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ARAŞTIRMA / RESEARCH

COVID-19'da hastane içi mortaliteyi tahmin etmede enflamatuvar temelli parametrelerin ve MELD-XI skorunun 4C mortalite skoru ile karşılaştırılması

Comparison of inflammation-based parameters and MELD-XI score with 4C mortality score in predicting in-hospital mortality in COVID-19

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Abstract

Purpose: In this study, we compared the roles of inflammatory parameters such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), C-reactive protein/lymphocyte ratio (CLR), monocyte/lymphocyte ratio (MLR), neutrophil/platelet ratio (NPR), neutrophil/monocyte ratio (NMR), CRP/albumin ratio (CAR), BUN/albumin ratio (BAR), MELD-XI score and 4C mortality score in predicting in-hospital mortality risk in COVID-19.

Materials and Methods: A total of 117 patients over 18 years old with a PCR-confirmed diagnosis of COVID-19 between June 2020 and February 2021 were retrospectively included. The roles of parameters for independently predicting in-hospital mortality were determined and compared with each other using appropriate statistical methods.

Results: Age, chronic kidney disease, diabetes mellitus, acute kidney injury, and length of hospital stay, urea, creatinine, LDH, AST, ferritin, D-dimer, CRP, albumin, Hb, CLR, BAR, CAR, MELD-XI score, and 4C mortality score were significantly correlated to in-hospital mortality. However, only the 4C mortality score and AST independently predicted in-hospital mortality in COVID-19 [OR 2.08 (%95 CI 1.06-2.36), for 4C mortality score, and OR 1.05 (%95 CI 1.00-1.10), for AST].

Conclusion: Unlike other mortality-related inflammatory parameters, the 4C mortality score and AST were independent and strong predictors of mortality in hospitalized COVID-19 patients.

Keywords:. AST, COVID-19, inflammatory parameters, 4C mortality score, MELD-XI score

Öz

Amaç: Bu çalışmada nötrofil/lenfosit oranı (NLR), monosit/lenfosit oranı (MLR), trombosit/lenfosit oranı (PLR) ve C-reaktif protein/lenfosit oranı (CLR), nötrofil /trombosit oranı (NPR), nötrofil/monosit oranı (NMR), CRP/albümin oranı (CAR), BUN/albümin oranı (BAR), MELD-XI skoru gibi enflamatuvar parametrelerin ve 4C mortalite skorunun COVID-19 tanısı olanlarda hastane içi mortalite riskini öngörmedeki rollerini karşılaştırdık.

Gereç ve Yöntem: Haziran 2020 ile Şubat 2021 arasında PCR ile COVID-19 tanısı doğrulanan 18 yaşından büyük toplam 117 hasta, geriye dönük olarak çalışmaya dahil edildi. Hastane içi ölümle ilişkili parametrelerin mortaliteyi bağımsız predikte etmedeki rolleri ve bunların birbirileriyle karşılaştırılmaları için uygun istatistiksel yöntemler yapıldı.

Bulgular: Yaş, diyabetes mellitus, kronik böbrek hastalığı, akut böbrek hasarı ve hastanede yatış süresi, üre, kreatinin, LDH, AST, ferritin, D-dimer, CRP, albümin, Hb, CLR, BAR, CAR, MELD-XI skoru ve 4C mortalite skoru hastane içi mortalite ile anlamlı olarak ilişkili bulundu. Bununla birlikte, sadece 4C mortalite skoru ve AST, COVID-19'da hastane içi mortalitenin bağımsız öngörücüleriydi [4C mortalite skoru için OR 2.08 (%95 GA 1.06-2.36; ve AST için OR 1.05 (%95 GA 1.00- 1.10]..

Sonuç: 4C mortalite skoru ve AST, hastaneye yatırılan COVID-19 hastalarında mortalite ile ilişkili diğer enflamatuvar parametrelerden farklı olarak aynı zamanda mortalitenin bağımsız ve güçlü öngörücüleridir.

Anahtar kelimeler: AST, COVID-19, enflamatuvar parametreler, 4C mortalite skoru, MELD-XI skoru

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INTRODUCTION

COVID-19 disease, caused by the SARS-CoV-2 virus and new variant strains, continues to be an important public health problem, leading to critical illness and death. From the first day of the pandemic to 2021 December 29, it caused 281,881,270 cases and 5,411,759 deaths[1]. Several clinical presentations ranging from mild upper respiratory tract infection to severe pneumonia, myocarditis, heart failure, severe respiratory failure, multiorgan failure, and even death can be insen during the course of the disease. While rapid diagnosis and treatment are vital in COVID-19, a quick analysis of prognostic risk factors in terms of disease severity and death is also important, considering the rapid spread and fatality rate of the virus.

The SARS-CoV-2 virus has variable effects on the cellular and humoral immune systems, resulting in severe inflammatory responses and deterioration of immune function. Therefore, inflammatory biomarkers can be beneficial for predicting mortality and other adverse outcomes in COVID-19. Recent studies have suggested that many biomarkers such as albumin, creatinine, high-sensitive cardiac troponin I (hs-cTnI), C-reactive protein (CRP), aspartate aminotransferase (AST), total bilirubin, lactate dehydrogenase (LDH), total bilirubin, neutrophil count, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), neutrophil/platelet ratio (NPR), neutrophil/monocyte ratio (NMR), monocyte/lymphocyte ratio (MLR), C-reactive protein/lymphocyte ratio (CLR), BUN/albumin ratio (BAR) are related to COVID-19 disease severity and mortality. Besides, age, albumin, NLR, CLR, BAR, low pulse arterial saturation, severe lymphopenia, procalcitonin, LDH obtained at admission have been shown to independently predict mortality or adverse outcomes in COVID-19[2-10]. Moreover, in one of the recent studies, the 4C mortality score was developed to predict the prognosis and risk associated with COVID-19. The 4C mortality score uses age, gender, number of comorbidities, respiratory rate per minute, peripheral oxygen saturation value, Glasgow Coma Scale score, urea, and CRP[11]. However, the MELD-XI score is based on blood total bilirubin level and albumin level and can be used to predict prognosis in patients with acute heart failure, critical illness, or inflammatory diseases such as infective endocarditis, end-stage heart failure, or myocardial infarction[12-16]. Since COVID-19 is a complex pro-inflammatory disease process, the MELD-XI score can help predict the prognosis of COVID-19. In our study, we hypothesized that the MELD-XI score, along with other inflammatory parameters, could predict short-term mortality in COVID-19 patients. Thus, we aimed to compare basic inflammatory parameters and the MELD-XI score with the 4C mortality score a previously validated mortality score for COVID-19, in predicting in-hospital mortality in hospitalized COVID-19 patients.

MATERIALS AND METHODS

Study population

We enrolled 228 COVID-19 patients with PCR positivity and/or CT signs plus the clinical features of the disease who were treated in Başkent University Konya Hospital between June 2020 and February 2021. Only 117 patients over the age of 18 were deemed eligible for the study after excluding patients with missing data for calculating the risk modalities and biomarkers, those with cancer actively treated with chemotherapy or radiotherapy, those using immunosuppressive therapy for any disorder, those with autoimmune diseases, and those who were transferred to other centers on the day of admission.

All patients included in the study were followed up in the COVID-19 ward, but those whose clinical signs and symptoms worsened in the regular ward were transferred to the intensive care unit. The treatment protocols of the COVID-19 patients were tailored by the hospital's infectious diseases and chest diseases departments. While 87 survived patients were PCR positive, 92 survived patients had positive CT signs of the disease. On the other hand, 15 of 16 deceased patients had a CT sign, while 14 them were PCR-positive.

This study complied with the Declaration of Helsinki and was approved by Başkent University Institutional Review Board (Project no: KA21/288) approval date: 17/11/2021; No: 21/152.) No patient informed consent was required because the study was retrospective and the data were completely anonymous.

Clinical characteristics and laboratory parameters

This study was conducted at Başkent University Konya Hospital. All data, including demographic features, preexisting comorbidities, laboratory

findings, chest-computed tomography results, and length of hospital stay, were obtained from the hospital's data automation system and written medical records.

Admission laboratory results including albumin, CRP, LDH, AST, alanine aminotransferase (ALT), total bilirubin, urea, creatinine, sodium, potassium, D-dimer, ferritin, and complete blood count were recorded before the start of the treatment. All inflammatory biomarkers, the 4C mortality score, and MELD-XI score were calculated by the same physician from the admission laboratory results. The 4C mortality score is a risk scoring system developed to predict in-hospital mortality in COVID-19 patients and is calculated using patient age, gender, respiratory rate, Glasgow coma score, pulse oxygen saturation level, number of comorbid diseases, BUN, and CRP levels [11].

The 4C mortality score is calculated using the follows: 1) age (0 points if <50 years old, 2 points if 50-59 years old, 4 points if 60-69 years old, 6 points if 70-79 years old, 7 points if >79 years old); 2) Gender (0 point if female, 1 point if male); 3) Number of comorbidities (chronic cardiac disease, chronic respiratory disease (excluding asthma), chronic renal disease (estimated glomerular filtration rate ≤30), mild to severe liver disease, dementia, chronic conditions, connective tissue disease, diabetes mellitus (diet, tablet, or insulin controlled), HIV or AIDS, and malignancy.); 1 point for each comorbidity;4)

Respiratory rate in terms of breaths/min (0 points if <20/min, 1 point if 20-29/min, 2 points if >29/min); 5) Peripheral oxygen saturation on room air (0 points if ≥92%, 1 point if <92%); 6) Glasgow Coma Scale score (0 points if 15, , 1 point if <15); 7) Urea level (0 points if <7 mmol/L or <42 mg/dL; 1 point if ≥7 to ≤14 mmol/L or ≥42mg/dL to ≤84 mg/dL; > 2 points if >14 mmol/L or >84 mg/dL); 8) CRP level (0 point if <50 mg/L or <5 mg/dL; 1 point if 50-99 mg/L or 5-9.9 mg/dL; 2 points if ≥100 mg/L or ≥10 mg/dL)[11]. We also used the following formula to calculate the MELD-XI score: 5.11 x ln (serum bilirubin in mg/dL) + 11.76 x ln (serum creatinine in mg/dL) + 9.44[12]. The primary endpoint in our study was considered in-hospital mortality (also called short-term mortality).

Statistical analysis

We used IBM SPSS Statistics volume 25.0 (SPSS Inc, IBM, USA) for all statistical analyses. Descriptive statistics were reported as mean and standard deviation for normally distributed continuous data and median and interquartile range (IQR) for non-normally distributed continuous data. Categorical variables were reported as number and percentage. Independent sample t-test was used for normally distributed numeric variables whereas Mann Whitney U test was used for non normally distributed numeric variables. Chi-square or Fischer's exact test was used for categorical variables.

Candidate variables that were significantly correlated to in-hospital mortality in univariate analysis were put into binary logistic regression analysis to identify independent predictors of mortality. Hosmer-Lemeshow goodness of fit statistics and Nagelkerke R square (R^2) were used to assess the fitness of the model. We also performed a ROC (Receiver Operating Characteristics) curve analysis to assess the predictive power of the independent predictors of short-term mortality. A p value of less than 0.05 was accepted as statistically significant.

RESULTS

One hundred and seventeen patients were included in this study, who had a mean age of 63.6 years; 63.2% (n=74) of the patients were male. The surviving patients had a mean age of 63 years; 35.6% (n=36) of them were female. The deceased patients (n=16) had a mean age of 69.5 years; 43.8% (n=7) of them were female. The baseline characteristics, laboratory parameters, and NLR, PLR, MLR, NPR, NMR, CLR, CAR, BAR, MELD-XI, and 4C mortality scores were shown on Table 1 and 2.

Among the baseline clinical characteristics, age, chronic kidney disease, diabetes mellitus, acute kidney injury, and length of hospital stay were significantly correlated to in-hospital mortality (p:0.026, p:0.012, p:0.004, p:0.020, and p<0.001, respectively). Among laboratory parameters, urea, creatinine, LDH, AST, ferritin, D-dimer, CRP, albumin, and Hb were found to be significantly correlated to in-hospital mortality (p:0.001, p<0.001, p:0.001, p:0.006, p:0.017, p:0.003, p:0.007, p<0.001, and p<0.001, respectively). Moreover, BAR, CLR, CAR, MELD-XI score, and 4C mortality score were significantly correlated to in-hospital mortality (p<0,001, p:0.003, p:0.002, p:0.007, and p<0.001, respectively).

Parameters correlated to in-hospital mortality in the univariate analysis with a Pearson correlation coefficient (r) value between -0.8 and +0.8 were put in the binary logistic regression analysis. In the logistic regression analysis of a total of 11 parameters, including baseline demographic features, laboratory parameters, CAR, BAR, CLR, MELD-XI score, and 4C mortality score, only 4C mortality score [OR 1.58 (95% CI 1.06-2.36), p:0.022] and AST [OR 1.05 (95% CI 1.00-1.10), p:0.005] were independently predictive of in-hospital mortality of COVID-19 patients (Table 3). The regression analysis performed to predict in-hospital mortality had a Hosmer-Lemeshow p-value of 0.639 and an explanatory coefficient Nagelkerke R^2 value of 0.576, which indicated the goodness of fit of the regression model.

Based on the mean 4C mortality score levels, the observed (post hoc) power was assessed using G*Power 3.1.9.7 program logistic regression analysis with two-tailed testing for an α=0.05 and a sample size of 117. It revealed a power (1-β) of 0.99 with a critical z value of 1.95. Since the 4C mortality score and AST were the only independent predictors of in-hospital mortality, we also performed a ROC curve analysis (AUC analysis) of the 4C mortality score and the AST (Table 4). The AUC of the 4C mortality score was 0.857 (95% CI 0.754-0.960; p<0.001) while the AUC of AST was 0.714 (95% CI 0.576-0.852; p:0.006) (Figure 1). For a cut-off value of 10.5, the 4C mortality score had a sensitivity of 81.3% and a specificity of 76.2%, a positive likelihood ratio (PLR) of 3.41, and a negative likelihood ratio (NLR) of 0.24 for predicting in-hospital mortality. For a cut-off value of 34.5 U/L, AST had sensitivity of 62.5%, specificity of 71.3%, a PLR of 2.17, and a NLR of 0.52, for in-hospital mortality prediction.

Table 1. Comparison of the demographic features and baseline clinical characteristics of the survived and deceased patients

Variables	**Survived Patients (N =101)** Mean (± SD)/Median (IQR)/frequency (%)	**Deceased Patients (N=16)** Mean (± SD)/Median (IQR)/frequency (%)	**P value**
Age	62.65 (±15.89)	69.5 (±9.79)	0.026
Sex category (male/female)	65 (64.4%)/ 36 (35.6%)	9 (56.3%)/7 (43.8%)	0.532
Smoking	26 (25.7%)	3 (18.7%)	0.758
Hypertension	58 (57.4)	12 (75%)	0.183
Diabetes mellitus	36 (35.6%)	11 (68.7%)	0.012
Atherosclerotic cardiovascular disease	26 (25.7%)	6 (37.5%)	0.369
Congestive heart failure	12 (11.8%)	2 (12.5%)	1.000
Atrial fibrillation	8 (7.9%)	2 (12.5%)	0.625
Cerebrovascular disease	5 (4.9%)	2 (12.5%)	0.244
Chronic pulmonary disease (except asthma)	21 (20.7%)	5 (31.2%)	0.346
Chronic kidney disease	20 (19.8%)	9 (56.3%)	0.004
Acute kidney injury	5 (4.9%)	4 (25%)	0.020
Thyroid disease (hypothyroidism)	6 (5.9%)	3 (18.7%)	0.106
Computed tomography findings	92 (91%)	15 (93.7%)	1.000
Positive PCR	87 (86.1%)	14 (87.5%)	1.000
Length of hospital stay (day)	7 (5)	17 (15.75)	<0.001

Abbrevations: SD: Standard derivation, IQR: Interquartile range (min-max)

Table 2. Comparison of the laboratory parameters and NLR, PLR, MLR, NPR, NMR, CLR, CAR, BAR, MELD-XI, and 4C mortality score of the survived and deceased patients

Variables	Survived Patients (N =101) Mean (± SD)/Median (IQR)/frequency (%)	Deceased Patients (N=16) Mean (± SD)/Median (IQR)/frequency (%)	P value
Urea (mmol/L)	6.43 (40.34)	12.67 (31.77)	0.001
Creatinine (µmol/L)	79.56 (1020.14)	251.94 (803.56)	<0.001
Na (mmol/L)	137 (24)	135.50 (17)	0.258
K (mmol/L)	4.26 (±0.60)	4.49 (±0.66)	0.158
LDH (U/L)	246.5 (1069)	411 (947)	0.001
AST (U/L)	25 (97)	39.50 (1884)	0.006
ALT (U/L)	25 (229)	21.50 (653)	0.703
Total bilirubin (mg/dL)	0.5 (3.65)	0.39 (0.63)	0.075
Ferritin (µg/L)	505.01 (±555.27)	1104.17 (±877.80)	0.017
D dimer (mg/L)	0.84 (13.81)	1.74 (13.72)	0.003
CRP (mg/L)	54.60 (410,6)	85 (303.1)	0.007
Albumin (g/L)	36.1 (±4.8)	30.6 (±4.6)	<0.001
Hemoglobin (g/L)	137.3 (±21.9)	114.6 (±13.9)	<0.001
WBC (10^9/L)	7.57 (±3.62)	8.01 (±5.04)	0.743
Neutrophil (10^9/L)	4.78 (19.87)	4.48 (13.92)	0.830
Lymphocyte (10^9/L)	1.13 (3.80)	0.86 (1.92)	0.094
Monocyte (10^9/L)	0.51 (±0.30)	0.53 (±0.29)	0.834
Eosinophil (10^9/L)	0.01 (0.86)	0.01 (0.57)	0.978
Platelet (10^9/L)	202 (496)	177.50 (370)	0.533
NLR	3.87 (33.58)	4.22 (28.73)	0.302
PLR	0.16 (0.81)	0.21 (1.06)	0.104
MLR	0.36 (1.90)	0.52 (1.13)	0.052
NPR	25.61 (108.94)	22.15 (132.25)	0.981
NMR	10.16 (246.81)	11.49 (31.58)	0.886
CLR	0.03 (0.68)	0.09 (1.31)	0.003
CAR	14.75 (152.14)	27.38 (105.82)	0.002
BAR	4.76 (35.59)	12.76 (35.45)	<0.001
MELD-XI score	8.67 (±3.73)	12.95 (±5.36)	0.007
4C mortality score	7.61 (±3.39)	12.25 (±2.91)	<0.001

Abbrevations: BAR: BUN to albumin ratio, CLR: C-reactive protein to lymphocyte ratio, NLR: Neutrophil to lymphocyte ratio, NPR: Neutrophile to platelet ratio, NMR: Neutrophile to monocyte ratio, MELD-XI score: Model for End-Stage Liver Disease Excluding INR score, MLR: Monocyte to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SD: Standard derivation, IQR: Interquartile range (max-min).

Table 3. Multivariable logistic regression analysis of the baseline characteristics, laboratory parameters, CAR, BAR, CLR, MELD-XI score, and 4C mortality score

Variables	B	SE	Wald	df	OR	P value	95% Confidence Interval	
							Lower bound	Upper Bound
Diabetes mellitus	0.463	0.953	0.242	1	1.598	0.623	0.247	10.334
LDH	0.000	0.003	0.001	1	1.000	0.970	0.994	1.006
AST	0.050	0.023	4.658	1	1.051	0.031	1.005	1.100
Ferritin	0.000	0.001	0.001	1	1.000	0.974	0.998	1.002
D-dimer	0.189	0.109	3.026	1	1.209	0.082	0.976	1.496
Hemoglobin	-0.302	0.193	2.457	1	0.739	0.117	0.506	1.079
CAR	0.008	0.019	0.187	1	1.008	0.665	0.971	1.047
BAR	0.027	0.067	0.164	1	1.027	0.686	0.901	1.171
CLR	-2.476	3.372	0.539	1	0.084	0.463	0.000	62.406
MELD-XI	0.013	0.153	0.008	1	1.013	0.931	0.750	1.369
4C mortality score	0.463	0.203	5.228	1	1.589	0.022	1.068	2.364

Abbrevations: BAR: BUN to albumin ratio, CAR: C-reactive protein to albümin ratio, CLR: C-reactive protein to lymphocyte ratio, MELD-XI score: Model for End-Stage Liver Disease Excluding INR score.

Table 4. Area under the curves (AUCs) of the 4C mortality score and AST

Test result variables	Area	Std. Error*	Asymptotic Sig.†	Asymptotic 95% Confidence Interval	
				Lower bound	Upper Bound
4C mortality score	0.857	0.052	<0.001	0.754	0.960
AST	0.714	0.070	0.006	0.576	0.852

The test result variables: 4C mortality score and AST have at least one tie between the positive actual state group and negative actual state group. Statistics may be biased; *Under the nonparametric assumption;
†Null hypothesis: true area= 0.5

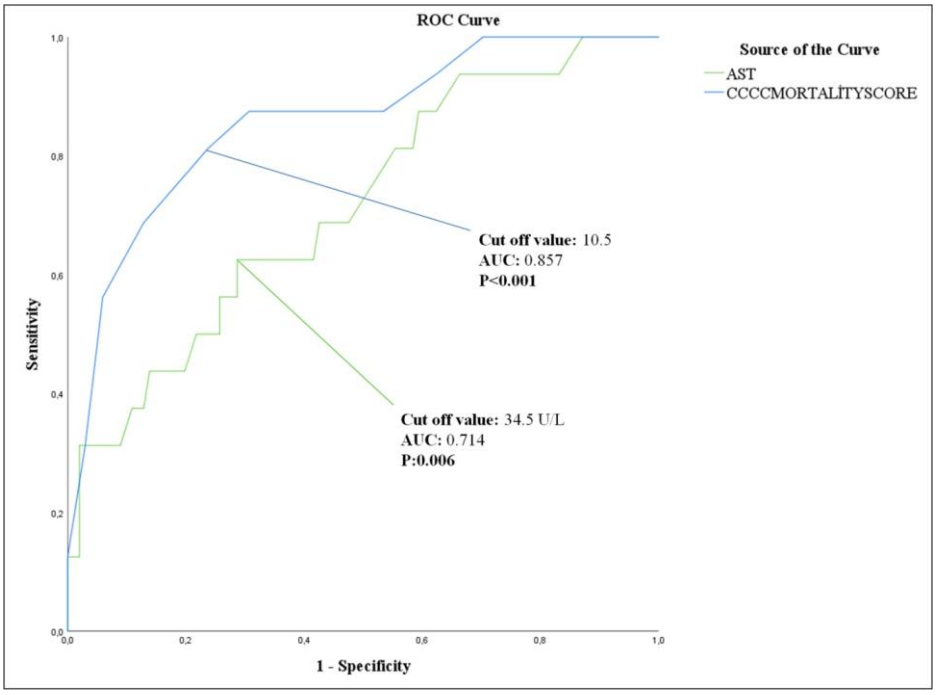

Figure 1. ROC curves of the 4C mortality score and AST

DISCUSSION

This study revealed that only the 4C mortality scoring system and AST independently predicted the short-term mortality risk in COVID-19 amongother inflammation-based parameters. In recent publications, NLR, PLR, CLR, BAR, and CAR are reportedly correlated to COVID-19 mortality[2,4,6-8]. Moreover, there are many demographic data and laboratory parameters significantly correlated to COVID-19 mortality, such as age, diabetes mellitus, white blood cell count, neutrophil count, platelet count, CRP, D-dimer, ferritin, LDH, albumin, creatinine, NLR, and PLR[2,3,9,17].

The 4C mortality score, an easy-to-use risk score that was developed and validated for COVID-19 patients, practically determines the prognosis of COVID-19 patients[11]. The 4C mortality score was scrutinized in different COVID-19 patient groups and was compared with other established critical care risk scores such as CURB65, CRB65, QSOFA, COVID-GRAM, NEWS, A-DROP, RISE UP, and REMS. Recent studies have showed that these scores are helpful for evaluating mortality risk and identifying patients at risk of critical illness at hospital admission. Nevertheless, the 4C mortality score outperformed existing scores in predicting in-hospital mortality in COVID-19 patients[18-21]. There is also another study

evaluating the strengths of improved scoring systems in mortality risk stratification in COVID-19, including the 4C mortality score, the quick COVID-19 Severity Index, and the COVID-GRAM Critical Illness Risk Score (COVID-GRAM) in older patients with COVID-19. This study revealed that the 4C mortality score and the COVID-GRAM score calculated at the time of admission showed the best performance in predicting mortality in elderly patients with COVID-19[22]. Furthermore, a recent study revealed that COVID-19 Mortality Score, COVID-19 Severity Index, 4C mortality score, and COVID-IRS NLR score were all predictive of in-hospital mortality in COVID-19[23]. Moreover, recent studies revealed that COVID-19 patients with abnormal liver tests including total bilirubin, ALP, GGT, AST, ALT at admission had a higher risk of progressing to severe disease[24] while AST and direct bilirubin were the independent predictors of mortality in COVID-19[25].

The MELD-XI score is used to predict prognosis and mortality in critically ill patients or patients with various acute or chronic inflammatory disease processes[12-16]. Because the MELD-XI score is based upon serum total bilirubin and creatinine level, we aimed to investigate whether this score was convenient in COVID-19 patients to assess the prognosis and mortality.

While our study was conducted, few studies were had already evaluated the relationship between in-hospital (short-term) mortality o, length of intensive care, length of hospital stay, and long-term mortality of COVID-19 and the MELD-XI score[26-27]. In one of these studies, a higher MELD-XI score was found to be associated with mortality in COVID-19 patients without liver disease, and it was stated that it could be a helpful tool for other risk modalities[26]. In another study, it was shown that the MELD-XI score may be useful in predicting early mortality in the elderly and critically ill patients[27].

However, no study in the literature has ever compared COVID-19 risk scoring systems such as MELD-XI score and 4C mortality score, and inflammatory parameters such as NLR, PLR, MLR, NPR, NMR, CAR, BAR, CLR. Therefore, we compared the MELD-XI score with the 4C mortality score and other inflammatory parameters to test their predictive power for in-hospital mortality of COVID-19. We found that CAR, CLR, BAR, 4C mortality score, and the MELD-XI score were significantly correlated to in-hospital mortality.

In conclusion, in line with previous reports, although age, chronic kidney disease, diabetes mellitus, acute kidney injury, length of hospital stay, urea, creatinine, LDH, AST, ferritin, D-dimer, CRP, albumin, Hb, CLR, BAR, CAR, MELD-XI score, and 4C mortality score were correlated to mortality in COVID-19, only the 4C mortality score and AST were the independent predictors of short-term mortality. Moreover, we found that the 4C mortality score was a useful risk modality for estimating in-hospital mortality with a ROC curve area (AUC) of 0.857, which had a sensitivity of 81.3% and a specificity of 76.2% for a cut-off value of 10.5. Remarkably, AST had a sensitivity of 62.5% and a specificity of 71.3% in predicting in-hospital mortality for a cut-off value of 34.5 U/L. Whereas it has been shown in the literature that admission AST and direct bilirubin levels independently predicted in-hospital mortality in COVID-19 patients[24], only basal AST level independently predicted mortality in our study.

This study has some limitations. Firstly, this is a retrospective single-center study with a relatively small sample size. Secondly, because of the retrospective design of this study and the lack of follow-up data, follow-up laboratory values could not be recorded. Therefore, we could not investigate the association of the peak blood levels or daily changes of biomarkers and other parameters with mortality and prognosis. In addition, oa higher prevalence of advanced age, diabetes, or chronic kidney disease may be another limitation of the study because these factors may have affected mortality rate. Finally, a few patients with mild disease did not have definite clinical and tomographic signs of the disease due to the lack of laboratory values and records at the time of patient admission. We referred to the existing international guidelines to define COVID-19 severity, and there were only nine patients without CT findings but clinical properties and PCR positivity. Furthermore, only one patient was clinically compatible with COVID 19 but had a negative CT and PCR.

In conclusion, The 4C mortality score calculated at hospital admission is a strong predictor of in-hospital mortality in COVID-19 patients. As the COVID-19 pandemic is still ongoing in a worldwide scale with poor outcomes, it is of utmost importance to rapidly assess prognosis and mortality in COVID-19 patients using effective and easy-to-use risk modalities such as the 4C mortality score along with other inflammatory risk factors, especially AST, at the time of admission.

Yazar Katkıları: Çalışma konsepti/Tasarımı: ÇOÇ; Veri toplama: ÇOÇ, NÖ; Veri analizi ve yorumlama: ÇOÇ, OÇ; Yazı taslağı: ÇOÇ; İçeriğin eleştirel incelenmesi: ÇOÇ, OÇ, NÖ, İHM; Son onay ve sorumluluk: ÇOÇ, OÇ, NÖ, İHM; Teknik ve malzeme desteği: ÇOÇ; Süpervizyon: ÇOÇ, OÇ, NE, İHM; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Başkent Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 17.11.2021 tarih ve KA21/288 Proje Numarası ve 21/152 sayılı kararı ile etik onay alınmıştır.
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