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ARAŞTIRMA / RESEARCH

C-reactive protein to albumin ratio is associated with increased risk of mortality in COVID-19 pneumonia patients

C-reaktif protein/albümin oranı COVID-19 pnömonisi olan hastalarda artan mortalite riski ile ilişkilidir

Selen Acehan[1], Müge Gülen[1], Cem Işıkber[1], Adem Kaya[1], Nurdan Unlu[2], Çağdaş İnce[1], Başak Toptaş Fırat[1], Gonca Köksaldı Şahin[1], Hilmi Erdem Sümbül[3], Salim Satar[1]

[1]Adana City Training and Research Hospital, Department of Emergency Medicine, [2]Department of Anesthesiology and Intensive Care, [3]Department of İnternal Medicine, Adana, Turkey

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Abstract

Purpose: The aim of this retrospective observational study is to compare C-reactive protein to albumin ratio and CURB-65 score in the emergency department in terms of predicting mortality in patients over the age of 18 who were hospitalized for COVID-19 pneumonia.
Materials and Methods: The study includes 613 patients hospitalized between March 15 and April 30, 2020 due to COVID-19 pneumonia detected on thorax computed tomography at the emergency department pandemic area. Hospitalized patients were divided into groups according to positive and negative real-time polymerase chain reaction results.
Results: While 73.1% (n: 448) of 613 patients included in the study were hospitalized in the ward, 26.9% (n: 165) were hospitalized in intensive care. 8.6% (n: 53) of the total patients died. In non-survivors patients the mean CURB 65 score was 4±1 (and C-Reactive Protein to Albumin Ratio was 5.6±4.2 Multivariate logistic regression analysis showed that CURB 65 and high C-Reactive Protein to Albumin Ratio are independent risk factors for COVID-19 pneumonia.
Conclusion: The C-reactive protein to albumin ratio is as sensitive as CURB 65 and can guide the clinician in the early detection of patients with poor prognosis COVID-19 pneumonia.
Keywords:. Reactive protein to albumin ratio, COVID-19 pneumonia, CURB 65, emergency department

Öz

Amaç: Bu retrospektif gözlemsel çalışmanın amacı, COVID-19 pnömonisi nedeniyle hastaneye yatırılan 18 yaş üstü hastalarda mortaliteyi öngörme açısından acil serviste bakılan C-reaktif protein/albumin oranı ile CURB-65 skorunun karşılaştırılmasıdır.
Gereç ve Yöntem: Çalışma 15 Mart-30 Nisan 2020 tarihleri arasında acil servis pandemi alanında toraks bilgisayarlı tomografisinde COVID-19 pnömonisi tespit edilerek hastaneye yatırılan 613 hastayı kapsamaktadır. Hastanede yatan hastalar pozitif ve negatif gerçek zamanlı polimeraz zincir reaksiyonu sonuçlarına göre gruplara ayrıldı.
Bulgular: Çalışmaya dahil edilen 613 hastanın %73,1'i (n:448) serviste yatarken, %26,9'u (n:165) yoğun bakımda yatmaktaydı. Toplam hastaların %8,6'sı (n:53) öldü. Ölen hastalarda CURB 65 skoru ortalama 4±1 ve C-reaktif protein/albümin oranı 5.6±4.2 idi.. Çok değişkenli lojistik regresyon analizi, CURB 65 skorunu) ve yüksek C-reaktif protein/albümin oranı olduğunu gösterdi.) COVID-19 pnömonisi için bağımsız risk faktörleri olarak göstermiştir.
Sonuç: C-reaktif protein/albumin oranı, kötü prognozlu COVID-19 pnömonisi olan hastaların erken tespitinde CURB 65 kadar duyarlı olup klinisyene yol gösterebilir.

Anahtar kelimeler: Acil servis, C-reaktif protein/albümin oranı, COVID-19 pnömonisi, CURB 65,

Yazışma Adresi/Address for Correspondence: Dr. Selen Acehan, Adana City Training and Research Hospital, Department of Emergency Medicine, Adana, Turkey E-mail adress: selenacehan@hotmail.com
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INTRODUCTION

Despite the fact that significant advances in global health have taken place, pneumonia is one of the most common infectious diseases requiring hospitalization and is associated with high morbidity and mortality[1,2]. SARS-CoV-2 (COVID-19), the 7th CoV known after SARS-, CoV and MERS-CoV, is the pathogen of the ongoing new pneumonia epidemic that infects humans[3].

The most common symptoms of SARS-CoV-2 during admission are respiratory system complaints such as fever, cough and shortness of breath. As of September 10, 2021, the number of cases of this contagious infection worldwide exceeded 219 million laboratory-confirmed cases, and deaths exceeded 4.5 million. Therefore, early isolation and effective treatment of patients infected with COVID-19 are of great importance in terms of reducing mortality and morbidity.

The CURB-65 (Confusion, Urea, Respiratory Rate) score is a pneumonia severity score developed to decide whether to care patients as outpatients or inpatients[4] and studies have shown that it can also be used to predict mortality[5-8]. In recent studies, the CURB-65 score was found to be significantly higher in deceased COVID-19 patients[9, 10]. Studies have shown that CURB 65 can also help clinicians during the COVID 19 pandemic period, as it has simple evaluation criteria and is easy to use in emergency situations. C-reactive protein (CRP) and albumin are used to predict mortality in critically ill patients because of their ability to demonstrate acute inflammatory conditions[11, 12]. CRP to albumin ratio, which is the ratio of these two laboratory parameters to each other, is a new and useful indicator that has been used in critical patients with sepsis, septic shock and malignancy[13-15].

In this study, it is aimed to compare C-reactive protein to albumin ratio (CAR) with CURB-65 score in predicting mortality in patients hospitalized with COVID-19 pneumonia from the emergency department pandemic area.

MATERIALS AND METHOD

This study was initiated after obtaining the approval of the Republic of Turkey Ministry of Health (2020-04-30T11_00_36.xml) and the local ethics committee (Approval Date: 06/05/2020, Decision Number: 841/56). Designed as a retrospective observational case series, the study included 613 patients transferred from the Tertiary hospital emergency department pandemic area to the ward as pneumonia was detected in Thorax computed tomography (CT), between 15/03/2020 and 30/04/2020. Patients under the age of 18, pregnant women, patients whose files and laboratory data could not be fully accessed, patients whose thorax CT could not be taken and/or whose thorax CT did not have typical pneumonia features were excluded from the study.

Data collection

Demographic characteristics, vital signs, additional diseases, laboratory parameters, Thorax CT reports, CURB 65 score, COVID-19 Real-time polymerase chain reaction (RT-PCR) test results, duration of hospitalization, mechanical ventilator, vasopressor and renal replacement therapy needs and outcome data of the patients included in the study were obtained from patient files and hospital electronic records and data processing system logs. Patients hospitalized in the emergency department with a diagnosis of pneumonia were divided into groups according to positive and negative RT-PCR results. Demographic characteristics, symptoms, vital signs, comorbidities, clinical and laboratory findings were recorded in the data collection form.

The patients included in the study were screened with a 64-channel multi-detector CT scanner Philips Ingenuity Core 128 (Philips Healthcare Eindhoven, The Netherlands, and June 2017). Radiologists (with at least 5 years of experience) interpreted all thorax CT images according to the COVID-19 Reporting and Data System (CO-RADS) classification, without knowing the clinical features and laboratory findings of the patients. The CO-RADS classification created by The Dutch Radiological Society, from 1 (very low) to 5 (very high), is a radiological diagnostic indicator to evaluate the suspicion of COVID-19 pulmonary involvement[16].

CO-RADS 1; implies a very low level of suspicion for pulmonary involvement by COVID-19 based on either normal CT results or CT findings of unequivocal noninfectious origin, CO-RADS 2; implies a low level of suspicion for pulmonary involvement by COVID-19 based on CT findings in the lungs typical of infectious origin that are considered not compatible with COVID-19, CO-RADS 3; implies equivocal findings for pulmonary involvement of COVID-19 based on CT features that can also be found in other viral pneumonias or

noninfectious causes, CO-RADS 4; implies a high level of suspicion for pulmonary involvement by COVID-19 based on CT findings that are typical for COVID-19 but also show some overlap with other (viral) pneumonias, CO-RADS 5; implies a very high level of suspicion for pulmonary involvement by COVID-19 based on typical CT findings[17]. Patients whose thorax CT findings were classified as CO-RADS 4 and 5 were included in the study.

Nasopharyngeal and oropharyngeal swab samples were taken from all patients for the diagnosis of COVID-19 in the emergency department. Nucleic acid isolation from nasopharyngeal and oropharyngeal swab samples was conducted using Bio-Speedy® Purification Kit (Bioeksen, Istanbul, Turkey).

Hemogram and biochemical parameters (Lactate dehydrogenase (LDH), Creatinine, Ferritin, Fibrinogen, D-dimer, Hs-Tn I, CRP, Albumin, and Procalcitonin (PCT)) were taken from all patients in the emergency department. In addition, CRP to albumin ratio (CAR), Neutrophil to Lymphocyte ratio (NLR), Fibrinogen to albumin ratio (FAR) and Urea to albumin ratio (UAR), which were created with the data obtained from laboratory parameters, were calculated mathematically.

CURB 65 was also calculated using the patients' pneumonia severity scores and recorded on the data collection form. The CURB-65 takes into account five risk factors: confusion or decreased consciousness, blood urea nitrogen >7 mmol/L, respiratory frequency ⩾30/min, systolic blood pressure <90 mmHg or diastolic blood pressure ⩽60 mmHg, and age ⩾65 years.

Statistical analysis

Data were expressed as mean ± SD for continuous variables and as percentages for categorical variables. The normal distribution of the variables was measured with the Kolmogorov-Smirnov test. The Student-t test was used to compare continuous variables with normal distribution, and the Mann-Whitney U-test was used to compare samples without normal distribution. Chi-square ($\chi 2$) test was used to compare categorical variables. Fisher's exact test was used when the chi-square ($\chi 2$) test conditions were not met. Kendall's tau_b and Spearmann correlation analysis were used for correlation analysis. The power of CURB-65 and laboratory parameters (CAR, NLR, FAR, UAR) to predict mortality was measured through ROC analysis. Sensitivity and specificity were calculated by finding a cut-off point that would have a high diagnostic accuracy for the parameters. Binary logistic regression analysis was applied using gender, age, comorbidities, CURB-65 and all laboratory parameters to identify predictors of mortality. As a result of the analysis, the parameters with Odds ratio above 1 are given in the table. SPSS 22.0 (SPSS 22.0 for Windows, Chicago, IL, USA) and MedCalc programs were used in the analysis. A p value of <0.05 was considered statistically significant for all analyses.

RESULTS

A total of 27364 patients were admitted to the emergency department during the study period. Throughout the study, 2518 patients were hospitalized for various reasons. 43.3% (n: 1090) of the hospitalized patients were hospitalized with a preliminary diagnosis of COVID-19 pneumonia. The study included 613 patients in whose Thoraks CT typical pneumonia findings (Table 1) was detected in the Tertiary hospital emergency department pandemic area and therefore hospitalized with the diagnosis of COVID-19 pneumonia. Of the 477 patients who were not included in the study, 211 did not have undergo Thorax CT procedure, 15 patients did not have typical pneumonia, 196 patients' laboratory data could not be accessed and 16 were pregnant.

Hospitalized patients were divided into groups according to positive and negative RT-PCR results. Group 1 consisted of Suspected COVID-19 patients with typical pneumonia features on Thorax CT and negative RT-PCR test and Group 2 consisted of confirmed COVID-19 patients with typical pneumonia features on Thorax CT with positive RT-PCR test. Group 1 and Group 2 constituted 66.4% (n: 407) and 33.6% (n: 206) of the total patients respectively (Table 1).

41.6% (n: 255) of the total patients were female and 58.4% (n: 358) were male. While 68% (n: 417) of the patients had at least one accompanying comorbidity, 39.3% (n: 241) had hypertension (HT) at most, 27.4% (n: 168) had coronary artery disease (CAD), 21.5% (n: 132) had diabetes mellitus (DM). The presence of accompanying comorbidity was found to be statistically significant in terms of mortality ($p<0.001$) (Table 1).

Table 1. Demographics and clinical presentation in COVID-19 pneumonia patients

	Total (n: 613)	**Grup 1 (n:407 %66.4)**	**Grup2 (n:206 %33.6)**	**p**	**Survıvor 560 (%91.4)**	**Non Survıvor 53 (%8.6)**	**p**
Sex							
Female	255 (41.6%)	170 (41.8%)	85 (41.3%)		230 (41.1%)	25 (47.2%)	0.387
Male	358 (58.4%)	237 (58.2%)	121 (58.7%)	0.931	330 (58.9%)	28 (52.8%)	
Age (year)	59.04±19.5	62±18.3	53.3±20.4	< 0.001	57.8±19.4	71.8±16.4	< 0.001
Fever (°C)	37.1±0.8	37.03±0.8	37.01±0.7	0.164	37.1±0.7	37.2±0.9	0.198
Pulse (beats/min)	95.3±22.3	93.9±21.1	98.1±24.4	0.035	94.01±21.8	108.9±23.9	< 0.001
MAP (mmHg)	86±19.3	85.9±18.5	86.1±20.8	0.884	87.6±18.7	68.3±16.8	< 0.001
Respiratory Rate (beats/min)	25.9±6.6	25.7±6.5	26.4±6.9	0.201	25.3±6.5	32.4±4.3	< 0.001
Saturation (%)	93.3±5.9	93.4±5.8	93.1±6.2	0.618	94.1±5.3	84.6±5.4	< 0.001
Accompanying Comorbidity	417 (68%)	311 (76.4%)	106 (51.5%)	< 0.001	371 (66.3%)	46 (86.8%)	< 0.001
HT	241 (39.3%)	162 (40.0%)	79 (38.3%)	0,793	227 (40.5%)	14 (26.4%)	0.055
DM	132 (21.5%)	108 (26.5%)	24 (11.7%)	< 0.001	119 (21.3%)	13 (24.5%)	0.600
CAD	168 (27.4%)	126 (31.0%)	42 (20.4%)	0,005	150 (26.8%)	18 (34%)	0,263
COPD	89 (14.5%)	66 (16.2%)	23 (11.2%)	0.114	82 (14.6%)	7 (13.2%)	1.000
CVD	55 (9%)	38 (9.3%)	17 (8.3%)	0,765	49 (8.8%)	6 (11.3%)	0,459
CKD	55 (9%)	34 (8.4%)	21 (10.2%)	0,457	49 (8.8%)	6 (11.3%)	0,459
Cancer	50 (8.2%)	40 (9.8%)	10 (4.9%)	0,041	39 (7%)	11 (20.8%)	0,002
Suspicious contact	156 (25.4%)	57 (14%)	99 (48.1%)	< 0.001	153 (27.3%)	3 (5.7%)	< 0.001
Fever	192 (31.3%)	123 (30.2%)	69 (33.5%)	0.409	176 (31.4%)	16 (30.2%)	1.000
Dry cough	326 (53.2%)	214 (52.6%)	112 (54.4%)	0.732	308 (55%)	18 (34%)	0.004
Dyspnoea	344 (56.1%)	236 (58%)	108 (52.4%)	0.197	295 (52.7%)	49 (92.5%)	< 0.001
Chest pain	61 (10%)	45 (11.1%)	16 (7.8%)	0.253	55 (9.8%)	6 (11.3%)	0.637
Abdominal pain	70 (11.4%)	45 (11.1%)	25 (12.1%)	0.689	66 (11.8%)	4 (7.5%)	0.498
Nausea - vomiting	150 (25.5%)	98 (24.1%)	52 (25.2%)	0.766	138 (24.6%)	12 (22.6%)	0.868
Symptoms onset to the first visit,(day)	3.8±2.0	3.6±1.9	4.2±2.1	<0.001	3.7±1.9	4.3±2.1	0.032
Emergency Service Outcome							
Service	448 (73.1%)	301 (74%)	147 (71.4%)	0.501	442 (78.9%)	6 (11.3%)	<0.001
İntensive Care Unit	165 (26.9%)	106 (26%)	59 (28.6%)		118 (21.1%)	17 (88.7%)	
Mortality	53 (8.6%)	40 (9.8%)	13 (6.3%)	0.171			
Vasopressor Requirement	161 (26.4%)	84 (20.7%)	77 (37.4%)	<0.001	121 (21.6%)	40 (75.5%)	<0.001
MV Requirement	148 (24.2%)	75 (18.5%)	73 (35.4%)	<0.001	102 (18.2%)	46 (86.8%)	<0.001
RRT	69 (11.3%)	43 (10.6%)	26 (12.6%)	0.499	60 (10.7%)	9 (17%)	0.173
NIMV	154 (25.1%)	101 (24.8%)	53 (25.7 %)	0.844	132 (23.6%)	22 (41.5 %)	0.007
Lenght of Hospital Stay	9.5±9.6	9.1±9.3	10.1±10.1	0.244	9.5±9.3	9.1±12.1	0.741
GGO	351 (57.3%)	227 (55.8%)	124 (60.2%)	0.300	329 (55.8%)	22 (41.5%)	0.020
Consolidation	133 (21.8%)	104 (25.7%)	29 (14.1%)	0.001	119 (21.3%)	14 (26.4%)	0.385
GGO + Consolidation	227 (37.2%)	137 (33.8%)	90 (43.7%)	0.021	206 (36.8%)	21 (39.6%)	0.766
Wall thickening	17 (2.8%)	11 (2.7%)	6 (2.9%)	1.000	17 (3%)	0 (0%)	0.385
Traction bronchiectasis	12 (2%)	6 (1.5%)	6 (2.9%)	0.233	12 (2.1%)	0 (0%)	0.613

Group 1: Suspected COVID 19 patients with typical pneumonia features on Thorax CT and negative RT-PCR test
Group 2: Confirmed COVID 19 patients with typical pneumonia on Thorax CT with positive RT-PCR test.
MAP: Mean arterial pressure HT: Hypertension, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease, CVD: Cerebrovascular Disease CKD; Chronic Kidney Disease, RT-PCR; Real-time polymerase chain reaction, MV: Mechanical Ventilator, RRT: Renal Replacement Therapy, NIMV; Non-Invazive Mechanical Ventilator, GGO; Ground glass opacity

When the admission symptoms of the patients were examined, there was no statistically significant difference between the groups. Nevertheless, the presence of dry cough (p=0.004) and dyspnea (p<0.001) were found to be statistically significant in terms of mortality (Table 1).

Demographic data and vital parameters of COVID-19 pneumonia patients are presented in Table 1. While 73.1% (n: 488) of the patients were admitted to the ward, 26.9% (n: 165) were admitted to the intensive care unit. The mean number of hospitalization days of the patients was determined to

be 10.7±12.1 days. 8.6% (n: 53) of our total patients died during their follow-up and treatment periods. When the groups were compared in terms of mortality, no statistically significant difference was found (p=0.171). Demographic data and vital parameters of pneumonia patients are presented in Table 1. The mean CURB 65 score was 1.8±1.7 in all of the patients. There was no statistically significant difference between the groups in terms of CURB 65 score (p=0.360). When the relationship between CURB 65 and mortality was examined, the CURB-65 score was 1.6±1.6 on average in survivor patients, while it was 4±1 on average in non-survivor patients (p <0.001) (Table 2).

Table 2. Score and laboratory parameters in COVID 19 pneumonia patients

	Total (n: 613)	Grup 1 (n:407 %66.4)	Grup2 (n:206 %33.6)	p	Survıvor 560 (%91.4)	Non Survıvor 53 (%8.6)	p
CURB 65	1.8±1.7	1.8±1.7	1.7±1.9	0.378	1.6±1.6	4±1	< 0.001
LDH (5-247 U/L)	359.7±404.3	365.8±469	347.9±228.4	0.605	340.9±361.1	558.5±691.6	0.028
Creatinine (0.51-0.95 mg/dl)	1.6±2.0	1.6±2.0	1.6±2,1	0.982	1.6±2.1	2.1±1.8	0.082
Ferritin (11-307 µg/L)	416±715.1	402.4±699.3	442.9±746.4	0508	308.8±475.7	1548.9±1467.6	< 0.001
Leukocyte (3.8-11.8 10^3/µl)	7.9±3.1	8.02±3.2	7.61±2.9	0.136	7.8±3.1	8.8±3.3	0.025
Neutrophils (1.9-8.2 10^3/µl)	6.8±2.4	6.9±2.5	6.6±2.2	0.159	6.7±2.4	8.1±2.6	< 0.001
Lymphocytes (1.1-3.1 10^3/µl)	1.2±0.7	1.24±0.7	1.2±0.5	0.058	1.3±0.7	0.8±0.4	< 0.001
Fibrinogen (180-350 mg/dl)	359.1±234.7	358.3±227.1	360.8±249.4	0.903	351.3±231.6	441.8±252.5	0.007
D-Dimer (0-630 µg/L)	2575.9±4644.2	2759.4±4948.7	2213.4±3961.3	0.169	2259.1±4277.7	5922.8±6681.5	< 0.001
Hs-Tn I (0-16 ng/L)	206.3±1283.5	249.6±1472	120.6±784.9	0.158	178.6±1201.3	498.4±1944.6	0.245
CRP (0-5 mg /l)	70.9±76.8	72.02±82	68.7±65.7	0.612	63.9±70.9	145.2±96.6	< 0.001
Albumin (35-55 g/l)	33.6±5.4	33.3±5.6	34.1±5,1	0.091	34.04±5.2	28.7±5,7	< 0.001
PCT (0-0.065 µg/L)	0.36±1	0.34±0.54	0.39±1.5	0.617	0.32±1	0.84±1.1	0.001
CAR	2.4±2.9	2.4±3.1	2.3±2.6	0.582	2.1±2.6	5.6±4.2	< 0.001
NLR	8.2±8.9	8.7±10.1	7.3±5.7	0.037	7.8±8.8	12.8±8.7	< 0.001
FAR	11.1±7.8	11.2±7.7	11±8.1	0.781	10.7±7.5	15.8±8.9	< 0.001
UAR	1.9±1.8	2±1.9	1.7±1.7	0.153	1.7±1.6	3.6±3	< 0.001

Group 1: Suspected COVID 19 patients with typical pneumonia features on Thorax CT and negative RT-PCR test
Group 2: Confirmed COVID 19 patients with typical pneumonia features on Thorax CT with positive RT-PCR test.
CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age≥65, LDH; Lactate dehydrogenase, hs-Tn I; High Sensitivity Troponin I, CRP; C-reaktive protein, PCT; Procalcitonin, CAR: CRP/Albumin Ratio, NLR; Neutrophils/Lymphocytes Ratio, FAR: FibrinoJen/Albumin Ratio; UAR: Ure/Albumin Ratio

Table 3. ROC analysis of the mortality prediction of CURB 65 and laboratory parameters in COVID-19 pneumonia patients

	AUC (%95 CI)	Cut off	p	Sensitivity (%)	Specifity (%)
CURB65	0.869 (0.832-0.905)	2.5	<0.001	96.2	70.2
CAR	0.790 (0.728-0.852)	2.1561	<0.001	73.6	68.4
UAR	0.750 (0.683-0.816)	1.5622	<0.001	73.6	67
NLR	0.743 (0.686-0.801)	7.7321	<0.001	67,9	67.5
FAR	0.668 (0.594-0.742)	11.1078	<0.001	62.3	57.5

AUC: Areas under the curve, SE: Standart Error, CI: Confidence Interval, CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age≥65, CAR: CRP/Albumin Ratio, NLR; Neutrophils/Lymphocytes Ratio, FAR: Fibrinojen/Albumin Ratio; UAR: Ure/Albumin Ratio

When the laboratory parameters of the patients were examined, it was determined that LDH, Ferritin, D-dimer, Troponin, Fibrinogen, CRP and PCT values were high, while lymphocyte and albumin values were low. There was no statistically significant difference between the groups in terms of laboratory

parameters. All laboratory parameters except for troponin (p=0.245) and creatinine (p=0.082) were significantly different in survivor and non-survivor groups. While CRP/Albumin ratio (CAR) was 2.1±2.6 on average in survivor patients, it was 5.6±4.2 on average in non-survivor patients (p <0.001). Scores and Laboratory Parameters in COVID-19 pneumonia patients are presented in Table 2.

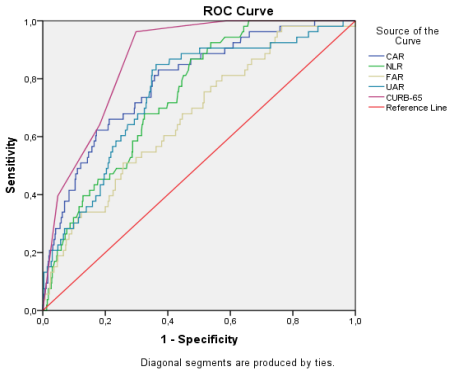

Figure 1. The graphic of ROC analysis performed to determine the mortality predictive characteristics of CURB 65 and laboratory parameters in COVID-19 pneumonia patients

CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age≥65, CAR: CRP/Albumin Ratio, NLR; Neutrophils/Lymphocytes Ratio, FAR: Fibrinojen/Albumin Ratio; UAR: Ure/Albumin Ratio

The ability of CAR, NLR, FAR, UAR and CURB 65 to predict in-hospital mortality was assessed using receiver operating characteristic (ROC) curves. The graphic of ROC analysis performed to determine the mortality predictive characteristics of CURB-65, CAR, NLR, FAR and UAR in the whole patients has been presented in Figure 1. When the ROC analysis performed to determine the mortality predictive characteristics of the scores was examined, it was determined that the AUC value of the CURB-65 (AUC: 0.869 95% CI 0.832-0.905, p <0.001) was the highest. When the cut-off value of CURB 65 was taken as 2.5 to predict mortality, the sensitivity was calculated as 96.2% and the specificity was calculated as 70.2%. CAR (AUC: 0.790, 95% CI 0.728-0.852, p <0.001) was found to be the highest of the laboratory parameters (Table 3).

Binary logistic regression analysis was applied using gender, age, comorbidities, CURB-65, all laboratory parameters determined in our study to determine the effective predictors of mortality. As a result of the analysis, the parameters with Odds ratio above 1 are given in the table. The Analysis indicated a 3.4-fold increased risk for mortality for each unit increase in CURB-65 value in COVID-19 pneumonia patients (OR = 3.416, 95% CI: 2.337-4.995, p <0.001) and 1.2-fold increased risk for mortality for each unit increase in CAR value (OR = 1.217, % 95 CI: 1.078-1.373, p <0.001) (Table 4).

Table 4. Binary logistic regression analysis for mortality

Variables	Odds Ratio	95% Confidence Interval	p
CURB-65	3.416	2.337-4.995	0.000
CAR	1.217	1.078-1.373	0.001
NLR	1.018	0.990-1.047	0.207
FAR	1.005	0.956-1.057	0.843

Binary Logistic Regression by Mortality; Variable(s): gender, age, comorbidities, CURB-65, All Laboratory Parameters
CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age≥65, CAR: CRP/Albumin Ratio, NLR; Neutrophils/Lymphocytes Ratio, FAR: Fibrinojen/Albumin Ratio;

DISCUSSION

In this study, we compared the predictive power of mortality the CRP to albumin ratio (CAR) with the CURB 65 score in patients hospitalized for COVID-19 pneumonia. In the analytical evaluation for mortality, the AUC of CURB 65 was 0.869, the AUC of CAR was 0.790. According to our study data, a cutoff value of CAR above 2.2 may be an indicator of mortality in patients diagnosed with COVID 19 pneumonia in the emergency department. Each unit increase in CAR increases mortality 1.2 times.

The use of scoring systems facilitates decision making as regards the location of treatment and assessment of the risk of death for pneumonia patients. Belated admission to the intensive care unit increases the mortality rate in pneumonia patients[18]. Community-acquired pneumonia guidelines recommend that

patients with CURB-65 scores of 0 and 1 be treated as an outpatient, those with a CURB-65 score of 2 should be hospitalized, and patients with a CURB-65 score of 3 or above should be evaluated for ICU admission[19]. In our study, 51.4% of the patients had a CURB 65 score of 0 and 1, 13.1% had a CURB 65 score of 2, and 35.6% had a CURB 65 score of 3 and above. Among the patients with a CURB 65 score of 0 or 1, we did not have any mortal patients. Since our study covered the first period of the pandemic period, patients with pneumonia were monitored and treated in hospital in isolation due to the COVID-19 epidemic, even if their CURB 65 score was 0 or 1. When the ROC analysis conducted to determine the predictive features of mortality was examined, it was determined that the AUC value of CURB-65 (AUC: 0.869 95% CI 0.832-0.905, p <0.001) was the highest. According to the study data, it was seen that the CURB-65 score calculated in the emergency department strongly predicted the mortality of pneumonia patients in the COVID-19 pandemic.

As reported in recent publications, ground-glass opacities on Thorax CT including multifocal irregular consolidation and/or peripherally distributed interstitial changes appear as typical radiographic features in almost all COVID-19 patients[20, 21]. These changes seen on Thorax CT were also observed in patients who had negative RT-PCR results but their clinical symptoms matched with COVID-19 Pneumonia. Small-scale studies have shown that the current RT-PCR test has limited sensitivity and that Thorax CT can reveal pulmonary changes consistent with COVID-19 even in patients with initial negative RT-PCR results[22, 23]. Patients with thorax CT compatible with typical COVID-19 pneumonia (CO-RADS 4 and 5) were included in the study. There was no statistically significant difference between the patients with negative RT-PCR test and those with positive RT-PCR test in terms of laboratory parameters. Laboratory parameters were consistent with COVID-19 pneumonia in both groups. Our data suggest that if there are clinical symptoms and thorax CT imaging features during the pandemic period, these patients should be isolated and treated in the early period, even if the RT-PCR test is negative.

The clinical features of COVID-19, which emerges with pneumonia symptoms, are still under investigation. COVID-19 is a systemic disease and the severity of the disease may be associated with the emergence of "cytokine storm syndrome" triggered by increased inflammatory markers [C-reactive protein (CRP), Procalcitonin (PCT), Neutrophil] [24]. It has been shown that increased serum ferritin, D-dimer, troponin I and lactate dehydrogenase (LDH) and lymphopenia are associated with poor prognosis and increased mortality[25-28]. In a meta-analysis, it was stated that CRP concentrations were high in patients who died of COVID-19 and that CRP could be used to assess severity of the disease[29]. It has been reported that COVID 19 patients with low Albumin levels have a higher risk of mortality[30, 31]. The patients in our study had low lymphocyte and albumin levels and high D-dimer, Fibrinogen, Ferritin, CRP and LDH levels, which were statistically significant in terms of mortality.

Recently, many simple inflammatory markers have been used as systemic inflammation markers to predict mortality in pneumonia patients[32-34]. In this study, we calculated the NLR, CAR, UAR and FAR values mathematically by using the emergency department laboratory parameters of the patients at the first admission and compared them with the outcomes of pneumonia patients during the pandemic. It is thought that the inflammatory cytokine storm may be associated with the progression of COVID-19[35-37]. CRP is an acute phase protein synthesized from hepatocytes in inflammatory conditions[38, 39]. Albumin is used as a negative acute phase reactant as a result of increased catabolism, inflammation, and decreased hepatic synthesis of the cytokine TNF-α[40]. Therefore, CRP to albumin ratio (CAR) can be considered as an important and sensitive predictor of systemic inflammatory response. High CAR has started to be used as a mortality indicator in new studies conducted in ICU inpatients[13, 14, 41, 42]. In study on COVID patients, Wang et al. found CAR to be associated with the severity of the COVID-19 disease [43].

In studies conducted as regards pneumonia patients before the pandemic, it was found that high Neutrophil to lymphocyte ratio (NLR) predicted mortality[44, 45] and admission to intensive care unit[46]. It has been stated that high NLR may be an independent prognostic biomarker that determines the severity of pneumonia in COVID-19 patients[47]. In another study, it was shown that severe COVID-19 cases tended to have high NLR[48]. Fibrinogen to albumin ratio (FAR)[49-51] and Urea to albumin ratio (UAR)[52-54] were studied in community-acquired pneumonia patients in some previous studies, and high FAR and UAR values were found to be

associated with mortality. In a study conducted in COVID 19 patients, increased UAR ratio[55] and increased FAR[56] were associated with increased mortality risk. In our study, inflammatory biomarkers (CAR, NLR, FAR, and UAR) were found to have a statistically significant relationship with mortality while the AUC value of CAR was the highest in the ROC analysis for mortality. When compared with NLR, FAR and UAR according to the study data, CAR (OR=1.217, 95% CI: 1.078-1.373, p <0.001) was observed as an independent risk factor for mortality in pneumonia patients. The fact that our study was single-centered and retrospective may be a limitation, as drawing out generalizations for all patients through the findings of this study conducted in a single hospital may cause misconceptions.

In conclusion ıf there are clinical symptoms, epidemiological features and Thorax CT imaging features of viral pneumonia compatible with COVID-19 infection, these patients should be isolated and treated in the early period, even if their RT-PCR tests are negative. Since the emergency departments have been rather busy recently, high CRP to albumin ratio (CAR) can identify COVID-19 pneumonia patients with poor prognosis during the pandemic, ensuring rapid isolation and effective treatment.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SA, MG, SS, NU, AK, CI, Çİ, HES; Veri toplama: SA, BTF, GKS, Çİ, CI, AK; Veri analizi ve yorumlama: SA, SS, MG, AC, HES, NU; Yazı taslağı: SA, MG, CI, AK, NU, Çİ, BTF, GKS, HES, SS; İçeriğin eleştirel incelenmesi: SA, MG, SS, HES; Son onay ve sorumluluk: SA, MG, CI, AK, NU, Çİ, BTF, GKŞ, HES, SS; Teknik ve malzeme desteği: SA, SS, BTF, GKS, Çİ, AK; Süpervizyon: SA, SS, HES, CI, NU; Fon sağlama (mevcut ise): yok.
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