



ORIGINAL ARTICLE

The Surrogate Marker for Coronary Thrombus Burden in Acute Coronary Syndrome Patients with COVID-19: The CHA₂DS₂-VAS_c Score

COVID-19'lu Akut Koroner Sendrom Hastalarında Koroner Trombüs Yükü İçin Bir Dolaylı Gösterge: CHA₂DS₂-VAS_c Skoru

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ABSTRACT

Aim: This study investigated whether the CHA₂DS₂-VAS_c score is an independent predictor of high thrombus burden and mortality in patients presenting with acute coronary syndrome (ACS) and Coronavirus Disease (COVID-19).

Materials and Methods: Patients with acute coronary syndrome (ACS) and COVID-19 (n = 76) were included in the study. They were categorized into low thrombus burden (LTB; grades 1-3) and high thrombus burden (HTB; grades 4 and 5) groups according to the final thrombus score. The CHA₂DS₂-VAS_c scores were then compared between the two groups.

Results: Post-procedural HTB developed in 50 patients (65.7%). The neutrophil-to-lymphocyte ratio (6.00 ± 3.73 vs. 11.45 ± 10.6; P < 0.05), creatinine (0.84 ± 0.22 vs. 1.51 ± 0.92 mg/dL; P < 0.05), blood urea nitrogen (42.27 ± 12.6 vs. 62.27 ± 48.2 mg/dL; P < 0.05), potassium (4.06 ± 0.35 vs. 4.51 ± 0.49 mEq/L; P < 0.05), ferritin (286 ± 55.2 vs. 730 ± 96.8 ng/mL; P < 0.05), interleukin-6 (18.12 ± 7.14 vs. 186.66 ± 56.8 pg/mL; P < 0.05), lactate dehydrogenase (425.7 ± 31.2 vs. 1002.7 ± 173.4 U/L; P < 0.05), and CHA₂DS₂-VAS_c score (2.84 ± 1.27 vs. 4.08 ± 1.61; P < 0.05) were significantly higher in the HTB group. Mortality [3 (11.5%) vs 23 (46.0%), P < 0.05] and CHA₂DS₂-VAS_c score (2.84 ± 1.27 vs 4.08 ± 1.61, P < 0.05) were higher in the HTB group (Table 1).

Conclusions: In this study, the easily calculated CHA₂DS₂-VAS_c score was an independent predictor of HTB in patients with COVID-19 presenting with ACS. In addition, it predicted mortality in the same patient group.

Keywords: Acute coronary syndrome, CHA₂DS₂-VAS_c score, COVID-19, high thrombus burden, low thrombus burden

ÖZ

Amaç: Bu çalışmada, akut koroner sendrom (AKS) ve Koronavirüs hastalığı (COVID-19) ile başvuran hastalarda CHA₂DS₂-VAS_c skorunun yüksek trombüs yükü ve mortalitenin bağımsız bir belirleyicisi olup olmadığını araştırılmıştır.

Gereç ve Yöntemler: AKS ve COVID-19 tanılı hastalar (n = 76) çalışmaya dahil edildi. Hastalar, son trombüs skoruna göre düşük trombüs yükü (DTY; derece 1-3) ve yüksek trombüs yükü (YTY; derece 4-5) olarak iki gruba ayrıldı. CHA₂DS₂-VAS_c skorları bu iki grup arasında karşılaştırıldı.

Bulgular: İşlem sonrası 50 hastada (%65,7) YTY tespit edildi. Nötrofil/lenfosit oranı (6.00 ± 3.73 vs. 11.45 ± 10.6; P < 0.05), kreatinin (0.84 ± 0.22 vs. 1.51 ± 0.92 mg/dL; P < 0.05), kan üre azotu (42.27 ± 12.6 vs. 62.27 ± 48.2 mg/dL; P < 0.05), potasyum (4.06 ± 0.35 vs. 4.51 ± 0.49 mEq/L; P < 0.05), ferritin (286 ± 55.2 vs. 730 ± 96.8 ng/mL; P < 0.05), interleukin-6 (18.12 ± 7.14 vs. 186.66 ± 56.8 pg/mL; P < 0.05), laktat dehidrojenaz (425.7 ± 31.2 vs. 1002.7 ± 173.4 U/L; P < 0.05) ve CHA₂DS₂-VAS_c skoru (2.84 ± 1.27 vs. 4.08 ± 1.61; P < 0.05) HTB grubunda anlamlı olarak daha yüksekti. Mortalite [3 (%11,5) vs. 23 (%46,0), P < 0.05] ve CHA₂DS₂-VAS_c skoru (2.84 ± 1.27 vs. 4.08 ± 1.61, P < 0.05) YTY grubunda daha yüksekti (Tablo 1).

Sonuçlar: Bu çalışmada, kolayca hesaplanabilen CHA₂DS₂-VAS_c skoru, COVID-19 ile birlikte AKS ile başvuran hastalarda YTY için bağımsız bir öngördürücü olarak bulundu. Ayrıca aynı hasta grubunda mortaliteyi de öngördürmekte olduğu izlenmiştir.

Anahtar Kelimeler: Akut koroner sendrom, CHA₂DS₂-VAS_c skoru, COVID-19, düşük trombüs yükü, yüksek trombüs yükü

Introduction

In December 2019, the first outbreak of Coronavirus Disease (COVID-19) was reported in Wuhan, China, and it quickly spread worldwide. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020 [1]. On the same day, the Ministry of Health of Türkiye announced the country's first confirmed COVID-19 case. Cardiovascular manifestations of COVID-19 include acute coronary syndrome (ACS), myocarditis, pericarditis, pericardial effusion, heart failure, and arrhythmias [2]. One proposed mechanism of myocardial injury involves the expression of angiotensin-converting enzyme 2 (ACE2) in the heart and coronary arteries, which leads to local inflammation, hypercoagulability, and thrombosis [3]. In patients with COVID-19, systemic inflammation promotes thrombosis, thereby triggering procoagulant activity and endothelial dysfunction [4]. Coagulation abnormalities have been identified in patients with COVID-19 and are associated with increased mortality and thrombotic complications, including acute limb ischemia, stroke, pulmonary embolism, venous thromboembolism, and catheter-associated thrombosis [5]. A nationwide study in Denmark involving more than 5,000 patients with COVID-19 found a 5.9-fold increase in myocardial infarction compared to a control group [6]. Another investigation reported higher incidences of cardiac multivessel thrombosis in patients with COVID-19 [7]. Coronary procedural complications, such as no-reflow and stent thrombosis, have been associated with a large thrombus burden [8]. A high thrombus burden is a major factor influencing prognosis in patients with ST-segment elevation myocardial infarction (STEMI) [8]. The presence of pre-procedural thrombus is also associated with poor short-term clinical outcomes, including higher rates of death and myocardial infarction in patients with non-ST-segment elevation myocardial infarction (NSTEMI) [9].

Approximately 10–30% of patients with acute coronary syndrome (ACS) experience the no-reflow phenomenon, which is defined as insufficient myocardial perfusion despite successful mechanical reopening of the occluded segment by percutaneous coronary intervention (PCI) [10]. Proposed mechanisms underlying no-reflow include vasospasm, microvascular obstruction, and distal embolization of thrombi [11].

In patients with non-valvular atrial fibrillation (AF), the CHA₂DS₂-VAS_c score is a straightforward, reliable, readily available, and practical classification system used to assess cardioembolic risk and guide anticoagulant therapy [12]. The score incorporates

factors such as congestive heart failure/left ventricular dysfunction, hypertension, age ≥ 75 years, diabetes mellitus, stroke/transient ischemic attack/systemic embolism, vascular disease, age 65–74 years, and sex category. A recent study indicated that the CHA₂DS₂-VAS_c score is a predictor of mortality in patients with COVID-19 [13]. It has also been shown that in patients with STEMI, the CHA₂DS₂-VAS_c score predicts high thrombus burden, no-reflow phenomenon, and both short- and long-term mortality [14–16]. Several parameters included in the CHA₂DS₂-VAS_c score, such as congestive heart failure, hypertension, and diabetes, are closely associated with microvascular dysfunction [17,18].

In this study, we aimed to investigate the ability of the CHA₂DS₂-VAS_c score to predict coronary thrombus burden and the no-reflow phenomenon in patients with acute coronary syndrome (ACS) and COVID-19.

Materials and Methods

Study Population

This retrospective, cross-sectional study included 76 patients diagnosed with acute coronary syndromes (STEMI and NSTEMI) and COVID-19 at our tertiary care hospital between March 2020 and June 2021 [19]. Patients were monitored throughout their hospital stay and for one month after discharge.

Patients' medical records were reviewed to collect baseline clinical and demographic data, including hypertension (HT), diabetes mellitus (DM), family history, hyperlipidemia (HL), smoking status, chronic heart failure, prior cerebrovascular accident (CVA), chronic renal disease (CRD), and peripheral arterial disease. COVID-19 diagnosis was confirmed either by detection of SARS-CoV-2 via nasal or pharyngeal swabs or by diagnostic chest imaging performed before the onset of COVID-19 symptoms. Exclusion criteria included hypercoagulable disorders, end-stage cancer, severe frailty as determined by the attending physician, pregnancy, death upon admission, age under eighteen years, and missing baseline data.

Prior to cardiac catheterization, baseline serological samples were obtained from all patients with acute coronary syndrome (ACS). These samples were used to measure levels of interleukin-6 (IL-6), high-sensitivity C-reactive protein, D-dimer, ferritin, albumin, and high-sensitivity (hs)-troponin T. The CHA₂DS₂-VAS_c score was calculated by assigning one point for each of the following: female sex, age between 65 and 74 years, history of hypertension (HT), diabetes mellitus (DM), heart failure (left ventricular

ejection fraction <40%), and vascular disease (myocardial infarction, complex aortic plaque, carotid disease, or peripheral artery disease); and two points for each of the following: age >75 years, history of stroke, or transient ischemic attack [12].

Angiographical Examination

Two experienced interventional cardiologists, blinded to the patients' clinical information, independently reviewed the coronary angiograms. Coronary angiography was performed using the Judkins technique via either the radial or femoral approach.

High thrombus burden was defined as a thrombolysis in myocardial infarction (TIMI) thrombus score >4, assessed using the TIMI thrombus grading scale (Table 1). Thrombus grade was determined immediately upon restoration of antegrade flow using a guidewire or gentle balloon dilatation in patients whose baseline angiography revealed an occluded infarct-related artery (IRA). Patients were classified into two groups based on their final thrombus score: low thrombus burden (LTB; grades 1–3) and high thrombus burden (HTB; grades 4 and 5) [20,21]. If IRA blood flow remained at TIMI 2 despite successful intervention and in the absence of mechanical complications, patients were considered to have the no-reflow phenomenon [10]. This retrospective study was approved by both the local ethics committee and the Republic of Türkiye Ministry of Health (No: Eİ-21-1941).

Statistical Analysis

All statistical analyses were performed using SPSS for Windows, version 19.0 (SPSS Inc., Chicago, IL). Sample size estimation was conducted with R version 3.0.1, an open-source application, indicating that at least 44 participants were required to achieve 90% power with a Type I error rate of 0.05. This calculation yielded an effect size of ± 0.18 . Descriptive statistics were expressed as mean, standard deviation, rates, and frequencies. The Kolmogorov–Smirnov test was used to assess the normality of continuous variable distributions. Parametric data were analyzed using the Student's t-test, while nonparametric data were analyzed with the Mann–Whitney U test. Categorical variables were compared between groups using the χ^2 test. Statistical significance was defined as $P < 0.05$. Logistic regression analysis was used to evaluate the effects of factors, with 95% confidence intervals and standardized beta coefficients reported.

Results

Demographic, clinical, angiographic, and laboratory findings of the patients are presented in Table 1.

The clinical characteristics of the two groups were statistically similar. Among the laboratory parameters, the neutrophil-to-lymphocyte ratio (6.00 ± 3.73 vs. 11.45 ± 10.6 ; $P < 0.05$), creatinine (0.84 ± 0.22 vs. 1.51 ± 0.92 mg/dL; $P < 0.05$), blood urea nitrogen (42.27 ± 12.6 vs. 62.27 ± 48.2 mg/dL; $P < 0.05$), potassium (4.06 ± 0.35 vs. 4.51 ± 0.49 mEq/L; $P < 0.05$), ferritin (286 ± 55.2 vs. 730 ± 96.8 ng/mL; $P < 0.05$), IL-6 (18.12 ± 7.14 vs. 186.66 ± 56.8 pg/mL; $P < 0.05$), and lactate dehydrogenase (425.7 ± 31.2 vs. 1002.7 ± 173.4 U/L; $P < 0.05$) were significantly higher in the HTB group than in the LTB group (Table 1).

Among the angiographic findings, the culprit lesion was most commonly located in the left anterior descending (LAD) coronary artery in the HTB group (9 [34.6%] vs. 30 [60.0%]; $P < 0.05$), while it was most common in the right coronary artery (RCA) in the LTB group (15 [57.7%] vs. 15 [30.0%]; $P < 0.05$). No significant differences were observed between the two groups regarding culprit lesions in other coronary arteries (Table 1).

Mortality [3 [11.5%] vs. 23 [46.0%]; $P < 0.05$] and the CHA₂DS₂-VAS_c score (2.84 ± 1.27 vs. 4.08 ± 1.61 ; $P < 0.05$) were significantly higher in the HTB group (Table 1).

Parameters considered as potential risk factors for a high thrombus burden were evaluated using logistic regression analysis. The variables included were neutrophil-to-lymphocyte ratio, creatinine, blood urea nitrogen, potassium, ferritin, IL-6, lactate dehydrogenase, and the CHA₂DS₂-VAS_c score. Each risk factor was first assessed with univariate analysis to examine its association with HTB. Variables demonstrating significant associations in univariate analysis—neutrophil-to-lymphocyte ratio, creatinine, blood urea nitrogen, potassium, IL-6, and CHA₂DS₂-VAS_c score—were subsequently included in a multivariate model. Multivariate logistic regression analysis demonstrated that a higher CHA₂DS₂-VAS_c score (odds ratio [OR]: 1.673; 95% confidence interval [CI]: 0.886–3.162; $P < 0.05$) and elevated interleukin-6 levels (OR: 1.049; 95% CI: 0.979–1.125; $P < 0.05$) were independent predictors of HTB (Table 2).

Multivariate logistic regression analysis also demonstrated that a higher CHA₂DS₂-VAS_c score (odds ratio [OR]: 1.673; 95% confidence interval [CI]: 0.886–3.162; $P < 0.05$), a higher thrombus grade score (OR: 2.412; 95% CI: 1.021–4.459; $P < 0.05$), and elevated lactate dehydrogenase levels (OR: 1.007; 95% CI: 1.000–1.015; $P < 0.05$) were independent predictors of mortality (Table 3).

Table 1. Characteristics and laboratory parameters of the study groups.

Variables	Low thrombus (n=26)	High thrombus (n=50)	p value
Age, year	67.0 ± 11.2	71.4 ± 13.0	0.208
Female, n(%)	8 (30.8%)	24 (48.0%)	0.149
STEMI, n(%)	18 (69.2%)	38 (76.0%)	0.430
PCR test positive, n(%)	9 (34.6)	15 (30.0)	0.681
CT diagnosis, n(%)	20 (76.9%)	42 (84.0%)	0.450
Coronary artery disease, n(%)	9 (34.6)	25 (50.0%)	0.201
Diabetes mellitus, n(%)	12 (46.2%)	32 (64.0%)	0.135
Hypertension, n(%)	14 (53.8%)	36 (72.0%)	0.114
Heart failure, n(%)	2 (7.7%)	8 (16.0%)	0.262
Chronic kidney disease, n(%)	0 (0.0%)	2 (4.0%)	0.544
Cerebrovascular accident, n(%)	0 (0.0%)	5 (10.0%)	0.159
Chronic obstructive pulmonary disease, n(%)	0 (0.0%)	4 (8.0%)	0.292
Laboratory Findings			
Peak troponin, ng/L	11740 ± 9281	16211 ± 9843	0.060
Hemoglobin, g/dL	13.4 ± 1.6	13.9 ± 1.7	0.212
White blood cell, 10 ³ /mm ³	17.2 ± 2.6	16.7 ± 2.5	0.923
Platelet, 10 ³ /mm ³	286 ± 93	276 ± 107	0.676
Lymphocyte, 10 ³ /mm ³	1.39 ± 0.72	1.20 ± 0.83	0.326
Neutrophile to lymphocyte ratio	6.00 ± 3.73	11.45 ± 10.6	0.016
Platelet to lymphocyte ratio	268.3 ± 110.6	261.6 ± 204.1	0.876
Creatinine, mg/dL	0.84 ± 0.22	1.51 ± 0.92	0.040
Blood Urea Nitrogen, mg/dL	42.27 ± 12.6	62.27 ± 48.2	0.042
Sodium, mEq/L	139.1 ± 2.3	138.4 ± 6.1	0.569
Potassium, mEq/L	4.06 ± 0.35	4.51 ± 0.49	<0.001
HDL-C, mg/dL	30.5 ± 7.3	31.9 ± 8.2	0.485
LDL-C, mg/dL	100.5 ± 33.0	97.9 ± 34.6	0.767
Triglyceride, mg/dL	133.3 ± 68.0	157.8 ± 91.3	0.265
Alanine transaminase, U/L	32.2 ± 13.2	119.8 ± 81.3	0.173
Ferritin, ml/ng	286 ± 55.2	730 ± 96.8	0.026
Interleukin 6, pg/ml	18.12 ± 7.14	186.66 ± 56.8	0.001
Lactate dehydrogenase, U/L	425.7 ± 31.2	1002.7 ± 173.4	0.004
CRP, mg/L	91.1 ± 39.5	107.7 ± 57.3	0.395
Albumin, g/dL	38.4 ± 4.8	38.1 ± 5.1	0.827
CRP to albumin ratio	2.56 ± 1.8	2.92 ± 1.7	0.510
D-Dimer, ng/mL	6.80 ± 4.5	8.07 ± 5.2	0.750
Mortality, n(%)	3 (11.5)	23 (46.0)	0.003
Angiographic Findings			
Culprit Lesion, n(%)			
LAD	9 (34.6)	30 (60.0)	0.036
CX	0 (0.0)	5 (10.0)	0.159
RCA	15 (57.7)	15 (30.0)	0.019
Saphenous graft	2 (7.7)	0 (0.0)	0.114
Additional coronary lesion, n(%)	15 (57.7%)	24 (48.0%)	0.846
No-Reflow Phenomenon, n(%)	0 (0.0%)	8 (16.0%)	0.028
Thrombus grade score	2.63 ± 0.49	4.62 ± 0.49	<0.001
SYNTAX score	12.8 ± 7.5	16.0 ± 9.0	0.137
CHA ₂ DS ₂ -VAS _c score	2.84 ± 1.27	4.08 ± 1.61	<0.001

Data are given as mean ± SD, n, as a percentage [n (%)]. STEMI, ST-elevation myocardial infarction; PCR, polymerase chain reaction; CT, computed tomography; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, C-reactive protein; LAD, left anterior descending artery, CX, circumflex artery; RCA, right coronary artery.

Table 2. Multivariate linear regression analysis showing the predictors of high thrombus burden.

Variables	Univariable		Multivariable	
	Beta (95% CI)	p value	Beta (95% CI)	p value
Neutrophile to lymphocyte ratio	1.029 (1.017- 1.254)	0.023	1.063 (0.850- 1.331)	0.591
Creatinine	18.713 (2.334-141.576)	0.006	0.552 (0.028-11.065)	0.698
Blood urea nitrogen	1.021 (1.000-1.043)	0.049	1.012 (0.955-1.073)	0.685
Potassium	9.826 (2.728-35.390)	<0.001	2.604 (0.292-23.198)	0.391
Ferritin	1.001 (1.000-1.002)w	0.168	-	-
Interleukin 6	1.060 (1.008-1.115)	0.015	1.049 (0.979-1.125)	0.047
Lactate dehydrogenase	1.001 (1.000-1.003)	0.056	-	-
CHA ₂ DS ₂ -VAS _c score	1.782 (1.225-2.591)	<0.001	1.673 (0.886-3.162)	0.005

CI, confidence interval; OR, Odds ratio.

Table 3. Multivariate linear regression analysis showing the predictors for mortality

Variables	Univariable		Multivariable	
	Beta (95% CI)	p value	Beta (95% CI)	p value
Neutrophile to lymphocyte ratio	1.031 (1.030- 1.200)	0.023	1.349 (0.915- 1.990)	0.131
Creatinine	8.403 (1.780-39.661)	0.007	15.773 (1.334-153.896)	0.181
Blood urea nitrogen	1.044 (1.019-1.069)	<0.001	0.878 (0.705-1.093)	0.244
Potassium	11.727 (2.986-46.064)	<0.001	2.300 (0.007-761.096)	0.778
Ferritin	1.002 (1.001-1.004)	0.002	1.001 (0.996-1.005)	0.735
Interleukin 6	1.008 (1.002-1.015)	0.013	1.022 (0.999-1.045)	0.065
Lactate dehydrogenase	1.004 (1.002-1.006)	<0.001	1.007 (1.000-1.015)	0.038
Thrombus grade score	1.852 (1.098-3.124)	<0.001	2.412 (1.021-4.459)	0.002
CHA ₂ DS ₂ -VAS _c score	1.858 (1.259-2.743)	<0.001	1.673 (0.886-3.162)	0.005

CI, confidence interval; OR, Odds ratio.

Discussion

This is the first study to evaluate the ability of the CHA₂DS₂-VAS_c score to predict high coronary thrombus burden and mortality in patients with acute coronary syndrome (ACS) and COVID-19.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the virus responsible for the COVID-19 pandemic [22]. Research has demonstrated two main pathways through which respiratory infections are linked to cardiovascular events, particularly coronary syndromes: hypoxemia and a proinflammatory state [23]. Recent studies have shown that serum levels of angiotensin II increase in direct proportion to SARS-CoV-2 viral load. Additionally, angiotensin II, together with the renin-angiotensin-aldosterone system, is known to exacerbate the systemic inflammatory response and significantly impact the coagulation cascade in COVID-19 [24]. Neutrophil extracellular traps (NETs) may also play a significant role in promoting inflammation and thrombosis in COVID-19 [25,26]. Due to aberrant stimulation of the coagulation system, the inflammatory response may damage the microvascular system, resulting in microthrombosis and vasculitis. This state is associated with severe COVID-19 [27,28]. Patients presenting with ACS during COVID-19 infection and exhibiting increased thrombogenicity have been found to have a larger

thrombus burden and a higher frequency of stent thrombosis, indicating a prothrombotic condition [7]. According to a recent study, patients had a five-fold higher risk of developing ACS within 14 days following a positive SARS-CoV-2 test [6].

Thrombus burden has been the subject of numerous previous studies. Toprak et al. investigated the association between the HbA1c/C-peptide ratio and angiographic thrombus burden, as well as short-term mortality, in patients presenting with ST-elevation myocardial infarction (STEMI) [29]. In another study, Toprak et al. examined the relationship between SCUBE1 levels and thrombotic complications, disease severity, and in-hospital mortality in COVID-19 patients, demonstrating that SCUBE1, a thrombotic marker, is an indicator of mortality in this population [30]. Similar studies on thrombus burden have identified various associated markers [31,32]. In patients with STEMI treated with drug-eluting stents, a large thrombus burden has been linked to very high rates of early and late IRA stent thrombosis, as well as higher 30-day mortality due to worse procedural outcomes [8]. Recent research indicates that the CHA₂DS₂-VAS_c score is independently associated with the severity of coronary artery disease, in-hospital, 12-month, and long-term mortality in STEMI patients, as well as an elevated all-cause mortality rate in patients with ACS after one year [33]. According to research by Barman et al., coronary artery ectasia

(CAE) is associated with the CHA₂DS₂-VAS_C score [15,34]. Seyis et al. reported that the CHA₂DS₂-VAS_C score is an independent predictor of intracoronary thrombus burden in patients with STEMI [35]. Similarly, Satilmis et al. demonstrated that NSTEMI patients with high thrombus burden in the IRA had significantly higher CHA₂DS₂-VAS_C scores compared to those with minimal thrombus burden [16]. The CHA₂DS₂-VAS_C score has also been linked to stent thrombosis in previous studies [36]. In treatments involving saphenous vein grafts, Maden et al. found that the CHA₂DS₂-VAS_C score was an independent predictor of significant thrombus burden and the no-reflow phenomenon [37,38]. Another study demonstrated that baseline troponin I levels, elevated CRP levels, lower serum albumin levels, higher CRP-to-albumin ratios, and higher neutrophil-to-lymphocyte ratios were all independent predictors of significant thrombus burden in ACS patients [39–41]. Choudry et al. reported that initial D-dimer levels are correlated with coronary thrombus burden and myocardial blush grade [7].

Insufficient myocardial perfusion despite mechanical reopening of the culprit lesion via percutaneous coronary intervention (PCI) is referred to as the “no-reflow” phenomenon. Proposed mechanisms underlying no-reflow include microvascular spasm, distal embolization, and microvascular obstruction caused by thrombosis [42, 43]. Components of the CHA₂DS₂-VAS_C score—such as diabetes mellitus, hypertension, heart failure, and female sex—are known risk factors for coronary microvascular dysfunction [17, 18]. Previous studies have suggested that the CHA₂DS₂-VAS_C score is an independent predictor of no-reflow during PCI in patients with STEMI and NSTEMI [44].

As a result, anticipating intracoronary thrombus burden prior to angiography may enable interventional cardiologists to take proactive measures to manage PCI-related complications in a timely manner. The CHA₂DS₂-VAS_C score is a simple and easily measurable tool that may help estimate thrombus burden in patients with a history of COVID-19 and MI. Additionally, it may serve as an indicator of early mortality. To confirm this relationship, further studies with larger patient populations are warranted.

Limitations of the Study

Our study has several important limitations that should be acknowledged. First, the retrospective and observational design inherently limits the ability to establish causal relationships between the CHA₂DS₂-

VAS_C score and high thrombus burden or mortality in ACS patients with COVID-19. While we observed significant associations, residual confounding cannot be excluded, given that not all potential confounders may have been measured or adjusted for in our analyses. Second, the relatively small sample size (n=76) limits the statistical power of the study and may increase the risk of type II errors. The limited sample also reduces the generalizability of our findings to broader or more diverse populations. Future studies with larger, multicenter cohorts are needed to validate our results. Third, our study was conducted at a single tertiary center, which may introduce selection bias and limit external validity. The patient population, treatment strategies, and local practice patterns may differ from those in other regions or health systems. Fourth, the follow-up duration was relatively short (up to one month after discharge), preventing assessment of longer-term outcomes such as reinfarction, late stent thrombosis, or long-term mortality. Therefore, the prognostic value of the CHA₂DS₂-VAS_C score over extended periods remains untested. Fifth, our diagnostic approach for COVID-19 included patients diagnosed either by PCR testing or by imaging criteria (CO-RADS scores). However, we did not differentiate outcomes between those with PCR-confirmed infection and those diagnosed radiologically. This heterogeneity in diagnostic criteria may have introduced misclassification bias. Sixth, although we assessed several inflammatory and biochemical markers, unmeasured confounding variables such as the use of specific antithrombotic or anti-inflammatory treatments, differences in revascularization techniques, or timing of presentation could have influenced both thrombus burden and outcomes. Finally, while our analysis suggests the CHA₂DS₂-VAS_C score may be useful for predicting high thrombus burden and mortality, this score was originally developed for risk stratification in atrial fibrillation and not specifically for ACS or COVID-19 populations. Its performance and clinical utility in this context require further prospective validation. Future studies should also explore whether incorporating COVID-19-specific markers or comorbidity indices could improve risk prediction in this unique patient population.

Conclusion

In this study, the easily calculated CHA₂DS₂-VAS_C score was an independent predictor of HTB in patients with COVID-19 presenting with ACS. In addition, it predicted mortality in the same patient group.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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