Mortality prediction with CHA2DS2-VASc, CHA2DS2-VASc-HS and R2CHA2DS2-VASc score in patients hospitalized due to COVID-19

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Abstract. – **OBJECTIVE:** We aimed to test the efficiency of CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS, $R_2CHA_2DS_2$-VASc score systems on the prediction of mortality in the patients with COVID-19.

PATIENTS AND METHODS: The data were collected from 508 hospitalized patients with COVID-19. Comorbidity features including coronary artery disease, peripheral arterial disease, congestive heart failure, hypertension, atrial fibrillation, diabetes mellitus, hyperlipidemia, smoking, chronic obstructive pulmonary disease, cerebrovascular event, cancer status, and renal disease were recorded. The patients were divided as surviving group (n=440) and non-survivors (n=68).

RESULTS: The in-hospital mortality rate of the patients with COVID-19 was 13.4%. Factors found to be associated with mortality in univariate analysis were CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS, $R_2CHA_2DS_2$-VASc, cancer state, atrial fibrillation, hemoglobin, lymphocyte count, CRP, albumin and ferritin. Model 1 multivariate cox regression analysis revealed CHA_2DS_2-VASc, hemoglobin, CRP and ferritin levels to be independently associated with mortality. Factors that were found to be independently associated with in-hospital mortality in Model 2 analysis were CHA_2DS_2-VASc-HS, $R_2CHA_2DS_2$-VASc, hemoglobin, CRP and ferritin whereas except hemoglobin in Model 3 analysis, the other variables had been the same. Predictive power of R2CHA2DS2-VASc was better than of both CHA2DS2-VASc (*p*=0.002) and CHA2DS2-VASc-HS (*p*=0.034) in determining the in-hospital mortality. Patients with higher R2CHA2DS2-VASc (> 3 points), CHA2DS2-VASc-HS (> 3 points) and CHA2DS2-VASc (> 2 points) scores exhibited the highest mortality rate in survival analysis by using Kaplan-Meier and long-rank tests.

CONCLUSIONS: CHA2DS2-VASc, CHA2DS2-VASc-HS, and R2CHA2DS2-VASc were found to be independent predictors of mortality in hospitalized COVID-19 patients. The current study revealed that the predictive ability of R2CHA2DS2-VASc was better than the both of CHA2DS2-VASc and CHA2DS2-VASc-HS score.

Key Words:
  SARS-COV-19, COVID-19, Pandemics, Mortality, CHA2DS2-VASc.

Introduction

The SARS-CoV-19 was first announced in China in December 2019. It rapidly spread worldwide and is accepted as pandemics by World Health Organization early in 2020[1]. The disease affects people at all age groups[1]. Although most of the otherwise healthy cases are either asymptomatic or mildy symptomatic, still COVID-19 is associated with serious mortality and morbidity without certain dicriminating factors indicating whom will be more severely affected.

Since the beginning of the disease, tremendous numbers of patients are hospitalized, many of them required treatment at the Intensive Care Units (ICUs) and unfortunately many lives were lost secondary to the complications of the COVID-19. COVID-19 is mainly associated with respiratory problems; however, disseminated coagulopathy is an unresolved complication of the disease as well, which also contributes to mortality, morbidity, and long-term health problems. Hence, anticoagulants are frequently prescribed for hospitalized COVID-19 patients[2].

There are worldwide ongoing searches for mortality predictors for COVID-19 hospitalized patients. CHA_2DS_2-VASc score is a clinical prediction tool for thromboembolic stroke in patients with non-valvular atrial fibrillation. Accordingly, anticoagulation and antiplatelet therapies are

determined depending on the scores[3]. The improved form of CHA_2DS_2-VASc was created by adding two other risk factors (hyperlipidemia and smoking) and named as CHA_2DS_2-VASc-HS[4]. $R_2CHA_2DS_2$-VASc is a modified form of CHA_2DS_2-VASc, created by adding reduced creatinin clearance[5]. All the scores are proven to be predictors of all cause mortality in the long-run in patients with cardiovascular disorders[4-6]. Since COVID-19 is strongly associated with dissemitated intravascular coagulation and thromboembolic events, with the same rationelle of using these scores for cardiac and thrombotic disorders, literature includes the application of modified CHA_2DS_2-VASc risk score in predicting mortality in patients hospitalized with COVID-19[7]. In the present research, we studied all these 3 risk score systems individually on mortality prediction in the patients receiving treatment at the Intensive Care Unit (ICU) against SARS-CoV-19 disease and investigated the reliability and superiority of each score over the others.

Patients and Methods

The diagnosis of first COVID-19 positive case in Turkey was declared on March 11, 2020, by the Ministry of Health[8]. The government and private health care facilities were immediately adapted to the new situation in the country and many hospitals including our hospital, were announced as 'pandemics hospital'. Necessary alterations were rapidly performed to take care of patients with COVID-19 disease. All the elective surgical and interventional procedures were postponed, and wards and ICUs of the hospital were dedicated for the care of the SARS-CoV-19 infected patients. The diagnosis was performed with nasopharyngeal swab and/or computerized tomography. Patient care was provided by the staff of the hospital from different branches. However, ICU reanimation team was the primary responsible personnelle for the care and discharge at the ICU and members of other branches worked under supervision of the anesthesiologists and reanimators. Extracorporeal membrane oxygenators were applied percutaneously by anesthesiologists or surgically by cardiovascular surgeons after team decision.

The age, gender, body weight, past medical history history, comorbidity features including coronary artery disease, peripheral arterial disease, congestive heart failure, hypertension, atrial fibrillation, diabetes mellitus, hyperlipidemia, cigarette smoking, chronic obstructive pulmonary disease, cerebrovascular accident, cancer status, and renal disease were recorded. Serial laboratory tests were performed and repeated. The laboratory markers presumed to be associated with COVID-19 multi-system collapse syndrome such as hemoglobin, white blood cell count, lymphocyte count, platelet count, D-Dimer, ferritin, CRP, highly sensitive troponin-I, uric acid, D-dimer and glomerular filtration rate were studied. The ICU and invasive mechanical ventilation requirement, myocardial and kidney injury, adult respiratory distress syndrome (ARDS), duration of hospital and ICU stays were researched. CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS, and $R_2CHA_2DS_2$-VASc were calculated for each patient treated at the hospital. The data collected from 508 hospitalized patients were analyzed for the surviving group (n=440) and the patients who died (non-survivors, n=68) during their hospital stay. The informed consent for patients were taken. The data were analyzed retrospectively in this observational research. Exclusion criteria included end stage cancer states, severe frailty determined by the attending physician's discretion, pregnancy, patients whom died at admission, patients under the age of 18 and patients who lacked baseline data. Among the screened patients 8 frail patients secondary to very old age (>95 years) and/or neuromuscular disorders, 4 due to end-stage disseminated malignancy and 5 due to loss of records were excluded from the study.

Ethical Committee Approval

All the studies regarding COVID-19 pandemics in the country required special permission from Republic of Turkey, Ministry of Health as a government policy. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices and was approved by the Republic of Turkey, Ministry of Health. Further Ethical aproval was obtained from the Institutional Ethics Committee (Date: May 29, 2020, No: 2020.05.2.12.068).

Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences version 24.0 software (IBM Corp., Armonk, NY, USA). ROC curves of the models were compared using with MEDCALC software (Software bvba 13, Ostend, Belgium).

Categorical variables are presented as frequencies and percentages. The chi-square (χ^2) test was used to compare the categorical variables between

the groups. Continuous variables are given as mean±standard deviation (if normally distributed) and medians (interquartile ranges) (if not normally distributed). The Kolmogorov–Smirnov test was used to assess whether the variables were normally distributed. The unpaired Student's *t*-test or Mann-Whitney U test was used to compare continuous variables between the groups whether they were normally distributed or not. Pearson's coefficient was calculated to describe the degree of correlation of parameters with each other.

In order to identify the independent risk factors for in-hospital mortality, univariate and Backward-LR stepwise multivariable cox regression analyses were performed. Only the variables with a *p*-value of less than 0.05 in univariate analysis were incorporated in the multivariate cox regression analysis. Variables already included in the CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS and R2CHA2DS2-VASc scores were not considered separately in the multivariable analysis independent of their significance in univariable analysis. In addition, to avoid model overfitting, the CHA2DS2-VASc, CHA2DS2-VASc -HS and R2CHA2DS2-VASc scoring systems were not included in the same multivariate logistic cox regression analysis model. We performed three different multivariable regression models defined as model 1 involving CHA2DS2-VASc, model 2 involving CHA2DS2-VASc-HSF and model 3 involving R2CHA2DS2-VASc. Results of the cox regression analysis were reported with hazard ratios (HR) and 95% confidence interval (CI). To determine the additional abilities of the CHA_2DS_2-VASc, CHA_2DS_2-VASc -HS and $R_2CHA_2DS_2$-VASc scores for prediction of in hospital mortality, the receiver operating characteristics (ROC) curve analysis was performed. The Area Under the Curve (AUC) was used as a measure of the predictive accuracy of all scoring systems. To compare the predictive performance of these scores, DeLong test was used. Survival evaluations for the low- and high CHA_2DS_2-VASc, CHA_2DS_2-VASc -HS and $R_2CHA_2DS_2$-VASc scores were determined by using Kaplan–Meier and long-rank tests. The results were evaluated within a 95% CI and at a significance level of *p*<0.05.

Results

The cohort comprised of 508 patients. The number of survivors was 440 whereas 68 patients died. The mortality rate of the patients with COVID-19 at the hospital was 13.4%. Overall, there were 270 male (53.1%) patients. Male / female ratio was 225/115 (51.1%) in surviving group and 45/23 (66.2%) among non-survivors. Mean age of the survivors was 58±15.5 years whereas it was 68.7±13.5 years in non-survivors. Gender did not have influence on mortality (*p*=0.02); however, increased age was significantly associated with death (*p*<0.01). Chronic obstructive pulmonary disease was not significantly associated with mortality (*p*=0.015; however, peripheral arterial disease had been detected as a significant predictor for mortality (*p*<0.001). The demographic features of the study cohort, clinical and laboratory parameters of the patients on admission are presented on Table I.

Overall, 97 patients out of hospitalized 508 patients required ICU admission. Although total mortality was 68 patients, 11 sudden deaths were observed either at the ward or at the emergency department. Myocardial injury, acute renal failure rates and the hospitalization time were significantly higher among the non-survivors when compared with the surviving patients (*p*<0.001) (Table I).

The laboratory parameters except the D-dimer and total platelet counts were significantly different between the groups. The hemoglobin levels, serum albumin levels, glomerular filtration rate and the lymphocyte fraction were found to be significantly decreased for the patients who lost their lives. However, the white blood cell count, CRP, ferritin, uric acid and troponin-I levels were significantly higher in the dying group (Table I).

Median CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS, and $R_2CHA_2DS_2$-VASc were calculated for survivors and non-survivors (Table I). The glomerular filtration rate was not included in multivariate analysis as it is a component of $R_2CHA_2DS_2$-VASc and it exhibited significant correlation with CHA_2DS_2-VASc (r=-613, *p*<0.001) and CHA_2DS_2-VASc-HS (r=-579, *p*<0.001). Factors that were found to be associated with in-hospital mortality in univariate anaylsis were CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS, $R_2CHA_2DS_2$-VASc, cancer state, atrial fibrillation, hemoglobin, lymphocyte count, CRP, albumin and ferritin. Model 1 multivariate cox regression analysis revealed CHA_2DS_2-VASc, hemoglobin, CRP and ferritin levels to be significantly associated with mortality (Table II). Factors that were found to be independently associated with in-hospital mortality in model 2 and model 3 multivariate cox regression analysis are presented on Table III. The parameters were CHA_2DS_2-VASc-HS, $R_2CHA_2DS_2$-VASc, hemoglobin, CRP and ferritin. When compared with CHA_2DS_2-VASc-HS, the $R_2CHA_2DS_2$-VASc revealed a more significant mortality predictor

Table I. Demographic, admission clinical and laboratory parameters of the study cohort. Values are n (%), median (interquartile range [IQR]), or mean± standart deviation.

Variables	All population (n= 508)	Survivors (n= 440)	Non-survivors (n= 68)	p
Male gender, n (%)	270 (53.1)	225 (51.1)	45 (66.2)	0.021
Age, year	58±15.5	56.4±15.1	68.7±13.5	< 0.001
CAD, n (%)	74 (14.6)	57 (13)	17 (25)	0.009
Peripheral artery Disease, n (%)	13 (2,6)	7 (1.6)	6 (8.8)	<0.001
Heart Failure, n (%)	33 (6.5)	22 (5)	11 (16.2)	0.001
Hypertension, n (%)	234 (46.1)	188 (42.7)	46 (67.6)	<0.001
Diabetes Mellitus, n (%)	165 (32.5)	139 (31.6)	26 (38.2)	0.276
Hyperlipidemia, n (%)	96 (18.9)	78 (17.7)	18 (26.5)	0.087
Current Smoking, n (%)	150 (29.5)	120 (27.3)	30 (44.1)	0.005
COPD, n (%)	54 (10.6)	41 (9.3)	13 (19.1)	0.015
Cancer, n (%)	34 (6.7)	24 (5.5)	10 (14.7)	0.004
CVA, n (%)	15 (3)	11 (2.5)	4 (5.9)	0.125
Chronic renal failure, n (%)	58 (11.4)	31 (7)	27 (39.7)	<0.001
Atrial fibrillation, n (%)	27 (5.3)	18 (4.1)	9 (13.2)	0.002
Needing ICU, n (%)	97 (19.1)	40 (9.1)	57 (83.8)	<0.001
Invasive mechanical ventilation n (%)	64 (12.6)	11 (2.5)	53 (77.9)	<0.001
ARDS, n (%)	87 (17.1)	32 (7.3)	55 (80.9)	<0.001
Myocardial Injury n (%)	85 (16.7)	40 (9.1)	45 (66.2)	<0.001
Acute kidney injury n (%)	28 (5.5)	11 (2,5)	17 (25)	<0.001
Hospitalization period, days, median, [IQR]	8 [5-12]	8 [5-12]	11 [6-18]	<0.001
CHA2DS2-VASc, median, [IQR]	2 [1-3]	1 [1-3]	3 [2-5]	<0.001
CHA2DS2-VASc-HS, median, [IQR]	2 [1-4]	2 [1-3]	4 [2-6]	<0.001
R2CHA2DS2-VASc, median, [IQR]	2 [1-3]	2 [1-3]	4 [2-6]	<0.001
Uric acid, mg/dL	5.1±2.1	4.9±1.8	6.4±2.9	<0.001
eGFR, mL/min/1.73m2, median, [IQR]	94 [70-104]	97 [79-106]	62.5 [34-87.5]	< 0.001
WBC, 10^3/uL, median, [IQR]	6.2 [4.8-8.7]	6.0 [4.6-7.9]	8.9 [5.7-12.7]	<0.001
Lymphocyte, 10^3/uL, median, [IQR]	1.1 [0.8-1.6]	1.2 [0.9-1.7]	0.8 [0.5-1.0]	<0.001
Haemoglobin, g/dL	12.5±1.9	12.7±1.8	11.3±2.3	<0.001
Platelet, 10^3/uL	233±95	236±97	212±64	0.043
D-Dimer, μg FEU/mL, median, [IQR]	0.4 [0.2-0.8]	0.3 [0.2-0.7]	0.8 [0.5-1.6]	0.053
Ferritin, ng/mL, median, [IQR]	204 [88-406]	184 [84-370]	400 [172-903]	<0.001
CRP, mg/L, median, [IQR]	35.5 [12.9-97]	28 [11-83.5]	136 [62.3-206]	<0.001
Albumin, g/L	35.5±5.5	36.2±5.2	31.0 ±5.0	<0.001
hs-TnI, pg/mL, median, [IQR]	3.0 [1.1-10.0]	2.4 [1.0-7.0]	29.2 [10.3-88.9]	0.003

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident (stroke or transient ischemic attack); ICU, intensive care unit; ARDS, acute respiratory distress syndrome; eGFR, estimated glomerular filtration; WBC, white blood count; CRP, C-reactive protein; hs-TnI, high-sensitive troponin I.

Table II. Factors that were found to be independently associated with in-hospital mortality in univariate anaylsis and in model 1 multivariate cox regression analysis.

Variables	Univariate HR (95% CI)	p	Model 1 Multivariate[1] HR (95% CI)	p
CHA2DS2-VASc	1.237 (1.086-1.408)	0.001	1.155 (1.003-1.329)	0.045
CHA2DS2-VASc-HS	1.219 (1.086-1.367)	0.001	- -	- -
R2CHA2DS2-VASc	1.304 (1173-1.451)	<0.001	-	-
Cancer	2.419 (1.233-4.744)	0.010	1.370 (0.643-2.920)	0.415
Atrial Fibrillation	2.093 (1.035-4.231)	0.040	1.047 (0.433-2.533)	0.919
Haemoglobin	0.834 (0.751-0.927)	0.001	0.890 (0.808-0.981)	0.019
Lymphocyte	0.444 (0.255-0.772)	0.004	0.729 (0.429-1.239)	0.243
CRP	1.006 (1.003-1.009)	<0.001	1.005 (1.002-1.008)	<0.010
Albumin	0.418 (0.265-0.658)	<0.001	0.721 (0.408-1.273)	0.260
Ferritin	1.001 (1.000-1.001)	0.002	1.001 (1.000-1.001)	0.016

1 the variables with a p-value of less than 0.05 in the univariate analysis were incorporated into the multivariate cox regression analysis by using Backward LR method. Abbreviations: CRP, C-reactive protein..

(p: 0.037 for CHA$_2$DS$_2$-VASc-HS *vs.* p=0.001 for R$_2$CHA$_2$DS$_2$-VASc). In addition, although hemoglobin had been a significant marker in model 2

multivariate analysis (p=0.018); in model 3 multivariate analysis, it was found to be insignificantly (p=0.069) associated with mortality. On the other

Table III. Factors that were found to be independently associated with in-hospital mortality in model 2 and model 3 multivariate cox regression analysis.
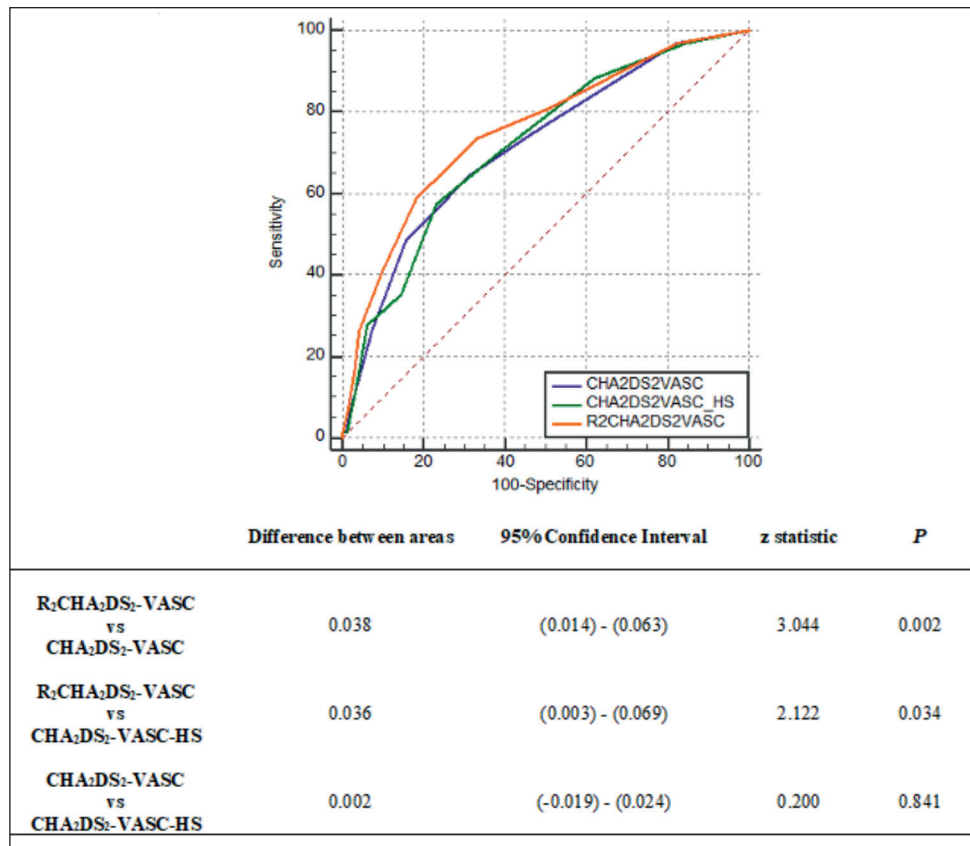
Variables	Model 2 Multivariate[1] HR (95% CI)	*p*	Model 3 Multivariate[1] HR (95% CI)	*p*
CHA2DS2-VASc-HS	1.139 (1.008-1.287)	0.037	-	-
R2CHA2DS2-VASc	-	-	1.219 (1.086-1.368)	0.001
Cancer	1.329 (0.624-2.831)	0.461	1.315 (0.621-2.784)	0.474
Atrial Fibrillation	1.073 (0.447-2.571)	0.875	0.804 (0.323-1.997)	0.638
Haemoglobin	0.891 (0.809-0.981)	0.018	0.911 (0.823- 1.007)	0.069
Lymphocyte	0.740 (0.435-1.259)	0.267	0.733 (0.433-1.240)	0.247
CRP	1.005 (1.002-1.008)	0.001	1.004 (1.001-1.007)	0.003
Albumin	0.715 (0.405-1.262)	0.247	0.759 (0.435-1.325)	0.332
Ferritin	1.001 (1.000-1.001)	0.036	1.001 (1.000-1.001)	0.017

[1]the variables with a p-value of less than 0.05 in the univariate analysis were incorporated into the multivariate cox regression analysis by using Backward LR method. **Abbreviations:** CRP, C-reactive protein.

hand, CRP and ferritin values were significantly associated with in-hospital mortality in model 2 and 3 multivariate analysis.

Comparison of the ROC curves of the $R_2CHA_2DS_2$-VASc (AUC:0.76, CI 95% 0.72-0.79, *p*<0.001), CHA_2DS_2-VASc (AUC: 0.72, CI 95% 0.68-0.76, *p*<0.001), and CHA_2DS_2-VASc-HS (AUC:0.72, CI 95% 0.68-0.76, *p*<0.001) for detecting the in-hospital mortality are presented on Figure 1. We detected a statistically significant difference when $R_2CHA_2DS_2$-VASc was compared with CHA_2DS_2-VASc and CHA_2DS_2-VASc-HS

	Difference between areas	95% Confidence Interval	z statistic	P
$R_2CHA_2DS_2$-VASC vs CHA_2DS_2-VASC	0.038	(0.014) - (0.063)	3.044	0.002
$R_2CHA_2DS_2$-VASC vs CHA_2DS_2-VASC-HS	0.036	(0.003) - (0.069)	2.122	0.034
CHA_2DS_2-VASC vs CHA_2DS_2-VASC-HS	0.002	(-0.019) - (0.024)	0.200	0.841

Figure 1. Comparison of the ROC curves of the R2CHA2DS2-VASc (AUC:0.76, CI 95% 0.72-0.79, *p*<0.001), CHA2DS2-VASc (AUC:0.72, CI 95% 0.68-0.76, *p*<0.001), and CHA2DS2-VASc-HS (AUC:0.72, CI 95% 0.68-0.76, *p*<0.001) for detecting the in-hospital mortality.
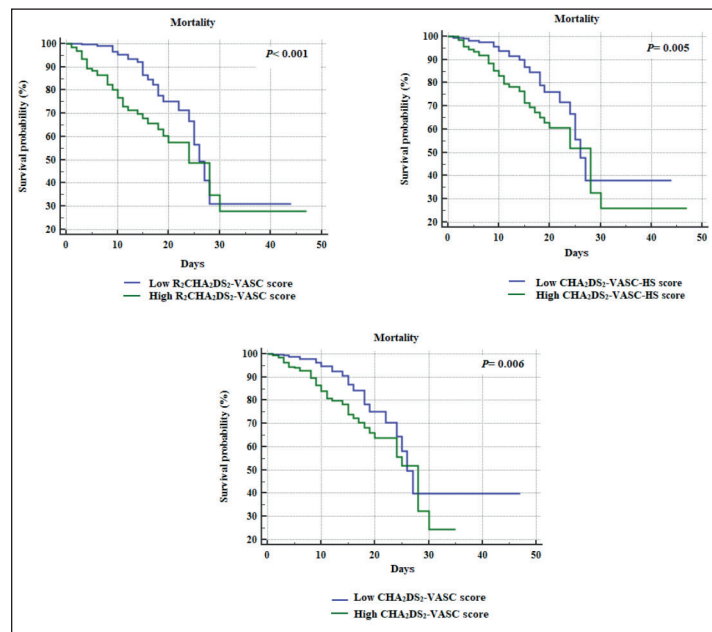
Figure 2. Kaplan-Meier plots of survival curves of patients with low- and high CHA2DS2-VASc, CHA2DS2-VASc-HS and R2CHA2DS2-VASc score categories.

(respectively $p=0.002$, $p=0.034$); however, the difference between CHA_2DS_2-VASc and CHA_2DS_2-VASc-HS was not significant ($p=0.841$). Kaplan-Meier plots of survival curves of patients with low- and high CHA_2DS_2-VASc, CHA_2DS_2-VASc-HS and $R_2CHA_2DS_2$-VASc score categories are presented on Figure 2. The sensitivity and specificity of each scoring system on mortality was seperately calculated. The AUC at ROC curves was calculated 0.72 (95% CI: 0.68-0.76) cut off> 2 for CHA_2DS_2-VASc which indicated 65% sensitivity and 68% specificity for mortality. The sensitivity of CHA_2DS_2-VASc-HS was 57% whereas its specificity was higher when compared with the CHA_2DS_2-VASc (77%), [AUC: 0.72 (95% CI: 0.68-0.76) cut off> 3]. On the other hand, the sensitivity of $R_2CHA_2DS_2$-VASc on mortality (59%) was similar with CHA_2DS_2-VASc-HS; however, its specificity to predict mortality was 82%, which was higher than CHA_2DS_2-VASc and CHA_2DS_2-VASc-HS [AUC: 0.76 (95%CI: 0.72-0.79) cut off> 3].

Discussion

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was first described by China in Wuhan and the virus has spread to the other regions of country as well as 210 countries and territories worldwide[9]. World Health Organization (WHO) officially declared disease as a pandemic on March 11, 2020[10]. The mortality rates secondary to COVID-19 has increased since then; however, the predictors of mortality remained controversial[10]. The main focus of studies had been severity, treatment and prevention of disease rather than the additional factors which may lead to death[10].

The literature includes various studies that examine the relationship between comorbidities and mortality rates in coronavirus disease. In a meta-analysis by Parohan et al[9], the older age ($\geq$65 years old) was found associated with higher mortality in COVID-19. The reason of severity of the disease in elderly population potentially depends on defects of B-cell and T-cell function, prolonged proinflammatory responses due to increased production of type 2 cytokines and defect in control of viral replication. Also, elderly patients may posses more comorbidities[9]. Some studies suggested that in older male patients, the progression of COVID-19 infection is more serious. The differences of sex hormones may affect the responses of immunity and influence the severity of disease[9].

In a study by Tian et al[10], the mortality rates were significantly higher in the patients with hypertension, coronary heart disease and diabetes mellitus. The non-survivor patients had increased levels of cardiac troponin, CRP, interleukin-6,

creatinine, alanine transaminase and decreased levels of albumin[10]. Hypertension was the most prevalent comorbidity in non-survivors as well as the second one had been diabetes mellitus. The cardiometabolic disease, increased acute inflammation and end-organ damage such as cardiac, renal, liver and hematologic pathologies were found to be associated with higher mortality rates in patients with COVID-19 infection[10]. Again, in a study by Wang et al[11] the patients with hypertension, diabetes mellitus, cardiovascular disease, or cerebrovascular disease were found associated with increased risk of mortality. Also chronic obstructive pulmonary disease was significantly associated with higher severity of COVID 19 disease determined by the same authors[11].

Up to date hypertension, diabetes mellitus, coronary artery disease, cerebrovascular disease, chronic obstructive pulmonary disease, and kidney dysfunction have been found to be associated with worse clinical outcomes in the patients with COVID-19 infection[12]. Besides, disease may lead to vascular complications due to advanced inflammation, hypoxia, immobilization, and diffuse intravascular coagulation. Vascular complications include both arterial and venous thromboembolic events. The inflammatory reaction may damage microvascular system and cause vasculitis and micro thrombosis due to abnormal activation of the coagulation system[13].

CHA_2DS_2-VASc score is used to predict stroke risk in patients with non-valvular atrial fibrillation (AF). Antithrombotic therapy is determined according to the results of score system[14]. The score system includes congestive heart failure, hypertension, age, diabetes mellitus, previous stroke/transient ischemic attack, vascular disease, and gender categories[12]. The system has been modified, detailed and improved in years. The CHA_2DS_2-VASc -CF score system includes family history and smoking habits, the CHA_2DS_2-VASc -HS score includes hyperlipidaemia and smoking[14] and $R_2CHA_2DS_2$-VASc score includes renal functions[15]. CHA_2DS_2-VASc score system has also been used in various cardiovascular disease scenarios such as acute coronary syndrome or acute stent thrombosis in patients with stable coronary artery disease to predict the risk of adverse cardiovascular events[12]. As the COVID-19 is strongly associated with widespread thromboembolic events through out the body, with the same rationelle of using CHA_2DS_2-VASc score and its further modifications in risk assessment secondary to cardioembolic events, literature includes

sparse application of modified CHA_2DS_2-VASc risk score in predicting mortality in patients hospitalized with COVID-19 [7].

In our study, we sought to investigate the COVID-19 related mortality using CHA_2DS_2-VASc, CHA_2DS_2-VASc -HS and $R_2CHA_2DS_2$-VASc score systems as well as to test the superiority of each score over the others. We detected that the mortality rates were higher in the patients with advanced age, coronary artery disease, peripheral artery disease, heart failure, hypertension and current smoking in accordance with the literature. By contrast, diabetes mellitus and hyperlipidemia were not significantly associated with mortality in our study. Additionally, a significant correlation between mortality and CHA_2DS_2-VASc and its variants was observed; however, $R_2CHA_2DS_2$-VASc was found to be more specific when compared with CHA_2DS_2-VASc and CHA_2DS_2-VASc-HS with similar sensitivity rates of the three forms.

Limitations

There are certain limitations of the study. The CHA_2DS_2-VASc scores are originally validated for thromboembolic stroke in patients with non-valvular atrial fibrillation. Since the COVID-19 is also associated with thromboembolic events, the justification regarding thrombotic phenomena may be questionable. However, literature includes many reports regarding the use of CHA_2DS_2-VASc and its variants in different cardiovascular scenarios and as well as recently for mortality prediction in COVID-19 disease[7]. Another limitation regards to the retrospective nature of the study. As a last limitation the sample size may be accepted as relatively small in the era of COVID-19 pandemics.

Conclusions

Although there have been many studies to examine the severity of disease, the literature includes many disorganized information about the pathology. When the mortality risk of disease is considered, the literature needs more and well-organized studies about the predictor factors of mortality in COVID-19 infection. The patients should be evaluated according to the risk factors and also some patients with high risk may be treated against the risk of thromboemboli to protect from vascular complications. Although multicenter and long-term studies are warranted,

depending on the need of a current score system about predictibility, the CHA_2DS_2-VASc and its variants may meet the need of a score system by including the approved risk factors of mortality of COVID-19 infection. However, our results indicated that the $R_2CHA_2DS_2$-VASc had higher specificity for mortality prediction than CHA_2DS_2-VASc and CHA_2DS_2-VASc-HS in patients with COVID-19. The system is applicable in clinical practice and the predictibility plays an important role in risk identification, treatment strategies, and management of healthcare resources during the COVID-19 pandemic.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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