RESEARCH ARTICLE

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Comparison of CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ Score Estimation of In-Hospital Mortality Among COVID-19 Patients

ABSTRACT

Objective: This study aims to compare of CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ score estimation of in-hospital mortality among COVID-19 patients and find a new scoring system that can better predict the hospital mortality by adding some laboratory parameters to the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores.

Materials and Methods: This is a cross-sectional study. A total of 1076 COVID-19 patients with confirmed COVID-19 PCR tests were included from September 2020 to March 2021. Age, sex, comorbidity, laboratory, survival times, and death status of the patients were recorded. The scores CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ of each patient were calculated. A new mortality prediction score was created to establish the most effective model with logistic regression analysis, including laboratory values.

Results: Of the 1076 patients hospitalized for COVID-19, 15.1% died, while 84.9% survived. There was no significant difference between the two groups in sex. All comorbidities were significantly higher in the deceased than in the survivors ($p<0.001$). The survivors' hemoglobin, thrombocyte, and eGFR values were significantly higher. The C-reactive protein (CRP), aspartate aminotransferase (AST), and neutrophil-to-lymphocyte ratio (NLR) were found to be associated with mortality, and the CAN-$R_2CHA_2DS_2VASc$ score was created by including these three laboratory parameters. The ROC curves of the scores CHA_2DS_2VASc (AUC=0.810), $R_2CHA_2DS_2VASc$ (AUC=0.824), and CAN-$R_2CHA_2DS_2VASc$ (AUC=0.909) were analyzed. The CAN-$R_2CHA_2DS_2VASc$ score was superior to other scores ($p<0.001$). The sensitivity and specificity of the CAN-$R_2CHA_2DS_2VASc$ score were 79.8% and 86.5%, respectively, while the criterion was >6 points.

Conclusions: The CAN-$R_2CHA_2DS_2VASc$ score is a useful tool for estimating hospital mortality in COVID-19 patients. The CAN-$R_2CHA_2DS_2VASc$ score was superior to the $R_2CHA_2DS_2VASc$ and CHA_2DS_2VASc score in predicting in-hospital mortality.

Keywords: Mortality, Hospitalization, COVID 19, Survival, Risk Factors, Comorbidity.

COVID-19 Hastalarında Hastane İçi Mortalitenin CHA_2DS_2VASc ve $R_2CHA_2DS_2VASc$ Skor Tahmininin Karşılaştırılması

ÖZET

Amaç: Bu çalışma, COVID-19 hastalarında hastane içi mortalitenin CHA_2DS_2VASc ve $R_2CHA_2DS_2VASc$ skor tahminini karşılaştırmayı ve CHA_2DS_2VASc ve $R_2CHA_2DS_2VASc$ skorlarına bazı laboratuvar parametreleri ekleyerek hastane mortalitesini daha iyi tahmin edebilen yeni bir skorlama sistemi bulmayı amaçlamaktadır.

Gereç ve Yöntem: Bu bir kesitsel çalışmadır. Eylül 2020'den Mart 2021'e kadar COVID-19 PCR testleri doğrulanmış toplam 1076 COVID-19 hastası dahil edildi. Hastaların yaş, cinsiyet, komorbidite, laboratuvar, hayatta kalma süreleri ve ölüm durumları kaydedildi. Her hastanın CHA_2DS_2VASc ve $R_2CHA_2DS_2VASc$ skorları hesaplandı. Laboratuvar değerleri de dahil olmak üzere lojistik regresyon analizi ile en etkili modeli oluşturmak için yeni bir ölüm tahmin skoru oluşturuldu.

Bulgular: COVID-19 nedeniyle hastaneye yatırılan 1076 hastanın %15,1'i öldü, %84,9'u hayatta kaldı. İki grup arasında cinsiyet açısından anlamlı fark yoktu. Ölenlerde tüm komorbiditeler yaşayanlara göre anlamlı derecede yüksekti ($p<0.001$). Hayatta kalanların hemoglobin, trombosit ve eGFR değerleri anlamlı olarak daha yüksekti. C-reaktif protein (CRP), aspartat aminotransferaz (AST) ve nötrofil-lenfosit oranı (NLR) mortalite ile ilişkili bulundu ve bu üç laboratuvar parametresi dahil edilerek CAN-$R_2CHA_2DS_2VASc$ skoru oluşturuldu. CHA_2DS_2VASc (AUC=0,810), $R_2CHA_2DS_2VASc$ (AUC=0,824) ve CAN-$R_2CHA_2DS_2VASc$ (AUC=0,909) skorlarının ROC eğrileri analiz edildi. CAN-$R_2CHA_2DS_2VASc$ skoru diğer skorlardan üstündü ($p<0.001$). CAN-$R_2CHA_2DS_2VASc$ skorunun duyarlılığı ve özgüllüğü sırasıyla %79,8 ve %86,5 iken, kriter >6 puandı.

Sonuç: CAN-$R_2CHA_2DS_2VASc$ skoru, COVID-19 hastalarında hastane mortalitesini tahmin etmek için yararlı bir araçtır. CAN-$R_2CHA_2DS_2VASc$ skoru, hastane içi mortaliteyi tahmin etmede $R_2CHA_2DS_2VASc$ ve CHA_2DS_2VASc skorundan üstündü.

Anahtar Kelimeler: Ölüm Oranı, Yataklı Tedavi, COVID-19, Sağ Kalım, Risk Faktörleri, Eşzamanlı Hastalık.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was defined as a pandemic by the World Health Organization on 11 March 2020, after its first detection in December 2019 in Wuhan, China, as the causal agent of COVID-19 disease (1, 2). COVID-19 remains a serious health problem worldwide. Although it mainly causes pneumonia in the lung, it can cause illness in more than one organ system (3). Age, male sex, and common cardiovascular comorbidities are associated with worse outcomes, and thromboembolic complications play an important role in the clinical course of these patients (4-6).

SARS-CoV-2 is a single-stranded RNA virus that enters cells by binding to angiotensin-converting enzyme two receptors found mainly in the lungs, heart, and vessels of the human body (7). Endothelial dysfunction is believed to play an essential role in the pathogenesis of thromboembolic events in COVID-19 (8, 9). The SARS-CoV-2 infection has been suggested to induce a process known as immunothrombosis, in which activated neutrophils and monocytes interact with platelets and the coagulation cascade, leading to the formation of intravascular clots in small and larger vessels (10, 11).

The $R_2CHA_2DS_2VASc$ scores, created by combining the CHA_2DS_2VASc score and the estimated glomerular filtration rate (eGFR), are simple scoring systems that are commonly used to predict the risk of systemic thromboembolism in patients with atrial fibrillation (AF) (12, 13). These risk scores have been shown to predict morbidity and mortality in various clinical conditions other than AF (14, 15). Taking into account the worse prognosis of the male sex in COVID-19 patients, it has been shown that the modified CHA_2DS_2VASc score, obtained by assigning 1 point to the male gender instead of the female gender, predicts in-hospital mortality (16-18). Renal dysfunction is also associated with increased morbidity and mortality in COVID-19 patients (19, 20). The R2CHA2DS2-VASc score, created by including renal (R) functions in the CHA2DS2VASc score, also predicts mortality in COVID-19 patients (16, 21). Similar to these, many other scoring systems have been created, including clinical, laboratory, and physiological parameters (20, 22-24). COVID-19 is a systemic infectious disease that causes cell destruction and inflammation. A new scoring system in which laboratory values that indicate cell damage and inflammation are included will be more effective in determining the prognosis. The aim is to compare CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ score estimation of in-hospital mortality among COVID-19 patients and find a new scoring system that can better predict hospital mortality by adding some laboratory parameters to the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores.

MATERIAL AND METHODS

This retrospective study was conducted at Health Sciences University Samsun Training and Research Hospital and included 1200 consecutive patients whose COVID-19 nasopharyngeal swab samples were positive by real-time reverse transcriptase-polymerase chain reaction (PCR) between September 1, 2020 and March 31, 2021. Those with active cancer, those receiving chemotherapy-radiotherapy treatment, immunosuppressive therapy for various reasons, those with severe liver disease, coagulation disorders, rheumatological diseases (Systemic Lupus Erythematosus, Behçet's Syndrome, Rheumatoid Arthritis, etc.), those using oral contraceptives and those aged under 18 years were excluded from the study. A total of 1076 patients with COVID-19 who met the appropriate criteria were included in the study. This study was carried out according to the Declaration of Helsinki, registered with the Ministry of Health Scientific Research COVID-19 Committee, and approved by the Local Ethics Committee.

Demographic, laboratory, and clinical information was obtained from patient electronic data at the emergency department and COVID-19 clinics, accessible at the individual patient level. Demographic and clinical data included age, sex, presence of prior diabetes mellitus, hypertension, hyperlipidemia, congestive heart failure, cardiovascular disease, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, chronic kidney disease, and smoking status. Detailed biochemical data and complete blood counts of all patients were obtained from the emergency department and the COVID-19 clinics. The estimated glomerular filtration rate (eGFR) was calculated using the Modified Diet in Renal Disease equation in kidney disease, using the mean of two different serum creatinine measurements in patients with steady-state renal function (one on emergency room admission and the second on the first day of pandemic hospital admission). Patients with acute kidney damage were excluded and an eGFR value <60 ml/min/1.73 m^2 was accepted as renal failure.

The CHA_2DS_2VASc and $R_2CHA_2DS_2VAScs$ scores of each patient were calculated during their hospitalization using clinical data from electronic medical health record history and routine biochemical tests. CHA_2DS_2VASc was calculated by giving 1 point for congestive heart failure, hypertension, age 65-74 years, diabetes mellitus, vascular disease, male sex, and 2 points for ischemic stroke history and/or transient ischemic attack (TIA) and age ≥75 years. When calculating the M-$R_2CHA_2DS_2VAScs$ score, the eGFR values >60 ml/min/1.73m^2, between 30-60 ml/min/1.73 m^2 and <30 ml/min/1.73m^2 were determined to be 0, 1 and 2 points, respectively. In addition to the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores, binary logistic regression analysis was used to select laboratory variables affecting the risk of in-hospital mortality. Parameter estimates were obtained using the stepwise selection method to identify the most effective model and variables that included all possible variations.

C-reactive protein (CRP) levels were evaluated according to the classification of 3-10 mg/L normal or minor elevation, 10-100 mg/L moderate elevation, and >100 mg/L marked elevation (25). These levels were evaluated as 0, 1, 2 points, respectively. Aspartate aminotransferase (AST) levels were evaluated as < 40 U/L normal, 40-80 U/L mild elevation, and >80 U/L moderate or marked elevation (26). These levels were evaluated as 0, 1, and 2 points, respectively. Since there is no standardized classification for AST value, an increase of 2 times the upper limit of normal was evaluated as moderate or marked. The Neutrophil/Lymphocyte ratio (NLR) was evaluated according to the classification of <6 normal, 6-9 mild stress, >9 critically ill patients (27). These levels were evaluated as 0, 1, and 2 points, respectively.

Statistical Analysis: Statistical analysis was performed using The conformity of continuous variables to the normal distribution was examined using visual graphics and the Kolmogorov–Smirnov/Shapiro–Wilk test. Continuous variables were presented as median

(quartile 1- quartile 3) and categorical variables as frequency and percentage. When appropriate, categorical variables were analyzed using the chi-square or Fisher's exact test. Continuous variables were analyzed using the Mann-Whitney U test.

In addition to the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores, binary logistic regression analysis was used to select laboratory variables affecting the risk of in-hospital mortality. Parameter estimates were obtained using the stepwise selection method to identify the most effective model and the variables that included all possible variations. Cox & Snell R^2, Nagelkerke R^2, accuracy, and p-values of the CAN-$R_2CHA_2DS_2VASc$ model created in this way were evaluated. The significance level was accepted as $p<0.05$. IBM SPSS Statistics version 26.0. was used for these analyses.

Receiver operating characteristic (ROC) analysis was performed for scores. The area under the curve (AUC) was evaluated. AUC and 95%CI values were given. The Delong test was used for the comparison of the ROC curve. The point of criterion at which sensitivity and specificity were optimal was selected using the Youden index. MedCalc® Statistical Software trial version 20.115 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2022) was used for these analyses.

RESULTS

While 15.1% (n=163) of 1076 patients hospitalized for COVID-19 died, 84.9% (n=913) survived. There were no significant differences between the two groups in sex, and 46.3% of the survivors and 41.7% of the deceased were women (p=0.276). There was a significant difference between survivors and deceased in terms of age (p<0.001). While 43.6% of the deceased were ≥75 years old, 27.6% were in the 65-74 age range, and 28.8% were in the 18-64 age range. On the other hand, 66.0% of the survivors were in the 18-64 age range. Of those who died, 28.8% had congestive heart failure, 85.3% hypertension, 14.7% Stroke/TIA/thromboembolism, 33.1% vascular disease, 50.9% diabetes, 57.1% chronic renal failure, and 17.8% COPD comorbidity. All comorbidities were significantly higher in the deceased than in the survivors (p<0.001). Initial laboratory evaluation revealed that the survivors' hemoglobin, thrombocyte, and eGFR values were significantly higher. In contrast, all other laboratory parameters in Table 1 were significantly higher in the deceased.

Table 1. Characteristics and initial laboratory results of COVID-19 patients

Parameters	**Survivor n=913**	**Non-survivor n=163**	**p-values**
Sex (Female), n (%)	423(46.3)	68(41.7)	0.276
Age group, n (%)			
18-64 years	603(66.0)	47(28.8)	<0.001
65-74 years	201(22.0)	45(27.6)	
≥75 years	109(12.0)	71(43.6)	
Comorbidities, n (%)			
Congestive heart failure	48(5.3)	47(28.8)	<0.001
Hypertension	393(43.0)	139(85.3)	<0.001
Stroke/TIA/thromboembolism	15(1.6)	24(14.7)	<0.001
Vascular disease	109(11.9)	54(33.1)	<0.001
Diabetes	242(26.5)	83(50.9)	<0.001
Chronic kidney disease	156(17.1)	93(57.1)	<0.001
COPD	57(6.2)	29(17.8)	<0.001
Initial laboratory results, Median (q1-q3)			
White Blood Cell ($x10^3/\mu L$)	6.2 (4.8-8.0)	8.1 (5.6-11.1)	<0.001
Hemoglobin (g/dL)	13.1 (12.0-14.2)	12.0 (10.8-13.0)	<0.001
Platelet ($x10^3/\mu L$)	211.0 (167.0-270.0)	184.0 (145.0-245.0)	<0.001
NLR	3.5 (2.4-5.2)	8.0 (5.0-11.0)	<0.001
Glucose (mg/dL)	124.0 (111.0-158.0)	163.0 (127.0-248.0)	<0.001
AST (U/L)	40.0 (32.0-52.0)	66.0 (45.0-89.0)	<0.001
ALT (U/L)	32.0 (23.0-45.0)	47.0 (35.0-70.0)	<0.001
eGFR ($ml/dk/1,73m^2$)	83.0 (67.0-98.0)	56.0 (36.5-75.6)	<0.001
BUN (mg/dL)	32.0 (25.0-41.0)	60,0 (45.0-85.0)	<0.001
Creatinine (mg/dL)	0.9 (0.8-1.0)	1.2 (0.9-1.7)	<0.001
BUN/Creatinine	16.9 (14,5-19.6)	21.5 (18.9-27.6)	<0.001
CRP (mg/L)	55.0 (30.0-100.0)	130.0 (88.0-185.0)	<0.001
Ferritin (mcg/L)	300.0 (167.0-490.0)	650.0 (345.0-953.0)	<0.001
D-dimer (mcg/mL)	0.7 (0.5-1.1)	1.4 (0.9-2.4)	<0.001
Fibrinogen (mg/dL)	450.0 (347.0-543.0)	519.0 (450.0-600.0)	<0.001
Troponin I (ng/mL)	0.1 (0.0-0.1)	0.2 (0.1-0.6)	<0.001
Creatine Kinase MB (ng/mL)	1.0 (0.9-2.0)	4.0 (3.0-6.0)	<0.001

TIA: transient ischemic attack; COPD: Chronic obstructive pulmonary disease; NLR: Neutrophil to lymphocyte ratio; AST: Aspartate aminotransferase; ALT: Alanine Aminotransferase; eGFR: Estimated glomerular filtration rate; BUN: Blood Urea Nitrogen; CRP: C-reactive protein

The stepwise logistic regression models in Table 1, which include all laboratory values not used in $R_2CHA_2DS_2VASc$ scoring, attempted to identify the most important factors explaining mortality. In these models, there were 3 variables other than $R_2CHA_2DS_2VASc$ in the model with the highest mortality explanation rate, and other criteria were excluded from the model because they decreased the model's mortality explanation rate. The C-reactive protein (CRP), aspartate aminotransferase (AST), and neutrophil-to-lymphocyte ratio (NLR) were found to be associated with mortality (Table 2). A new scoring system was created by adding these three new laboratory values associated with mortality to the current scoring system (Table 3). The CAN-$R_2CHA_2DS_2VASc$ score was established by assigning letter C for C-reactive protein (CRP), letter A for aspartate aminotransferase (AST), and letter N for neutrophil to lymphocyte ratio (NLR) (Table 3).

Table 2. Regression analysis of the predictive model for COVID-19 patients (CAN-$R_2CHA_2DS_2VASc$)

Predictive Model	OR (95%CI)	p
$R_2CHA_2DS_2VASc$	1.901 (1.686-2.144)	<0.001
NLR	1.207 (1.131-1.289)	<0.001
AST	1.009 (1.006-1.013)	<0.001
CRP	1.020 (1.014-1.027)	<0.001

Model fit: p < 0,001; Cox & Snell R^2= 0,3051; Nagelkerke R^2= 0,5326; Accuracy=90%

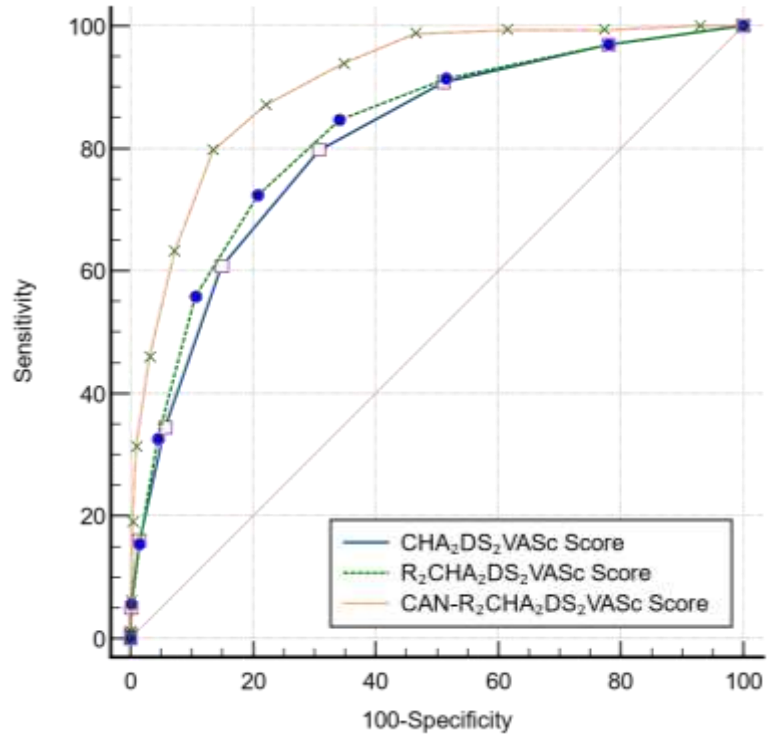
Table 3. Criteria of CAN-$R_2CHA_2DS_2VASc$

Criteria	Category	Points
Congestive heart failure history		+1
Hypertension history		+1
Age	<65 years old	0
	65-74 years old	+1
	≥75 years old	+2
Diabetes mellitus history		+1
Previous stroke, transient ischemic attack, thromboembolism history		+2
Vascular disease history (prior myocardial infarction, peripheral artery disease, or aortic plaque)		+1
Sex	Female	0
	Male	+1
Renal Function (estimated glomerular filtration rate (eGFR)) (ml/dk/1,73m^2)	> 60	0
	30-60	+1
	<30	+2
CRP (mg/L)	<10	0
	10-100	+1
	>100	+2
AST (U/L)	<40	0
	40-80	+1
	>80	+2
NLR	<6	0
	6-9	+1
	>9	+2

AST: Aspartate aminotransferase; CRP: C-reactive protein; eGFR: Estimated glomerular filtration rate; NLR: Neutrophil to lymphocyte ratio;

ROC curves of CHA_2DS_2VASc, $R_2CHA_2DS_2VASc$, and CAN-$R_2CHA_2DS_2VASc$ scores were analyzed (Figure 1). The area under the curve (AUC) was calculated as 0.810 for CHA_2DS_2VASc, 0.824 for $R_2CHA_2DS_2VASc$, and 0.909 for CAN-$R_2CHA_2DS_2VASc$. The Delong test was used for the comparison of the ROC curve. The AUC of the $R_2CHA_2DS_2VASc$ score was significantly higher than the CHA_2DS_2VASc score (p=0.009).

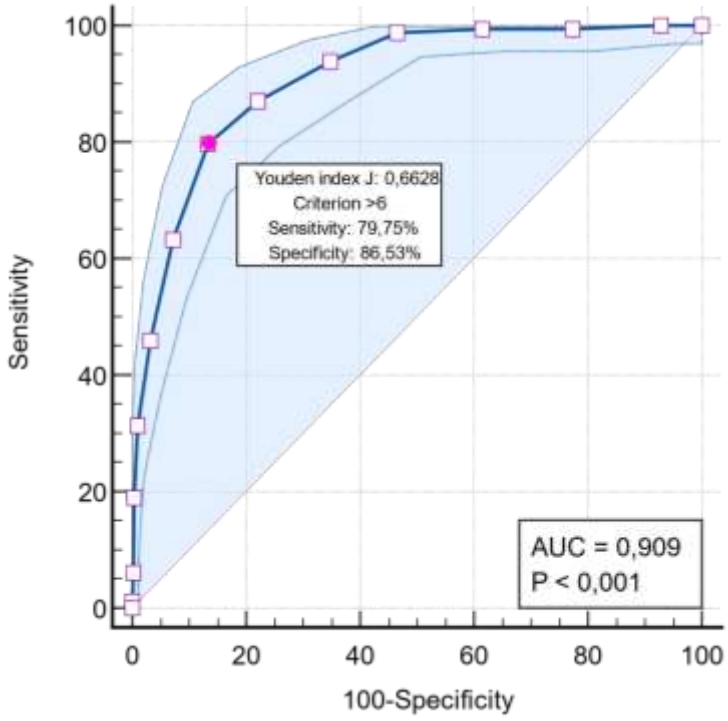
The AUC of the CAN-$R_2CHA_2DS_2VASc$ score was significantly higher than the AUC of both $R_2CHA_2DS_2VASc$ and CHA_2DS_2VASc scores (p<0.001). The point of criterion at which sensitivity and specificity were optimal was selected using the Youden index. The CAN-$R_2CHA_2DS_2VASc$ score sensitivity was 79.8%, specificity was 86.5%, +LR was 5.92, -LR was 0.23, while the criterion was >6 points (Figure 2).



Scores	AUC¥	95% CI	$R_2CHA_2DS_2VASc$	CAN-$R_2CHA_2DS_2VASc$
CHA_2DS_2VASC	0.810	0.785 - 0.833	z= 2.623 **p= 0.009***	z= 7.599 **p< 0,001***
$R_2CHA_2DS_2VASC$	0.824	0.800 - 0.847		z= 6.954 **p< 0,001***
CAN-$R_2CHA_2DS_2VASC$	0.909	0.890 - 0.925		

¥ p<0.001; *DeLong test used for comparison.

Figure 1. Comparison of Scores' ROC curves for survivors.



Statistic	Value	95% CI
Sensitivity	79.75%	72.76% to 85.64%
Specificity	86.53%	84.14% to 88.68%
Positive Likelihood Ratio	5.92	4.94 to 7.10
Negative Likelihood Ratio	0.23	0.17 to 0.32

Figure 2. ROC curve of the CAN-$R_2CHA_2DS_2VASc$ scores, sensitivity, specificity, and criterion.

DISCUSSION

Although COVID-19 was initially thought to be primarily a respiratory disease, evidence suggests that the primary and perhaps most important target of the virus is the endothelium. Endothelial dysfunction is believed to play an important role in the pathogenesis of thromboembolic events in COVID-19.(8, 9) COVID-19 has been suggested to induce a process known as immunothrombosis, in which activated neutrophils and monocytes interact with platelets and the coagulation cascade, leading to the formation of intravascular clots in small and larger vessels (10, 11). Endothelial hemostasis plays a vital role in the regulation of fibrinolysis and vessel wall permeability, and its dysfunction triggers immunothrombosis (10, 11, 28). Endothelial dysfunction is associated with atherosclerotic risk factors such as diabetes mellitus, hypertension, hyperlipidemia, inflammation, coronary artery disease, and peripheral artery disease (29, 30). Comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease associated with endothelial dysfunction have been found to be more common in hospitalized patients with COVID-19. These comorbidities have also been observed to be associated with a predisposition to severe COVID-19 and an increased risk of death (31-33).

The CHA_2DS_2VASc score and $R_2CHA_2DS_2VASc$ score, which is formed by including the estimated glomerular filtration rate (eGFR), are simple scoring systems that are commonly used to predict the risk of systemic thromboembolism in patients with AF (10, 11). These scores are primarily designed to predict the risk of thrombosis, and many of their components are also prognostic risk factors for COVID-19. As the patients' CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores increase, their susceptibility to endothelial dysfunction and thrombosis increases. Since endothelial dysfunction and thrombosis play an important role in the pathogenesis of COVID-19, these scores were thought to predict in-hospital mortality in this patient population (9, 10). Studies have shown that in COVID-19 patients, the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ obtained by scoring the male sex predicts in-hospital mortality (16-18, 21).

This study supports previous studies. Both the CHA_2DS_2VASc and $R_2CHA_2DS_2VASc$ scores demonstrated increased in-hospital mortality. Some studies have shown that renal dysfunction is associated with increased morbidity and mortality in COVID-19 (19, 20). In light of these studies, we investigated whether the $R_2CHA_2DS_2VASc$ score, which was created by including eGFR in the CHA_2DS_2VASc score, was superior in predicting mortality, since kidney functions are an important cause of mortality in this population of patients. As a result, the $R_2CHA_2DS_2VASc$ score was superior to the CHA_2DS_2VASc score in terms of mortality prediction.

Since COVID-19 is a systemic infectious disease, it causes destruction and increases cell inflammation. Therefore, it is not surprising that the CRP, AST, and NLR values increase in COVID-19 patients. Studies have shown that inflammatory markers such as CRP and NLR are associated with increased mortality in COVID-19 (34-37). Significant increases in AST have also been reported in COVID-19 patients. The increase in AST, which is found not only in the liver but also in many organs, can be explained by the resulting multiorgan dysfunction (38-40). In the model created with the CRP, AST, and NLR values added to the $R_2CHA_2DS_2VASc$ score, and it was possible to evaluate endothelial dysfunction and thrombosis together with cell destruction and inflammation parameters.

Consequently, early estimation of the risk of death in COVID-19 patients is of great importance in terms of clinical patient management and treatment strategies, and we found that the ability of the CAN-$R_2CHA_2DS_2VASc$ score to predict mortality is better than the $R_2CHA_2DS_2VASc$ and CHA_2DS_2VASc scores. *The CAN-$R_2CHA_2DS_2VASc$ score we defined had sufficient sensitivity and specificity and was more successful in predicting mortality.* Unlike other scores, it includes both clinical and laboratory parameters, making it a strong prognostic indicator.

This study has some limitations. First, this study is a retrospective and single-center study. This may limit the generalizability of this study's findings. Furthermore, this study was carried out in the early period of the pandemic, when variants of COVID-19 (delta, omicron, etc.) had not yet emerged and vaccination had not started in Türkiye. Different viral strains and vaccination status can influence the risk of complications and prognosis among infected patients. The performance of this new scoring system may differ between currently infected patients with different viral strains and vaccination status. Due to increased vaccinations and newly emerging variants, the efficacy of this model must be tested in a population of new dominant variants. Racial differences may also affect the severity and prognosis. The generalizability of the results and the usability of the score in clinical practice should be evaluated with larger studies.

CONCLUSION

The results of this study showed that the CAN-$R_2CHA_2DS_2VASc$s score could be useful in predicting in-hospital mortality in patients with COVID-19. Furthermore, the predictive ability of CAN-$R_2CHA_2DS_2VASc$ was better than the $R_2CHA_2DS_2VASc$ and CHA_2DS_2VASc scores to predict mortality in this patient population. Since it is an easily calculable score, it can help determine clinical patient management and treatment strategies by estimating the risk of mortality early.

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