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Estimation of biochemical factors affecting survival in intensive care COVID-19 patients undergoing chest CT scoring

A retrospective cross-sectional study

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Abstract

Coronavirus disease 2019 (COVID-19) is a rapidly spreading deadly respiratory disease that emerged in the city of Wuhan in December 2019. As a result of its rapid and widespread transmission, the WHO declared a pandemic on March 11, 2020 and studies evaluating mortality and prognosis in COVID-19 gained importance. The aim of this study was to determine the factors affecting the survival of COVID-19 patients followed up in a tertiary intensive care unit (ICU) and undergoing chest computed tomography (CT) scoring. This retrospective cross-sectional study was conducted with the approval of Uşak University Medical Faculty Ethics Committee between July and September 2020. It included 187 symptomatic patients (67 females, 120 males) with suspected COVID-19 who underwent chest CT scans in the ICU. Demographics, acute physiology and chronic health evaluation (APACHE II), chest CT scores, COVID-19 real-time polymerase chain reaction (RT PCR) results, and laboratory parameters were recorded. SPSS 15.0 for Windows was used for the data analysis. The ages of the patients ranged from 18 to 94 and the mean age was 68.0 ± 13.9 years. The COVID-19 RT PCR test was positive in 86 (46.0%) patients and 110 patients (58.8%) died during the follow-up. ICU stay ($P = .024$) and total invasive mechanical ventilation time ($P < .001$) were longer and blood urea nitrogen (BUN) was higher ($P < .001$) in the nonsurvivors. Patients with an APACHE II score of 23 and above had a 1.12-fold higher mortality rate (95% CI 0.061–0.263). There was no significant difference in total chest CT score between the survivors and nonsurvivors ($P = .210$). Chest CT score was not significantly associated with mortality in COVID-19 patients. Our idea that COVID-19 will cause greater mortality in patients with severe chest CT findings has changed. More studies on COVID-19 are needed to reveal the markers that affect prognosis and mortality in this period when new variants are affecting the world.

Abbreviations: APACHE = acute physiology and chronic health evaluation, BUN = blood urea nitrogen, COVID-19 = coronavirus disease 2019, CT = computed tomography, ICU = intensive care unit, MV = mechanical ventilation, RT PCR = real-time polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, WHO = World Health Organization.

Keywords: chest CT scoring, COVID-19, intensive care unit, pneumonia

1. Introduction

Coronavirus disease 2019 (COVID-19), caused by the new coronavirus severe acute respiratory syndrome coronavirus 2, is a highly contagious respiratory disease that has emerged, causing a large number of deaths and impairing quality of life.[1,2] COVID-19 first appeared in the city of Wuhan in China Hubei province in December 2019.[3] The World Health Organization (WHO) declared a public health emergency and a pandemic on March 11, 2020, after the disease spread rapidly around the world and the disease was seen in all continents and in more than 190 countries.[3]

COVID-19 is a disease with a very variable clinical course that may have a symptomless or mild course and may leave patients needing oxygen support for the rest of their lives and even lead to death. With this disease, the number of presentations to health centers dramatically increased and the capacities of hospitals and intensive care units (ICUs) were put under pressure. Therefore, the management of disease severity is important for prevention of earlier death due to COVID-19 and poor

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prognosis in critical care patients. For this purpose, many studies have explored the factors affecting the course and mortality of the disease. There are studies showing that there is a relationship between advanced age, presence of comorbidity, high c-reactive protein, high D-dimer, lactate dehydrogenase level, procalcitonin level, lymphocyte count, need for mechanical ventilation (MV), chest computed tomography (CT) score, and the course of the disease.[4,5] The aim of our retrospective study was to determine the factors affecting the survival of COVID-19 patients followed up in a tertiary intensive care unit (ICU) and undergoing chest CT scoring.

2. Materials and methods

2.1. Ethical approval

This retrospective cross-sectional study was carried out in Uşak Research and Training Hospital. The study protocol was approved by Uşak University Medical Faculty Local Ethics Committee with the number/date 26.11.20/01.07.2020. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was waived due to the retrospective nature of the study.

2.2. Study design and population

This retrospective cross-sectional study was conducted with the approval of Uşak University Medical Faculty Ethics Committee between July and September 2020. The study included 187 symptomatic patients (67 females, 120 males) with suspected COVID-19 who underwent chest CT scans in the ICU.

The exclusion criteria were as follows:

1. Patients under the age of 18,
2. Pregnant and lactating women,
3. Those with a diagnosis of any malignancy,
4. Patients hospitalized in the ICU for <24 hours,
5. Patients transferred from Uşak University Faculty of Medicine Training and Research Hospital to an external center,
6. Patients with at least 1 value missing in the parameters to be evaluated in the study,
7. Patients who had not had a chest CT scan.

All patients who were older than 18 years of age and were followed up in the intensive care unit for at least 24 hours with the suspicion of symptomatic COVID-19 in the Uşak University Faculty of Medicine Training and Research Hospital between June and September 2020 and who did not meet the exclusion criteria were included.

Patients with symptoms of high fever and respiratory tract infection (cough, shortness of breath, use of accessory respiratory muscles); patients with oxygen saturation in room air below 90%; patients with a respiratory rate above 30; laboratory-tested COVID-19 patients with supporting findings (high C-reactive protein, lymphopenia, high procalcitonin, high D-dimer, etc); patients with bilateral lobular, peripheral localized patchy ground-glass opacities on thorax CT imaging; and patients with positive reverse transcriptase polymerase chain reaction (RT PCR) results and symptomatic COVID-19 were considered patients.[6]

2.3. Data collection

Demographics, COVID-19 RT PCR test results, comorbidities, survival, length of hospital stay, duration of MV, acute physiology and chronic health evaluation (APACHE II) score, chest CT score, the first and last routine blood tests including arterial blood gas analysis, complete blood count, electrolytes, renal-liver function tests, coagulation, and inflammatory parameters were evaluated. A low-dose chest CT device (Toshiba Aquilion 16 CT Scanner, Kyoto, Japan) for imaging COVID-19 patients was used for all assessments.

2.4. Statistical analysis

All statistical calculations were performed with SPSS 15.0 (SPSS for Windows, Chicago, IL, USA). The chi-square test, Student t-test, and multivariate logistic regression analysis were used for analysis of the data. The results were presented as mean ± standard deviation and median (minimum-maximum) for the quantitative data and as frequency (percentage) for the categorical data. In the analyses, $P < .05$ was accepted as statistically significant.

2.5. Chest CT scoring

Chest CT scoring of the patients was performed in the form of semiquantitative CT severity scoring recommended by Pan et al and Francone et al[7,8] The bilateral lungs were divided into 5 regions according to the anatomical structure: left upper lobe, left lower lobe, right upper lobe, right middle lobe, and right lower lobe. The score was calculated according to the severity of each lobe involvement as follows: 0: No involvement, 1: <5% involvement, 2: 5% to 25% involvement, 3: 26% to 50% involvement, 4: 51% to 75% involvement, 5: 75% to 100% involvement. The total chest CT score was calculated by summing the separately calculated scores for the 5 lobes. Accordingly, the lowest score was 0 and the highest score was 25.

Table 1

Demographics and clinical characteristics of the patients.

Parameters	n (%)
Gender	
Male	120 (64.2)
Female	67 (35.8)
Age, y	
Mean ± SD	68.0 ± 13.9
BMI	
<30.0	149 (79.7)
≥30.0	38 (20.3)
Total chest CT scoring	
Mean ± SD	14.89 ± 6.59
IVIG therapy	
(+)	72 (38.5)
(–)	115 (61.5)
Tocilizumab treatment	
(+)	67 (35.8)
(–)	120 (64.2)
Hemofiltration	
(+)	27 (14.4)
(–)	160 (85.6)
Plasma treatment	
(+)	57 (30.5)
(–)	130 (69.5)
COVID-19 RT PCR test results	
Negative	101 (54.0)
Positive	86 (46.0)
Comorbidities	
Hypertension	99 (52.9)
Coronary artery disease	60 (32.1)
Congestive heart failure	37 (19.8)
Chronic obstructive pulmonary disease	68 (36.4)
Diabetes mellitus	65 (34.8)
Chronic renal failure	9 (4.8)
APACHE score	
Mean ± SD	21.79 ± 8.62

APACHE = Acute Physiology and Chronic Health Evaluation, BMI = body mass index, IVIG = intravenous immunoglobulin, RT PCR = reverse transcriptase polymerase chain reaction.

3. Results

While 64.2% (n = 120) of the patients were male, 35.8% (n = 67) were female, and the ages of the patients ranged from 18 to 94, with a mean age of 68.0 ± 13.9 years. The distribution of the study group according to demographics and clinical characteristics is given in Table 1.

The COVID-19 PCR test was positive in 86 patients (46.0%) in the study group, and 110 of the patients (58.8%) died in the ICU follow-up. The mean age of the patients who died during intensive care follow-up was significantly higher than the age of those who survived ($P = .002$). The total chest CT score was 14.89 ± 6.585 points on average. There was no significant difference in total chest CT scores between living and deceased patients ($P > .210$). The length of stay in the ICU of the patients who died during the intensive care follow-up was significantly longer than that of the surviving patients ($P = .024$). The duration of treatment with a mechanical ventilator in patients who died during intensive care follow-up was significantly longer than that of the patients who survived ($P < .001$). The distribution of the survivors and nonsurvivors according to clinical parameters is given in Table 2.

Blood urea nitrogen (BUN) was significantly higher in the nonsurvivor group ($P < .001$). The comparison of the patients in the study group according to their laboratory results is given in Table 3.

Multivariate logistic regression analysis was performed with age, gender, COVID-19 RT PCR results, presence of comorbidity, and APACHE II scores thought to be related to mortality in the study group. Mortality was 1.12 times higher in patients with an APACHE II score of 23 and above compared to patients with an APACHE II score of 22 and below (95% CI 0.061–0.263). The results of the multivariate logistic regression analysis with variables related to mortality in the study group are shown in Table 4.

4. Discussion

In the present study, we examined the variables affecting mortality in patients who were followed up in the ICU due to COVID-19 and whose chest CT score was calculated. Most of the patients followed up in the ICU were men and the mean age was over 68 years. The most common comorbid disease in patients was hypertension. In the literature, it was seen that patients with COVID-19 were mostly advanced age males, and the most common accompanying comorbidity was hypertension.[9–11]

Table 2

Clinical parameters of the survivors and nonsurvivors.

Variables	Nonsurvivors	Survivors	Total	Test value; *P*
Gender				
Female	40 (36.4)	27 (35.1)	67 (35.8)	0.033;.855
Male	70 (58.3)	50 (64.9)	120 (64.2)	
Age, y				
Mean ± SD	70.5 ± 13.3	64.3 ± 13.9	68.0 ± 13.9	3.091;.002
BMI				
<30	90 (81.8)	59 (76.6)	149 (79.7)	0.468;.494
≥30	20 (18.2)	18 (23.4)	38 (20.3)	
Total chest CT score				
Mean ± SD	14.38 ± 6.86	15.61 ± 6.14	14.89 ± 6.585	−1.229;.210
COVID-19 RT PCR				
Negative	54 (49.1)	47 (61.0)	101 (54.0)	2.603;.107
Positive	56 (50.9)	30 (39.0)	86 (46.0)	
Length of stay in ICU				
Mean ± SD	8.65 ± 4.60	7.08 ± 4.75	8.01 ± 4.71	2.276;.024
Total MV duration				
Mean ± SD	8.20 ± 4.99	4.29 ± 3.88	6.59 ± 4.95	5.765; <.001

CT = computed tomography, ICU = intensive care unit, MV = mechanical ventilation, RT PCR = real-time polymerase chain reaction.

Table 3

Comparison of the laboratory findings of the nonsurvivors and survivors.

Variables	Nonsurvivors (mean ± SD)	Survivors (mean ± SD)	Total (mean ± SD)	Test value; *P*
Hemoglobine	12.06 ± 2.34	12.28 ± 2.13	12.15 ± 2.25	−0.662;.509
White blood cell	11.89 ± 13.60	9.85 ± 5.37	11.05 ± 11.01	1.225;.222
Platelet	232.18 ± 114.41	240.44 ± 110.73	235.61 ± 112.66	−0.485;.628
pH	9.06 ± 14.30	8.13 ± 4.40	8.67 ± 11.28	0.541;.589
Lymphocyte	4.78 ± 30.93	8.03 ± 42.97	6.13 ± 36.36	−0.591;.555
C-reactive protein	144.64 ± 82.68	142.43 ± 90.39	143.73 ± 85.54	0.132;.895
D-dimer	2070.24 ± 1460.48	1898.19 ± 1461.26	1996.83 ± 1458.41	0.713;.477
Fibrinogen	536.45 ± 153.91	548.29 ± 158.44	541.21 ± 155.15	−0.395;.694
Activated partial thromboplastin time	16.61 ± 1.78	51.70 ± 6.90	31.77 ± 34.61	−0.530;.597
Prothrombin time	86.57 ± 27.94	90.71 ± 21.45	88.18 ± 25.61	−0.945;.346
Calcium	8.07 ± 0.74	8.24 ± 0.64	8.14 ± 0.70	−1.635;.104
Potassium	4.29 ± 0.89	4.27 ± 0.71	4.28 ± 0.82	0.138;.891
Sodium	138.35 ± 14.12	139.58 ± 4.68	138.87 ± 11.12	−0.739;.461
Creatinine	1.61 ± 1.19	2.43 ± 5.85	1.96 ± 3.93	−1.396;.164
BUN	46.76 ± 33.30	30.99 ± 20.62	40.14 ± 29.65	**3.652; <.001**

BUN = blood urea nitrogen.

Table 4

Multivariate regression analysis results of variables related to mortality.

Variables	OR	95% CI	*P*
Age	0.680	0.332–1.396	.294
Reference: <65 age			
Gender	1.156	0.577–2.317	.682
Reference: female			
COVID-19 RT PCR	0.507	0.256–1.001	.050
Reference: negative			
Comorbidities	1.209	0.509–2.874	.667
Reference: (–)			
APACHE II Score	**1.127**	**0.061–0.263**	**<.001**
Reference: <22			
Constant	6.983		<.001

APACHE = acute physiology and chronic health evaluation, COVID-19 = coronavirus disease, RT PCR = real-time polymerase chain reaction.

The COVID-19 RT PCR result was positive in 86 of the patients in the study, and 56 of these patients died. The mortality rate was significantly higher in elderly patients (>70.5), those who stayed longer in the ICU, and those who had longer MV. In many studies, advanced age has been found to be a risk factor that increases mortality in COVID-19.[12,13] In the study by Alharty et al,[14] the mortality rate was high in patients with advanced age and long ICU stay. However, no correlation was found between the duration of MV and mortality.[14] In the study by Bayrak et al,[15] no significant relationship was found between the length of stay in the ICU and the mortality rate in patients with COVID-19, but mortality was significantly higher in patients with long intubation and MV times.

In our study, the mortality rate was significantly higher in patients with high BUN levels, which is one of the laboratory parameters. Except for BUN, no significant correlation was found between biochemistry, hemogram, blood gas, and coagulation parameters and mortality. In many studies in the literature, high BUN has been found to be associated with increased mortality in COVID-19 patients and this supports our study.[16–18]

The APACHE II score is a frequently used system to predict the mortality rate of patients treated in the ICU. In our study, the mortality rate of patients with an APACHE II score of 23 and above was significantly higher. In many studies in the literature, APACHE II score has been found to be associated with an increased mortality rate.[15,19,20]

Since the start of the COVID-19 pandemic, many patients have presented to our tertiary health care center. We were the only pandemic hospital in our city center. During this time, we realized that the mortality of patients with severe chest CT findings was not as high as we expected, and so we designed the present study. When we reviewed the literature, in some studies, a significant relationship was found between chest CT scoring and the prognosis and mortality of COVID-19 patients.[4,8,15,21,22] However, in our study, the chest CT score was not significantly associated with mortality.

Our study has some limitations. We performed a retrospective analysis with data from a limited number of patients for a period of 3 months. During the current pandemic, it was predicted that a prospective study involving a larger number of patients would take longer and be more complex to complete. Patients with clinical symptoms and laboratory findings or chest CT findings compatible with COVID-19 and whose clinical conditions could not be explained by any other diagnosis were included in the study as symptomatic COVID-19 patients. The inclusion of patients with negative RT PCR results but clinical symptoms and laboratory or chest CT imaging compatible with COVID-19 is also a limitation.

5. Conclusion

There are many situations that are still not understood regarding COVID-19. This disease has caused many deaths all over the world, resulting in life style changes. In this retrospective study we conducted in order to contribute to knowledge of the criteria affecting predictable mortality, advanced age, male gender, and hypertension comorbidity were risk factors for mortality. Patients who received long-term mechanical ventilation therapy and were hospitalized in the ICU had high mortality. Those with higher BUN and APACHE II scores had higher mortality. Moreover, chest CT score was not significantly associated with mortality. Our prejudice that COVID-19 would cause greater mortality in patients with severe chest CT findings was dispelled. At present, when new variants are exerting their effect worldwide, there is a need for more studies on COVID-19.

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Author contributions

Dagtekin G, Can S, Yilmaz H, Yaman E, and Diker S contributed to the analysis of the data; Dal H and Keklik KSE to the data collection; and Dal H, Keklik KSE, and Avcil M to the preliminary studies and the design of the study. All authors contributed to the preparation and revision of the article.

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