.300
CURB-65	1.68 ± 0.17	0.55 ± 0.05	< 0.001	3.411	2.265-5.136
C - Reactive Protein (CRP) (mg/L)	112.28 ± 14.68	61.55 ± 4.88	< 0.001	1.007	1.003-1.011
Procalcitonin (ug/L)	3.22 ± 1.64	0.63 ± 0.22	0.034	1.074	1.005-1.147
Creatinine (mg/dl)	1.81 ± 0.26	3.17 ± 1.02	0.607	0.990	-
Creatinine kinase (CK) (U/L)	527.52 ± 206.71	159.92 ± 24.54	0.010	1.001	-
D-dimer (mg/L)	3.69 ± 0.97	1.2 ± 0.09	0.001	1.348	1.135-1.602
Ferritin (ug/L)	1844.4 ± 860.7	540.5 ± 96.1	0.067	1.000	-
Leucocyte count (/mm3)	10394 ± 1838	8107 ± 390	0.088	1.000	-
Lymphocyte count (/mm^3)	1221 ± 211	1679 ± 95	0.026	0.999	-
Thrombocyte count (/mm^3)	173902 ± 17488	222914 ± 7128	0.006	1.000	-
Neutrophile / Lymphocyte Ratio	10.18 ± 1.59	5.21 ± 0.57	0.019	1.048	1.008-1.091
Thrombocyte / Lymphocyte Ratio	215.81 ± 31.45	180.34 ± 10.75	0.247	1.001	-
Aspartate aminotransferase (AST) (U/L)	58.38 ± 9.06	37.34 ± 3.37	0.040	1.006	-
Alanine aminotransferase (ALT) (U/L)	45.51 ± 9.88	35.21 ± 3.25	0.264	1.003	-
Albumin (g/L)	30.83 ± 0.64	36.13 ± 0.7	0.003	0.755	0.628-0.909
Hemoglobin (g/dL)	11.8 ± 0.36	13.06 ± 0.15	0.002	0.794	0.685-0.920
Glucose (mg/dL)	156.68 ± 13.39	127.33 ± 4.27	0.019	1.005	1.001-1.010
CK-MB (U/L)	42.23 ± 7.91	20.35 ± 1.05	< 0.001	1.028	1.013-1.043
Fibrinogen (mg/dL)	295.71 ± 50.16	554 ± 40.89	0.031	0.984	0.970-0.999
Lactate Dehydrogenase (LDH) (U/L)	486.12 ± 68.05	309.10 ± 20.49	0.005	1.004	1.001-1.007
INR	1.00 ± 0.03	0.92 ± 0.01	0.150	2.380	0.731-7.746
Sodium (mmol/L)	135.78 ± 1.48	136.66 ± 0.23	0.292	0.961	-
Potassium (mmol/L)	4.59 ± 0.13	4.19 ± 0.03	0.001	2.693	1.523-4.762

Table 2. Multivariate logistic regression analysis of the risk factors for the 30-day mortality.

Variables	*p* value	Odds Ratio	95% CI
One point increase of SOFA score on admission (per one-point increase)	< 0.001	1.868	1.420-2.458
One point increase of CURB-65 score on admission (per one-point increase)	0.001	2.600	1.477-4.578

Nagelkerke R^2 : 0.493.

Mortality and associated factors

The 30-day overall mortality rate was 14.4% (n = 37); 5.9% for patients with moderate illness, 25.9% for patients with severe illness and as high as 75% for patients with critical illness. The mortality rate among male patients was higher than in females but the difference was not significant (23/140 *vs*. 14/117, p = 0.312). On the other hand, mean age was found to be significantly higher in patients who died (66.51 ± 2.74 *vs*. 54.28 ± 1.09, $p < 0.001$).

Laboratory findings at admission of COVID-19 patients: CRP ($p < 0.001$), procalcitonin ($p = 0.034$), creatinine kinase (CK) ($p = 0.010$), CK-MB ($p < 0.001$), D-dimer ($p = 0.001$), lactate dehydrogenase (LDH) ($p = 0.005$), aspartate aminotransferase (AST) ($p = 0.04$), glucose ($p = 0.019$) and potassium ($p = 0.001$) levels were all significantly elevated in patients who died, whereas mean lymphocyte ($p = 0.026$), mean thrombocyte ($p = 0.006$), albumin ($p = 0.003$), hemoglobin ($p = 0.002$) and fibrinogen ($p = 0.031$) levels were all significantly lower (Table 1). In addition, there was a significantly higher neutrophil-to-lymphocyte ratio on admission in patients who subsequently deceased ($p = 0.019$) (Table 1).

Mean CCI, SOFA, qSOFA, CURB-65 and MEWS scores on admission were all significantly higher in deceased patients ($p < 0.001$) (Table 1).

Univariate analysis for mortality

In univariate analysis, age, chronic renal failure, malignancy, cerebrovascular disease, number of comorbidities >2, dyspnea, cough, NIH severe and critical illness, pulse oxygen saturation, respiratory rate, systolic and diastolic blood pressure, qSOFA, GCS, MEWS, SOFA, CURB-65, CCI, CRP, procalcitonin, CK, D-dimer, lymphocyte and thrombocyte levels, neutrophil-to-lymphocyte ratio, AST, albumin, hemoglobin, CK-MB, fibrinogen, LDH and potassium levels were all associated with mortality ($p < 0.05$) (Table 1).

Multivariate analysis for mortality

Certain variables with a $p < 0.05$ in univariate analysis (NIH severe and critical illness, qSOFA, MEWS, SOFA, CURB-65, CCI, CRP, procalcitonin, CK, D-dimer, neutrophil-to-lymphocyte ratio, AST, hemoglobin, glucose, CK-MB and potassium levels) were included in multivariate logistic regression analysis. However, variables with a $p < 0.05$ in univariate analysis such as age, chronic renal failure, malignancy, cerebrovascular disease, number of comorbidities > 2, dyspnea, cough, pulse oxygen saturation, respiratory rate, systolic and diastolic blood pressure, GCS, lymphocyte, thrombocyte count were excluded from the multivariate analysis as they were variables themselves in the clinical score systems. Meanwhile, albumin, fibrinogen, and LDH were also excluded due to the high number of missing values. In logistic regression analysis, both higher SOFA ($p < 0.001$, OR = 1.86, 95% CI = 1.42-2.45) and CURB-65 scores on admission ($p = 0.001$, OR = 2.60, 95% CI = 1.47-4.57) were associated with mortality on day 30 (Table 2).

Clinical score systems on admission such as SOFA, qSOFA, MEWS, GCS, CCI and CURB-65 were analyzed via receiver operating characteristic (ROC) curve analysis for 30-day mortality prediction. The highest area under curve (AUC) value was recorded for SOFA score with AUC: 0.84 (95% CI = 0.79-0.88) which was followed by CURB-65 score as AUC: 0.79 (95% CI = 0.73-0.83). Regarding the prediction of 30-day mortality, the optimal cut-off values were found as

Table 3. Area under curve (AUC) and cut-off values of score systems for 30-day mortality.

Variable	AUC (95% CI)	Standart error	*p* value	Youden Index	Optimal Cut-off Value	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
SOFA	0.840 (0.790-0.883)	0.0407	< 0.0001	0.5572	> 2	70.27 (53-84.1)	85.45 (80.1-89.8)
CURB-65	0.791 (0.736-0.839)	0.0409	< 0.0001	0.4582	≥ 2	59.46 (42.1-75.2)	86.36 (81.1-90.6)
CCI	0.779 (0.723-0.828)	0.0408	< 0.0001	0.4330	≥ 1	86.49 (71.2-95.5)	56.82 (50-63.5)
qSOFA	0.740 (0.681-0.792)	0.0431	< 0.0001	0.4391	≥ 1	70.27 (53-84.1)	73.64 (67.3-79.3)
MEWS	0.714 (0.655-0.768)	0.0472	< 0.0001	0.3118	> 1	70.27 (53-84.1)	60.91 (54.1-67.4)
GCS	0.610 (0.547-0.670)	0.0360	0.0023	0.2205	< 15	24.32 (11.8-41.2)	97.73 (94.8-99.3)

>2 points for SOFA score with 70.27% sensitivity, 85.45% specificity and ≥ 2 points for CURB-65 score with 59.46% sensitivity, 86.36% specificity (Table 3).

Subgroup Analysis of the laboratory results on day 0, 3, 7, and 14 among inpatient deaths

Friedman's two-way analysis by ranks was performed for the subgroup analysis of laboratory parameters on day 0, 3, 7 and 14 among patients who died. In these patients, there were significant differences between the baseline, day 3, 7 and 14 results of D-dimer (chi-square (χ^2) (3, n = 11): 11.40, $p = 0.01$), Ferritin (χ^2 (3, n = 12): 8.19, $p = 0.042$), leucocyte (χ^2 (3, n = 12): 10.00, $p = 0.019$) and neutrophil counts (χ^2 (3, n = 12): 12.20, $p = 0.007$). In deceased patients, median values of D-dimers were 1.59 for day 0; 1.60 for day 3; 3.85 for day 7 and 4.46 for day 14; median values of Ferritin were 588.5 for day 0; 799.5 for day 3; 988.5 for day 7 and 1080 for day 14; and median leukocyte and neutrophil counts were 8,245 and 6,615 for day 0; 9,985 and 9,065 for day 3; 10,210 and 9,095 for day 7; 18,185 and 15,755 for day 14, respectively.

In pairwise comparison analysis of day 0 and day 14 of these inpatient deaths, there was a statistically significant increase in median levels of D-dimer (Bonferroni corrected $p = 0.006$), Ferritin (Bonferroni corrected $p = 0.034$), leukocyte (Bonferroni corrected $p = 0.027$) and neutrophil (Bonferroni corrected $p = 0.009$) counts from baseline to day 14.

Discussion

We believe that identifying the prognostic factors have a vital importance in order to set priorities for the management of COVID-19 patients. Regarding the baseline variables relating to clinical and laboratory characteristics of COVID-19 on admission, one point increase of SOFA and CURB-65 scores were found as independent risk factors for the mortality and this study emphasizes the prognostic value of clinical scoring systems on admission for COVID-19 patients from our country.

Zheng *et al.* conducted a meta-analysis among critical/mortal and non-critical COVID-19 patients regarding the risk factors and they concluded that leucocyte count, AST, creatinine, PCT, LDH, hs-Troponin I and D-dimer could imply the progression of COVID-19 [13]. In addition, Cheng *et al.* investigated a total number of 10614 confirmed COVID-19 patients and they found out that non-survivors had a significantly higher ferritin level compared with the one in survivors (WMD = 677.17, 95% CI = 391.01-963.33, $p < 0.001$) [14]. In our study, we also found out that D-dimer, Ferritin, leucocyte and neutrophile counts had increased significantly during the follow-up in patients with mortality.

A prospective cross-sectional study with a total number of 140 critically ill patients without trauma revealed that the area under the ROC curve of SOFA score in predicting mortality was 0.73 (95% CI = 0.65-0.81) with the best cut-off point as ≥ 7 (sensitivity 75%, specificity 62.23%) in predicting 30-day mortality [15]. Karakuzu *et al.* investigated 167 critically ill patients with the diagnosis of ventilator-associated pneumonia (VAP) and they found that SOFA score of > 6 on the day of VAP diagnosis was an independent risk factor for mortality (OR = 1.4, 95% CI = 1.2-1.6, $p < 0.001$) [16]. On the other hand, a retrospective study with a total of 976 patients diagnosed with sepsis revealed that the ability to predict in-hospital sepsis-related mortality was statistically significant for the SOFA score with a high distinctive ability to predict in-hospital mortality ($p < 0.0001$) and cut-off value for SOFA score in terms of predicting in-hospital mortality was found as high as > 9 points with the sensitivity as 65.8% and specificity as 75.5% [17].

Zhou *et al*. investigated a total number of 191 laboratory-confirmed COVID-19 patients and they showed that a higher SOFA score on admission could be helpful for the clinicians to identify patients with poor prognosis at an early stage (OR = 5.65, 95% CI = 2.61–12.23; $p < 0{\cdot}0001$) in terms of in-hospital mortality [18]. Similar to our study results, an observational retrospective study with a total number of 238 hospitalized COVID-19 patients from Spain revealed that SOFA (19% Hazard ratio, HR, increase per 1-point increase, 95% CI = 5-34) and CURB-65 (76% HR increase per 1-point increase, 95% CI = 23-143) scores were found as the baseline factors that were associated with a greater hazard of death [19]. Izcovich *et al*. conducted a systematic review with a total number of 57044 confirmed or suspected COVID-19 patients and revealed that a SOFA score > 2 (Odds ratio as 1.97, 95% CI: 1.22-3.2; Risk diffences as 7.3%, 95% CI: 1.8%-15%) was associated with poor outcome in terms of survival with moderate certainty of the evidence [20]. Chauhan *et al*. also revealed that a higher SOFA score at admission is a poor prognostic factor and showed a SOFA score cut-off value as ≥ 3.5 with 91.7% sensitivity and 87.5% specificity rates via ROC analysis [21]. On the other hand, among the 47 intensive care unit (ICU) patients with confirmed COVID-19, lower SOFA score (≤ 4) on admission was found as a protective factor in an observational study from China [22]. Similar to these findings, Wang *et al*. also showed

that a SOFA score above 4 (OR = 5.16, 95% CI = 1.29-20.55) were identified as risk factors for mortality of critically ill ICU patients with COVID-19 [23]. Regarding the difference of SOFA score cut-off values between the COVID-19 and critically ill sepsis patients, a hypothesis may be described as the main organ dysfunction in COVID-19 patients seems to be respiratory failure and acute respiratory distress syndrome is one of the major cause of mortality among them. Thus, possible reason of lower SOFA score cut-off values for COVID-19 patients than the other septic patients in terms of predicting mortality might be the rapid deterioration of respiratory system parameters.

A retrospective cohort study from China revealed that MEWS score could be useful for predicting in-hospital mortality among a total number of 235 elderly (older adults aged 60 or above) patients with COVID-19 and the optimal cut-off value of MEWS in the male patients aged 75 years or above was found as 2.5 (84.3% specificity, 84.6% sensitivity) [24]. Wang *et al.* showed that the AUROCs in predicting in-hospital mortality for SOFA as 0.926 (95% CI = 0.877–0.975); MEWS as 0.913 (95% CI = 0.864–0.941); qSOFA as 0.886 (95% CI = 0.804–0.969) and CURB-65 as 0.845 (95% CI = 0.740–0.951), respectively [24]. In our study, we found that AUROC in predicting mortality for MEWS score as 0.714 (95% CI = 0.655–0.768) with a cut-off value as two points or above (70.27% sensitivity, 60.91% specificity). The possible explanations for these results might be the differences of mean age which was recorded as 56.04 ± 1.05 years in our study and disease severity at the presentation.

Az *et al*. investigated a total of 540 confirmed COVID-19 patients for predictive factors and found CRP levels (OR = 1.02, 95% CI = 1.009-1.032; $p < 0.001$) and CURB-65 scores (OR = 4, 95% CI = 1.28-12.44; $p = 0.017$) to be independently associated with disease severity and mortality [25]. When Shi *et al*. evaluated 257 hospitalized patients with laboratory-confirmed COVID-19 pneumonia, they showed that the CURB-65 score (AUC = 0.84, 95% CI = 0.67-0.93) had better prognostic value for in-hospital mortality than other pneumonia prognostic scores, reporting a negative predictive value of CURB-65 ≥ 2 of 97.2% [26]. Similar to these findings, Rodriguez-Nava *et al*. also evaluated a total of 313 confirmed COVID-19 patients and found the CURB-65 score to have higher numerical AUC to predict in-hospital mortality (AUC 0.78), in comparison to the quick COVID-19 Severity Index (qCSI) score (AUC 0.71) and Brescia-COVID Respiratory Severity Scale (BCRSS) (AUC 0.66) [27]. In addition to this, a prospective study in India evaluated the capacity of early warning scores taken at ICU admission to predict mortality in 140 confirmed COVID-19 patients, and results indicated that CURB-65 performed better in predicting ICU mortality (AUC = 0.72, 95% CI = 0.63-0.81) than the National Early Warning Score (NEWS)2, qSOFA or SIRS score systems [28].

Our study is limited by its retrospective design and single-center data, which was collected from patients' hospital records. However, despite these limitations, our results indicate that SOFA and CURB-65 scores on admission are of more benefit in predicting mortality in our COVID-19 patients than other parameters.

Conclusions

In conclusion, SOFA and CURB-65 scores on admission seem to be promising factors for predicting the prognosis of hospitalized COVID-19 patients in terms of mortality. Based on our results, these scores could be useful for triaging high-risk patients. The optimal cut-off values for predicting 30-day mortality, seem to be >2 points for SOFA and ≥ 2 points for CURB-65 scores. In addition, we found D-dimer, ferritin, leukocyte and neutrophil counts were all significantly increased in patients who died in our study. Thus, these laboratory parameters should also be tracked in high-risk patients.

Acknowledgements

We would like to thank the Pandemic Study team members for their work: Mustafa Hacı Mustafaoglu, Erol Armagan, Cagri Hunutlu, Aynur Urhan, Fahir Ozkalemkas, Solmaz Celebi, Gurkan Uncu, Alpaslan Turkkan, Alis Ozcakir, Levent Ozdemir, Cuneyt Ozakın, Nermin Kelebek, Fatma Duzgun, Nevin Bor, Sevginar Sakarya, Fahri Durmaz, Mufit Parlak, Mustafa Gullulu, Suna Goren, Ali Aydınlar, Kemal Durak, Remzi İscimen, Bedrettin Akova, Saduman Balaban Adim, Suheda Ozcakir, Ayse Melda Payaslioglu, Haluk Barbaros Oral, Ekrem Kaya, İrfan Kiristioglu, Ridvan Ali.

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Corresponding author
Uğur Önal, MD
Uludağ University, Faculty of Medicine, 16100, Bursa, Turkey
Phone: +90 533 776 91 71
Fax: +90 224 295 00 19
Email: uguronal@uludag.edu.tr

Conflict of interests: No conflict of interests is declared.