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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Usefulness of APACHE-II, SOFA, ISARIC/WHO 4C Mortality Score and CO-RADS for Mortality Prediction of Critically Ill Coronavirus Disease-2019 Patients

APACHE-II, SOFA, ISARIC/WHO 4C Mortalite Skoru ve CO-RADS'nin Kritik Koronavirüs Hastalığı-2019 Hastalarının Mortalite Tahmininde Kullanımı

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ABSTRACT *Objective:* It was aimed to report the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow coma scale (GCS), 4C mortality score and the coronavirus disease-2019 (COVID-19) Reporting and Data System (CO-RADS) in predicting the outcome of critically ill COVID-19 patients.

Materials and Methods: Patients with laboratory-confirmed COVID-19 infection or clinical and radiological confirmed COVID-19 infection who were admitted to adult intensive care unit (ICU) were included. Clinical characteristics, outcomes, APACHE-II score, SOFA score, International Severe Acute Respiratory and Emerging Infections Consortium/World Health Organization 4C mortality score and CO-RADS classification were reported at admission.

Results: Two hundred seventy six patients were included in this study. The mean age was higher in non-survivor patients. The most common cause of hospitalization was respiratory failure (67%). The common co-morbidities were hypertension (51.8%), cardiac disease (43.4%) and diabetes (33.6%). Organ failure was present in 61.5% of the patients. The mean APACHE-II, SOFA, GCS and 4C mortality scores were higher in non-survivor patients. 4C mortality and SOFA scores showed higher predictive accuracy for mortality with an area under the curve 0.736 and 0.706, respectively. 4C mortality had sensitivity of 78.9% and specificity of 58.1% whereas of SOFA had a sensitivity of 78.9% and a specificity of 53.3%.

Conclusion: 4C mortality and SOFA scores could be a predictors of mortality in COVID-19 patients in the ICU.

Keywords: COVID-19, intensive care, CO-RADS classification, 4C mortality score, SOFA score, APACHE-II score

ÖZ *Amaç:* Kritik koronavirüs hastalığı-2019 (COVİD-19) hastalarının mortalite tahmininde Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skoru, Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skoru, Glasgow koma skalası (GCS), 4C mortalite skoru ve COVİD-19 Raporlama ve Veri Sistemi'nin (CO-RADS) araştırılması amaçlanmıştır.

Gereç ve Yöntem: Laboratuvarca doğrulanmış COVİD-19 enfeksiyonu veya klinik ve radyolojik olarak doğrulanmış COVİD-19 enfeksiyonu olan erişkin yoğun bakım ünitesine (YBÜ) kabul edilen hastalar dahil edildi. Klinik özellikler, sonuçlar, APACHE-II skoru, SOFA skoru, Uluslararası Şiddetli Akut Solunum ve Ortaya Çıkan Enfeksiyonlar Konsorsiyumu/Dünya Sağlık Örgütü *(International Severe Acute Respiratory and Emerging Infections Consortium/World Health Organization)* 4C mortalite skoru ve CO-RADS sınıflandırması yatış esnasında kaydedildi.

Bulgular: Bu çalışmaya 276 hasta dahil edildi. Ölen hastalarda yaş ortalaması daha yüksekti. En sık hastaneye yatış nedeni solunum yetmezliğiydi (%67). En sık eşlik eden hastalıklar hipertansiyon (%51,8), kalp hastalığı (%43,4) ve diyabet (%33,6) idi. Hastaların %61,5'inde organ yetmezliği mevcuttu. Ortalama APACHE-II, SOFA, GCS ve 4C mortalite skorları ölen hastalarda daha yüksekti. Mortalite için 4C mortalite ve SOFA skorları, sırasıyla eğri altındaki alan 0,736 ve 0,706 alan ile daha yüksek öngörü bulundu. 4C mortalite skoru %78,9 duyarlılık ve %58,1 özgüllüğe sahipken, SOFA'nın duyarlılığı %78,9 ve özgüllüğü %53,3 idi.

Sonuç: 4C mortalite ve SOFA skorları, YBÜ'deki COVİD-19 hastalarında mortalitenin tahmin ettirici bir göstergesi olabilir.

Anahtar Kelimeler: COVİD-19, yoğun bakım, CO-RADS sınıflandırması, 4C mortalite skoru, SOFA skoru, APACHE-II skoru

Introduction

The severe acute respiratory syndrome coronavirus disease-2019 (COVID-19) began in Wuhan, China, and has spread worldwide, infecting millions of people since than December 2019. The COVID-19 pandemic has caused an intense loss of human life worldwide and presents an extraordinary challenge to public health systems and the world economy.

Predicting the outcomes in intensive care patients is very important in terms of both guiding the treatment and preventing unnecessary treatments. Various laboratory tests, clinical findings or scoring systems are used to predict outcomes in intensive care patients. Research and large-scale vaccination campaigns are ongoing for effective treatment of COVID-19. Meanwhile, it is very important to predict in-hospital mortality during hospitalization for COVID-19.

The Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores was designed to calculate the severity of disease of intensive care unit (ICU) patients and to predict mortality. The APACHE-II score is calculated based on body temperature, heart and respiratory rate, mean arterial pressure, pH. Range of APACHE-II is 0 to 71. Increasing score is associated with an increasing risk of hospital death (1). The SOFA score was designed to assess the severity of organ dysfunction in critically ill septic patients. The original SOFA score was studied from a cohort of 1449 patients admitted to ICUs in sixteen countries (2). It was published that a high correlation between hospital mortality and the SOFA score in COVID-19 patients. They reported that SOFA score was a risk factor for death in COVID-19 patients (3). However the discriminant accuracy of the SOFA score for mortality prediction in patients with COVID-19 pneumonia requiring mechanical ventilation was poor (4).

In a review for prediction models for COVID-19 patients, they identified 107 prognostic models for patients with a diagnosis of COVID-19. The suggested use of these models was not visibly described. The most frequently used categories of prognostic factors (included at least 20 times for any outcome) included age, comorbidities, vital signs, image features, sex, lymphocyte count, and C-reactive protein (CRP) (5). It was recommended the models by Knight et al. (6) and Jehi et al. (7) are good candidates for validation studies in other data for prediction models. Knight et al. (6) published the International Severe Acute Respiratory and emerging Infections Consortium/World Health Organization (ISARIC/WHO) 4C mortality score for COVID-19. ISARIC/WHO 4C mortality score includes the biological and clinical variables, like breathing rate, peripheral oxygen saturation, age, sex, Glasgow coma scale (GCS), urea, CRP levels and number of comorbidities. The score ranges from zero to twenty-one points. A score of ≤3 had a 1% mortality risk compared with 62% mortality risk for those with a score of ≥15.

Chest computerized tomography (CT) scans are used as a valuable tool in the diagnostic process of COVID-19 viral pneumonia cases. Chest CT specificity (82.9% to 96%) and sensitivity (80% to 90%) were reported to be higher than real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing for COVID-19 diagnosis. This highlights the need to recognize and understand imaging findings of the lungs (8). COVID-19 Reporting and Data System (CO-RADS) is published in Mid-March of 2020 that grades the findings on how likely the diagnosis of COVID-19 is. It was evaluated using 105 randomly selected chest CT scans of patients admitted to the emergency department with clinical suspicion of COVID-19. CO-RADS system has seven categories. Categories zero and grade 1 to 6. Grade 1 to 6 means that from very low risk to proven infection with a positive RT-PCR assay. The system very well in estimating COVID-19 in patients with moderate to severe clinical disease (9).

The objective of this paper is to report APACHE-II score, SOFA score, the 4C mortality score and the CO-RADS classification in predicting outcome of COVID-19 in the ICU.

Materials and Methods

This is a single-center; retrospective cohort study that was analyzed anonymized data. After the Non-Invasive Clinical Researches Ethics Committee of the Pamukkale University this study was performed (no: 60116787-020-14366, date: 02.02.2021). Informed consent was waived because of the retrospective design of the study. Between September 1, 2020 and January 30, 2021 (the second wave of the COVID-19 pandemic), all adult patients (over than 18 years of the age) with RT-PCR assay confirmed COVID-19 infection or clinical and radiological confirmed COVID-19 infection were included.

Diagnosis of COVID-19 was accepted according to these findings: 1) Positive result of RT-PCR assay for COVID-19, 2), Typical COVID-19 lung CT scan abnormalities, 3)

COVID-19 clinical findings and symptoms and/or the recent contact and/or travel history with certain case of COVID-19, associated with CO-RADS 3, 4 chest CT scan. Laboratory confirmation for COVID-19 was defined as a positive result of RT-PCR test from a specimen collected on an endotracheal aspirate or nasopharyngeal swab. RT-PCR assays (COVID-19 RT-qPCR, Bio-Speedy) were performed according to the protocol approved by WHO in the General Office of Public Health Microbiology Reference Laboratory and laboratories in the specified areas (10). Patient's data was obtained from hospital information systems. Data was recorded on daily basis.

Data Collection

The demographics and characteristics, clinical findings, therapies and laboratory data were recorded. The demographics and characteristics were age, sex, smoking history, APACHE-II, GCS, SOFA, the 4C mortality score, laboratory data, clinical symptoms or signs, the recent exposure and travel history, comorbidities. The demographics and characteristics APACHE-II, GCS, SOFA, the 4C mortality score, clinical symptoms or signs, the recent exposure and travel history, comorbidities were recorded at admission.

Laboratory data consisted of complete blood count, alkaline phosphatase, alanine aminotransferases, aspartate aminotransferases (AST), lactate dehydrogenase, serum creatinine (Cr), serum potassium, phosphate, sodium, D-dimer, prothrombin time, international normalized ratio (INR), partial thromboplastin time, serum CRP, and serum procalcitonin. Invasive and noninvasive mechanical ventilation parameters were recorded. Arterial blood gas analysis were performed according to the patient's needs.

The ISARIC/WHO 4C mortality score was calculated on admission for each patient. This score includes eight parameters: age, sex, peripheral oxygen saturation, respiratory rate, number of comorbidities, level of consciousness (assessed using the GCS) and results of laboratory tests: serum urea and CRP (6). CT was performed at 1st day and as needed. All chest CT scans were performed without contrast agent and with a section thickness of 5 mm. The chest CT scans were reported according to CO-RADS. The CO-RADS scoring system has classification such as CO-RADS category 0 for technically insufficient imaging and CO-RADS category 6 for the confirmed disease through RT-PCR testing (9).

Outcome

Patients' length of mechanical ventilation in ICU and discharge status (non-survivor, survivor) was entered patent's data form. Patients were treated according to the guide was prepared by scientific committee of the Ministry of Health and available literature (11). Therapies of the patients were documented daily. Since there was not enough evidence at the beginning of the pandemic, we did not routinely use steroids in our patients. Microbial cultures from blood tracheal aspirate, and urine were taken at admission and in need of clinical situation.

Statistical Analysis

Statistical analyses were performed with SPSS for Windows 19 software. Continuous variable are shown as mean (standard deviation), median and minimum-maximum, categorical variables were reported as frequency with odds ratio and 95% confidence interval (CI). The conformity of data to normal distribution were evaluated with Shapiro-Wilk test. The comparisons between groups were evaluated with Mann-Whitney U test for continuous variables, chi-square test and Fisher's Exact chi-square test for categorical values. Receiver operating characteristic (ROC) curves of APACHE-II, SOFA, the 4C mortality score and CO-RADS were presented with area under curve (AUC), 95% CI, cut-off value, sensitivity, specificity. Statistical analyses were evaluated with 95% CI and $p<0.05$ was accepted as a significant difference.

Results

Two hundred seventy six patients included to this study. Total 276 patients were grouped into two groups, depending on the survival status. One hundred seventy one patients (61.9%) were included in the non-survivor group. The rest of 105 patients (38.1%) had included in the survivor group. Total female and male patient were 98 (36.6%) and 178 (64.4%) respectively. The mean age was 68.6 (13.3) years for all patients. In non-survivor patient group, the mean age were higher than in survivor patients ($p<0.001$) (Table 1, 2). One hundred eighty nine patients (68.4%) were admitted from emergency department. The most common cause of hospitalization was respiratory failure with a rate of 67%. The second most common cause was sepsis (33%). The reasons for hospitalization was statistically different between survivor and non-survivor patients. Sepsis is higher in non-survivor group than survivor group at admission ($p<0.001$).

Table 1. Demographics and clinical characteristics of the patients

Variable	Alive			Ex			All			p
	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	
Age	64.4±13.6	66	23-95	71.2±12.5	72	23-96	68.6±13.3	70	23-96	<0.001
BMI	29.7±3.4	30	22-42	29.5±3.6	29	20-46	29.6±3.5	29.3	20-46	0.566
Duration of symptom (day)	6.0±3.9	5	0-30	6.8±4.4	6	0-30	6.3±4.2	5	0-30	0.273
APACHE-II	17.8±8.6	15	5-42	21.6±9.8	21	5-44	20.2±9.5	18	5-44	0.001
SOFA	5.0±2.5	4	0-12	7.4±3.5	7	0-18	6.5±3.3	6	0-18	<0.001
GCS	14.0±2.6	15	3-15	10.4±5.3	13	3-15	11.7±4.8	15	3-15	<0.001
4C mortality	11.2±3.5	11	4-19	14.2±3.3	15	6-21	13.0±3.7	13	4-21	<0.001
CO-RADS	5.0±0.9	5	2-6	5.0±0.9	5	2-6	5.0±0.9	5	2-6	0.784
Fever	37.0±0.5	37	35.8-38.6	37.1±0.8	37	35.7-39.0	37.0±0.7	37	35.7-39.0	0.346
Heart rate (/min)	90.7±12.7	89	60-130	99.0±15.5	100	52-150	95.8±15.0	96	52-150	<0.001
Mean arterial pressure (mmHg)	81.1±9.1	80	66-120	77.7±12.7	75	50-122	79.0±11.5	78	50-122	0.003
FiO_2	50.9±7.8	50	40-80	63.1±10.1	60	40-90	58.5±11.0	60	40-90	<0.001
SPO_2	91.9±3.0	92	78-99	90.9±5.0	91	62-100	91.3±4.3	91	62-100	0.053
PEEP	6.0±1.1	6	5-10	7.8±1.9	8	5-14	7.1±1.9	7	5-14	<0.001
Tidal volume	388.6±46.2	390	320-450	418.3±43.9	420	300-600	416.0±44.6	410	300-600	0.032
Compliance mL cmH_2O	23.4±5.0	22	20-34.7	24.5±6.2	24	12-45	24.4±6.1	23.6	12-45	0.549
Driving pressure	15.5±4.7	14	10-25	15.6±4.4	14	9-24	15.6±4.4	14	9-25	0.637
PaO_2/FiO_2	143.2±50.5	134	75-381	125.2±51.4	112	45-353	132.0±51.7	122	45-381	<0.001
Max PEEP during ICU	6.8±1.6	7	5-12	10.3±2.5	10	5-16	8.9±2.7	8	5-16	<0.001
Min PEEP during ICU	5.2±0.5	5	5-8	7.1±1.6	7	5-13	6.4±1.6	6	5-13	<0.001
Max PaO_2/FiO_2	279.3±74.8	261.5	132-520	186.7±70.4	180	17-456	221.7±89.7	220	17-520	<0.001
Min PaO_2/FiO_2	136.8±43.4	127	65-319	100.8±34.3	95	43-213	114.4±41.8	108	43-319	<0.001
Max PaO_2	109.9±34.9	99	55-202	98.8±37.6	88	42-212	103.0±36.9	93	42-212	0.003
Min PaO_2	61.6±22.0	54	41-185	59.1±19.7	52	30-132	60.1±20.6	53	30-185	0.204
Invasive mechanical ventilation (day)	9.6±8.4	7.5	1-27	7.1±7.7	4	1-36	7.2±7.7	4	1-36	0.197
Noninvasive mechanical ventilation (day)	7.9±5.7	6	1-26	4.8±4.4	3	1-27	6.6±5.4	5	1-27	<0.001

BMI: Body mass index, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, ICU: intensive care unit, SD: standard deviation, min: minimum, max: maximum, PEEP: positive-end-expiratory respiration

Table 2. Data frequencies of the patients

Variable	Alive (n=105)	Ex (n=171)	p	OR	CI	Variable	Alive (n=105)	Ex (n=171)	p	OR	CI
Gender (F/M)	36/69	62/109	0.740	0.92	0.51-1.53	CT (-/+)	8/97	16/155	0.782[a]	0.80	0.33-1.94
Comorbidity (-/+)	27/78	20/151	0.004[a]	2.61	1.38-4.95	CT bilateral ground glass opacification (-/+)	17/77	44/127	0.207[a]	0.64	0.34-1.19
Hypertension (-/+)	58/47	75/96	0.066	1.58	0.97-2.58	CT pleural effusion (-/+)	80/14	119/52	0.008[a]	2.50	1.30-4.81
Diabetes mellitus (-/+)	66/39	114/57	0.519	0.85	0.51-1.41	CT nodul (-/+)	86/6	163/8	0.712[b]	0.70	0.24-2.09
Cardiac disease (-/+)	70/35	86/85	0.008	1.98	1.19-3.27	Therapies and interventions					
Pulmonary disease (-/+)	93/12	130/41	0.016	2.44	1.22-4.90	Recruitment (-/+)	103/2	146/25	0.001	8.82	2.04-38.050
Malignity (-/+)	93/12	138/33	0.121[a]	1.85	0.91-3.77	Prone position (-/+)	69/36	156/15	<0.001	0.18	0.10-0.36
Chronic renal failure (-/+)	94/11	145/26	0.349[a]	1.53	0.72-3.25	Renal replacement therapy (-/+)	104/1	158/13	0.031[a]	8.56	1.10-66.39
Immune deficiency (-/+)	104/1	166/5	0.524[b]	3.13	0.36-27.19	Plasma therapy (-/+)	99/6	158/13	0.721[a]	1.36	0.45-3.69
Symptom (-/+)	3/102	1/170	0.311[b]	5.00	0.51-48.70	Hidroxy chloroquine (-/+)	99/6	167/4	0.262[a]	0.40	0.11-1.44
Fever (-/+)	77/28	124/47	0.882	1.04	0.60-1.80	Antibiotic therapy (-/+)	5/100	6/165	0.825[b]	1.38	0.41-4.62
Dyspnea (-/+)	6/99	8/163	0.922[a]	1.24	0.42-3.66	Antiviral (-/+)	1/104	4/167	0.740[b]	0.40	0.04-3.64
Cough (-/+)	45/60	105/66	0.003	0.47	0.29-0.77	Vasopressor (-/+)	93/12	17/154	<0.001	70.21	32.1-153.5
Smoking (-/+)	74/31	127/44	0.492	0.83	0.48-1.42	Tocilizumab (-/+)	98/7	162/9	0.827[a]	0.78	0.28-2.16
Contact history (-/+)	80/25	136/35	0.513	0.82	0.46-1.48	Cytokine adsorption (-/+)	104/1	157/14	0.021[a]	9.27	1.20-71.59
						Aspirin (-/+)	0/105	2/169	0.383[b]	0.54*	0.06-5.21
Reason for admission (respiratory failure/sepsis)	84/21	101/70	<0.001	2.77	1.57-4.89	Low molecular weight heparin (-/+)	0/105	2/169	0.383[b]	0.54*	0.06-5.21
PCR at admission (-/+)	12/93	5/166	0.009[a]	4.28	1.46-12.53	Microbial culture (-/+)	74/31	116/55	0.646	1.13	0.67-1.92
Radiography (-/+)	27/78	42/129	0.830	1.06	0.61-1.86	Organ failure (-/+)	49/56	57/114	0.027	1.75	1.06-2.88
Radiography bilateral infiltrate (-/+)	29/76	44/127	0.730	1.10	0.64-1.91	Organ failure (-/single/ multiple)	49/52/4	57/55/59	<0.001	-	-
Radiography effusion (-/+)	92/13	125/46	0.007[a]	2.60	1.33-5.10	Invasive mechanical ventilation (-/+)	95/10	4/167	<0.001	396.6	121.1-1299.0
Radiography ground glass opacities (-/+)	30/75	47/124	0.845	1.06	0.62-1.81	Noninvasive mechanical ventilation (-/+)	3/102	74/97	<0.001	0.04	0.01-0.13

[a]Yates corrected chi-square, [b]Fisher's Exact chi-square. PCR: Polymerase chain reaction, F: female, M: male, OR: odds ratio, CI: confidence interval, CT: computed tomography

Table 3. Laboratory data of the patients

Variable	Alive			Ex			All			p
	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	Mean ± SD	Median	Min-max	
White blood cell (per mm^3)	10893.1±5811.0	9720	100-28900	13116.3±13903.8	11090	340-171000	12270.5±11551.8	10870	100-171000	0.110
Lymphocyte (per mm^3)	822.7±1356.4	530	78-10100	684.0±459.3	520	100-2800	737.0±912.7	520	78-10100	0.883
Platelet (per mm^3)	1061.4±8369.7	225	36-86000	230.2±167.3	216	15-1900	546.4±5164.6	218	15-86000	0.232
Neutrophil to lymphocyte ratio	16.3±11.4	13.2	1.5-67	17.3±12.8	15	1.2-82	16.9±12.3	14.2	1.2-82	0.679
INR	1.2±0.5	1.1	0.9-4.6	1.4±1.8	1.2	0.9-9.3	1.3±0.7	1.2	0.9-9.3	<0.001
D-dimer ng/mL	1991.9±5589.1	570	48-46000	3556.6±6716.2	1290	106-55046	2961.4±6346.5	915	48-55046	<0.001
Fibrinogen mg/dL	583.1±246.5	586	99-1567	541.0±248.6	528	97-2000	557.0±248.2	550	97-2000	0.166
Creatinine mg/dL	1.2±1.3	0.9	0.4-9.7	1.7±1.3	1.2	0.3-8.9	1.5±1.3	1.1	0.3-9.7	<0.001
Aspartate aminotransferase	54.3±155.9	33	8-1612	143.9±530.1	38	8-6145	109.8±429.9	35.5	8-6145	0.009
Alanine aminotransferase	38.4±34.5	30	241	103.7±329.9	24	2-2864	78.9±262.1	26	2-2864	0.376
Ferritin ug/L	794.2±549.1	676.5	54-2000	852.7±627.0	663	32-3162	830.3±598.1	668.5	32-3162	0.745
C-reactive protein	98.9±70.6	88	0.9-388	136.1±143.8	106	6.7-1654	121.9±122.4	99.5	0.9-1654	0.006
Procalcitonin	1.6±6.8	0.2	0.03-66	5.3±13.0	0.7	0.01-80	3.9±11.2	0.4	0.01-80	<0.001
Lactate ug/L	1.7±0.4	1.8	0.8-3.1	2.4±1.9	2	0.8-16	2.2±1.7	1.9	0.8-16	0.005
IL-6	58.5±76.4	32.5	3.4-397.8	256.3±701.1	63.5	12.1-3700	163.7±521.1	51.2	3.4-3700	0.001
Amylase	73.7±57.6	51	18-233	87.9±76.0	59	10-338	80.8±67.3	58.5	10-338	0.553
Lipase	41.8±42.5	28.3	10-232	79.0±134.8	42.5	4-726	60.1±100.4	32.6	4-726	0.259
Urea	56.8±32.4	49	13-159	93.3±60.2	75	19-353	79.4±54.3	62	13-353	<0.001

SD: Standard deviation, min: minimum, max: maximum, INR: international normalized ratio

Two hundred twenty nine patients have comorbidities. Comorbidities have higher in the non-survivor group than survivor group. The most common co-morbidities were hypertension (51.8%), cardiac disease (43.4%) and diabetes (33.6%). Compared to the survivor group, non-survivor group had a significantly higher proportion of cardiac disease and pulmonary disease; the differences were statistically significant ($p<0.05$). Dyspnea was the most common symptom. Ninety five percent of the patients have dyspnea. The other common symptoms were, coughing and fever. Coughing was significantly higher in non-survivor patients than survivor patients were ($p=0.003$) (Table 2).

Heart rate and FiO_2 was lower in survivor patients than non-survivor patients ($p<0.001$), whereas the mean arterial pressure, was higher in survivor patients ($p=0.003$). In terms of comparison laboratory biomarkers taken during admission between 2 groups, it was found INR, D-dimer, Cr, urea, CRP, AST, procalcitonin, lactate and IL-6 were significantly lower in the survivor group ($p<0.001$) (Table 3). Chest radiography was available in 207 patients at admission. Pleural effusion were seen significantly higher in non-survivor patients ($p=0.007$). Two hundred fifty two patient got CT scan at admission. Same as the radiography pleural effusion were shown significantly higher in non-survivor patients on CT scan ($p=0.008$) (Table 2).

Seventy percent of the patients were underwent invasive mechanical ventilation therapy. Invasive mechanical ventilation therapy was applied to the majority of patients who died whereas non-invasive mechanical ventilation therapy was applied to the majority of survivor patients. This difference was statistically significant (p<0.001) (Table 2). Positive-end-expiratory respiration and tidal volume values statistically were different between survivor and non-survivor groups. When we compared arterial blood gas analysis, it was found that non-survivor group had lower PaO_2 and PaO_2: FiO_2 ratio than the survivor group (p<0.001) (Table 1). Therapies and interventions were given in Table 2. Recruitment maneuver, prone position, renal replacement therapy, vasopressor usage and cytokine adsorption were higher in non-survivor patients and were statistically different from survivor patients (p<0.001). Organ failure was present in 61.5% of all patients. Multiple organ failure was more common in the non-survivor -group. The length of invasive and non-invasive mechanical ventilation were statistically significantly longer in survivor group (p<0.001) Table 2.

The mean APACHE-II, SOFA, GCS and the 4C mortality scores were higher in non-survivor patients than in survivor patients (p<0.001) (Table 2). The mean CO-RADS classification value was not different between groups. ROC curves were computed to assess the accuracy of scores and CO-RADS in predicting mortality. 4C mortality and SOFA scores showed higher predictive accuracy for mortality with an area AUC 0.736 and 0.706 respectively (p<0.001) (Figure 1) (Table 4). The 4C mortality cut-off value of 11.5 had a sensitivity of 78.9% and specificity of 58.1%. The cut-off value of SOFA was 4.5, which corresponded to a sensitivity of 78.9% and a specificity of 53.3%. CO-RADS have not good results for predicting mortality with 5.5 cut-off value in ICU patients (p=0.802).

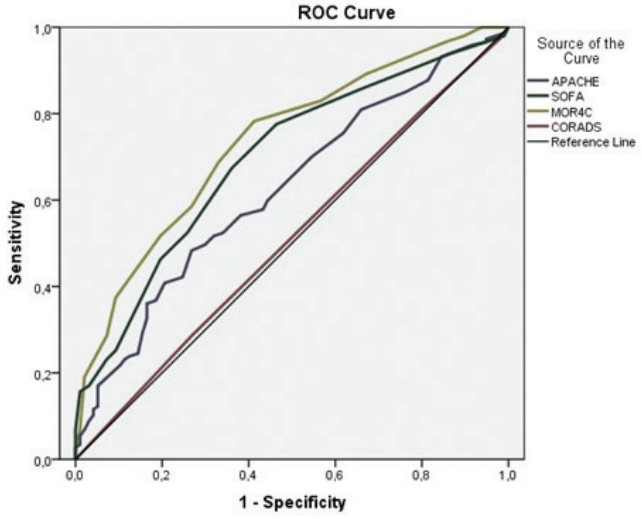

Figure 1. Four score ROC
ROC: Receiver operating characteristic, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, MOR4C: 4C mortality

Discussion

It was aimed to report APACHE-II score, SOFA score, the 4C mortality score and the CO-RADS classification in predicting outcome of COVID-19 in the ICU in this study. Mortality was 61.9% and was higher in older patients and septic patients.

Previous studies from China, Europe, and United States, have described different mortality rates among critically ill patients ranging from 53.8% to 60.4% (12-14). Studies from have reported that critically ill COVID-19 patients are generally older and have underlying medical conditions, such as hypertension and diabetes (12-14). Intensive Care National Audit & Research Centre have evaluated data for 12,420 admissions of 10,873 patents critically ill with confirmed COVID-19. They reported that mortality was 55.9% patients with confirmed COVID-19 and any advanced respiratory

Table 4. ROC analysis results by mortality

	Area under the curve (ROC)	95% CI	p	Cut-off	Sensitivity	Specificity
APACHE-II	0.616	0.549-0.684	0.001	≥19.5	53.2	65.7
SOFA	0.706	0.644-0.768	<0.001	≥4.5	78.9	53.3
GCS	0.688	0.626-0.750	<0.001	≤13.5	50.9	83.8
CO-RADS	0.509	0.435-0.583	0.802	≥5.5	28.6	26.8
4C mortality score	0.736	0.676-0.796	<0.001	≥11.5	78.9	58.1

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow coma scale, CO-RADS: coronavirus disease-2019 Reporting and Data System, ROC: receiver operating characteristic, CI: confidence interval

support (13). In our study, we found also that older patients and patients have comorbidities higher mortality than others.

COVID-19 mainly in severe cases in addition to lung involves different organs such as heart, liver, and kidney, as well as hematological and nervous system, and induce multi-organ failure (15). In our study, patients have high percentage of respiratory failure and sepsis.

Despite advances in patient care, distance measures, and population vaccination campaigns COVID-19 still causes a high rate of death, especially in elderly and comorbid patients. As of 21 October 2021 more than 250 million cases of COVID-19 have been stated with more than 4 million deaths globally since than December 2019 (16). Hospitals all over the world are confronted with an influx of patients with COVID-19. There is an urgent need for a practical risk identification which will allow which patients are at the highest risk of death. Clinicians should consider prioritizing some therapies for patients at highest risk of clinical progression because of the optimize resource allocation and to guide management. Prediction models for COVID-19 are quickly entering the COVID-19 literature to support therapeutic choice making at a time when needed.

Yang et al. (17) were reported that APACHE score and SOFA score were higher in died patients than in surviving patients. It was admitted fifty-two critically ill adult patients were with COVID-19 pneumonia in their study. Zou et al. (18) was aimed to investigate the APACHE score as a predictor for survival to facilitate decision-making for treatment in Wuhan. In predicting hospital mortality, APACHE-II score showed better discriminative ability (AUC, 0.966; 0.942-0.990, 95% CI) than SOFA score (AUC, 0.867; 0.808-0.926, 95% CI). APACHE-II demonstrated a sensitivity and specificity of 96% and 86%, respectively in ICU patients. Stephens et al. (19) wrote a letter to the editor for Zou's study (18) and stated that raising questions about the calibration of APACHE-II for COVID-19 patients. They noticed mortality higher than expected compared to relatively low APACHE-II scores. One hundred and sixteen COVID-19 patients admitted to the ICU were retrospectively analyzed in Vandenbrande et al. (20) study. They calculated APACHE-II, APACHE-IV scores and SOFA scores at admission. APACHE-IV had a higher value for AUC than APACHE-II (AUC, 0.67 vs. 0.63). APACHE-IV and APACHE-II have moderate discriminative power whereas the SOFA score had poor discriminative power (AUC: 0.53) in all patients. In another paper, it was used multivariable logistic regression methods to investigate the risk factors associated with in-hospital mortality. It was reported increasing odds of in-hospital mortality associated with higher SOFA score in 191 adult COVID-19 patients (21). In our study, we also reported that higher APACHE-II, SOFA, GCS and 4C mortality scores in non-survivor patients. APACHE-II and SOFA have AUC 0.616 and 0.706 respectively in our ICU paients. APACHE-II and SOFA have same sensitivity such as 78.9%. SOFA score have better AUC data than APACHE-II for predicting mortality in ICU COVID-19 patients.

The ISARIC/WHO 4C mortality score and the Jehi diagnostic model were reported as encouraging prediction models for COVID-19 (5). It was compared the ISARIC/WHO 4C mortality score to the CURB65, CRB65 and quick SOFA scores for to estimate 30-day mortality in patients with variety of respiratory infection in 606 patients. Fifty-three of 606 patients had COVID-19 infection. The ISARIC/WHO 4C mortality score had the highest AUC in COVID-19 patients for predicting mortality with value of 0.83 (22). Yildiz et al. (23) prospectively evaluated 4C mortality score, COVID-GRAM, NEWS2, CURB-65 and compare them for progress of critical disease and poor outcome in a COVID-19 patients. The ISARIC/WHO 4C mortality score, COVID-GRAM, CURB-65 and NLR on admission showed strong predictive accuracy for mortality with an AUC of 0.80, 0.74, 0.74 and 0.76 respectively. 4C mortality score had the highest value for mortality prediction in COVID-19 hospitalized patients. In this model, a total score was calculated. In our study, the highest predictive score was 4C mortality score in our critically ill patients.

Chest CT imaging shows a vital role in the diagnosis and evaluation of COVID-19 patients. The predictive value of high-resolution CT findings was reported in 181 mild-to-moderate and severe COVID-19 patients. It was shown that CT severity score might be a significant predictor of mortality in COVID-19 patients. The major chest CT finding is ground-glass opacity in both lungs, and multiple lobes in COVID-19 patients (24). The CO-RADS assessment scheme allows for the categorization of a chest CT scan. CO-RADS chest CT was greatly accurate for detecting COVID-19 pneumonia. The highest AUC (0.865) and accuracy (86.0%) was reported in the CO-RADS 4/5 group with a specificity of 112/132 (84.9%) and a sensitivity of 60/80 (88.2%) for diagnosing COVID-19 by RT-PCR test as the gold standard. Diagnostic value of CO-RADS on chest CT for the diagnosis of COVID-19 infection using the final clinical diagnosis as the standard of reference also have good result with AUC:

0.902 and accuracy (90.5%) in the CO-RADS 4/5 group (25). In our critically ill patients, CO-RADS was used for predicting of mortality in critically ill COVID-19 patients. CO-RADS was poor in predicting mortality in COVID-19 intensive care patients. In literature, there is no study that CO-RADS used COVID-19 for predicting mortality purposes.

If we were to comment on the mortality prediction of these five scorings used in our study, first, ROC curves studies may reach different values in different studies because of the difference in the patient population and the cut-off value chosen in the statistical method. In our study, CO-RADS did not give a significant result for predicting mortality. Although the most appropriate cut-off value is 5.5 and above, sensitivity and specificity values are quite low. The other four scores gave meaningful results and can be recommended for use mortality prediction. In our study, SOFA and 4C mortality score had the highest rates of accurate determination of mortality with 78.9%, but the probability of accurately determining survival in both was low.

This study has several limitations. It is a single center retrospective study and the study population was small. It was based on data mainly recorded hospital data base systems. Observer bias could be possible for CO-RADS evaluation.

Conclusion

SOFA and the 4C mortality score can be used to triage, guide decisions, and the clinical settings, to analyze early assessment of outcomes at admission. These scores may provide clinicians with a clue to discharge patients with low mortality scores or to manage early in patients whom need extra treatments. Future large studies should be aimed at developing and validating diagnostic and/or prognostic models for COVID-19 in ICU.

Ethics

Ethics Committee Approval: This is a single-center; retrospective cohort study that was analyzed anonymized data. After the Non-Invasive Clinical Researches Ethics Committee of the Pamukkale University this study was performed (no: 60116787-020-14366, date: 02.02.2021).

Informed Consent: Informed consent was waived because of the retrospective design of the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.S., M.K., Mi.K., M.A., F.A., A.Ç., Concept: H.S., Design: H.S., Data Collection and Process: F.S., M.K., Mi.K., M.A., S.K., Analysis or Interpretation: H.S., F.A., Literature Search: H.S., F.S., M.K., Mi.K., M.A., Writing: H.S.

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