SELCUK UNIVERSITY PRESS

GENEL TIP DERGİSİ
The Journal of General Medicine

Received: 04 Jun 2025 | **Accepted:** 07 Oct 2025 **Genel Tıp Derg. Volume** 36 (2026), 1-8

DOI: 10.54005/geneltip.1714674

ORIGINAL ARTICLE

The Surrogate Marker for Coronary Thrombus Burden in Acute Coronary Syndrome Patients with COVID-19: The CHA_2DS_2-VAS_C Score

COVID-19'lu Akut Koroner Sendrom Hastalarında Koroner Trombüs Yükü için Bir Dolaylı Gösterge: CHA_2DS_2-VAS_C Skoru

[1]Yasin ÖZEN, [1]Hüseyin TEZCAN, [2]Mehmet Hakan UZUN, [3]Mehmet Uğur ÇALIŞKAN, [4]Cem ÇÖTELİ

[1]Department of Cardiology , Faculty of Medicine , Selcuk University, Konya, Türkiye
[2]Department of Cardiology , Republic of Türkiye Ministry of Health Kutahya City Hospital, Kütahya, Türkiye
[3]Department of Cardiology , Republic of Türkiye Ministry of Health Kızılcahamam State Hospital, Ankara, Türkiye
[4]Department of Cardiology , Faculty of Medicine , Hacettepe University, Ankara, Türkiye

Correspondence

Mehmet Hakan UZUN
Evliya Çelebi Mh. Eken Paşa Cd. Kütahya City Hospital No:19 43100 Kütahya, Türkiye.

E-Mail: mdmehmetuzun@gmail.com

How to cite ?

Özen Y, Tezcan H, Uzun MH, Çalışkan MU, Çöteli C. The Surrogate Marker for Coronary Thrombus Burden in Acute Coronary Syndrome Patients with COVID-19: The CHA_2DS_2-VAS_C Score, Genel Tıp Derg. 36 (2026), 1-8.

ABSTRACT

Aim: This study investigated whether the CHA_2DS_2-VAS_C score is an independent predictor of high thrombus burden and mortality in patients presenting with acute coronary syndrome (ACS) and Coronavirus Ddisease (COVID-19).
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 CHA_2DS_2-VAS_Cscores 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 CHA_2DS_2-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-VASc 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 CHA_2DS_2-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, CHA_2DS_2-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 CHA_2DS_2-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. CHA_2DS_2-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), interlökin-6 (18.12 ± 7.14 vs. 186.66 ± 56.8 pg/mL; P < 0.05), laktat dehidrogenaz (425.7 ± 31.2 vs. 1002.7 ± 173.4 U/L; P < 0.05) ve CHA_2DS_2-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 CHA_2DS_2-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 CHA_2DS_2-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, CHA_2DS_2-VAS_C skoru, COVID-19, düşük trombüs yükü, yüksek trombüs yükü

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
Complaints: geneltip@selcuk.edu.tr

Introduction

In December 2019, the first outbreak of Ccoronavirus Ddisease (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 CHA2DS-VASc 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 CHA_2DS_2-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 CHA_2DS_2-VAS_C score predicts high thrombus burden, no-reflow phenomenon, and both short- and long-term mortality [14–16]. Several parameters included in the CHA_2DS_2-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 CHA_2DS_2-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 CHA_2DS_2-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: E1-21-1941).

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 CHA_2DS_2-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 CHA_2DS_2-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 CHA_2DS_2-VAS_C score—were subsequently included in a multivariate model. Multivariate logistic regression analysis demonstrated that a higher CHA_2DS_2-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 CHA_2DS_2-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_2DS_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.

	Univariable		Multivariable	
Variables	**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_2DS_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

	Univariable		Multivariable	
Variables	**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_2DS_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 CHA_2DS_2-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 proinflammatorya 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 CHA_2DS_2-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 CHA_2DS_2-VAS_C score [15,34]. Seyis et al. reported that the CHA_2DS_2-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 CHA_2DS_2-VAS_C scores compared to those with minimal thrombus burden [16]. The CHA_2DS_2-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 CHA_2DS_2-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 CHA_2DS_2-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 theCHA_2DS_2-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 CHA_2DS_2-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 CHA_2DS_2-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 analysesanalysis. 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 CHA_2DS_2-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 CHA□DS□-VASc 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 CHA_2DS_2-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.

Financial support

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Acknowledgement

The authors declare that there are no acknowledgements to be stated.

References

1. Ugurlucan M, Yildiz Y, Oztas DM, Coban S, Beyaz MO, Sari G, et al. Congenital cardiac interventions during the peak phase of COVID-19 pandemics in the country in a pandemics hospital in Istanbul. Cardiol Young. 2020;30(9):1288-96.

2. Kunal S, Gupta K, Sharma SM, Pathak V, Mittal S, Tarke C. Cardiovascular system and COVID-19: perspectives from a developing country. Monaldi Arch Chest Dis. 2020;90(2).

3. Hottz ED, Azevedo-Quintanilha IG, Palhinha L, Teixeira L, Barreto EA, Pao CRR, et al. Platelet activation and platelet-monocyte aggregate formation trigger tissue factor expression in patients with severe COVID-19. Blood. 2020;136(11):1330-41.

4. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020;5(7):802-10.

5. Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, et al. ST-segment elevation in patients with COVID-19: a case series. N Engl J Med. 2020;382(25):2478-80.

6. Modin D, Claggett B, Sindet-Pedersen C, Lassen MCH, Skaarup KG, Jensen JUS, et al. Acute COVID-19 and the incidence of ischemic stroke and acute myocardial infarction. Circulation. 2020;142(21):2080-2.

7. Choudry FA, Hamshere SM, Rathod KS, Akhtar MM, Archbold RA, Guttmann OP, et al. High thrombus burden in patients with COVID-19 presenting with ST-segment elevation myocardial infarction. J Am Coll Cardiol. 2020;76(10):1168-76.

8. Sianos G, Papafaklis MI, Daemen J, Vaina S, van Mieghem CA, van Domburg RT, et al. Angiographic stent thrombosis after routine use of drug-eluting stents in ST-segment elevation myocardial infarction: the importance of thrombus burden. J Am Coll Cardiol. 2007;50(7):573-83.

9. Goto K, Lansky AJ, Nikolsky E, Fahy M, Feit F, Ohman EM, et al. Prognostic significance of coronary thrombus in patients undergoing percutaneous coronary intervention for acute coronary syndromes: a subanalysis of the ACUITY trial. J Am Coll Cardiol Cardiovasc Interv. 2011;4(7):769-77.

10. Ito H, Maruyama A, Iwakura K, Takiuchi S, Masuyama T, Hori M, et al. Clinical implications of the no-reflow phenomenon: a predictor of complications and left ventricular remodeling in reperfused anterior wall myocardial infarction. Circulation. 1996;93(2):223-8.

11. Rezkalla SH, Kloner RA. No-reflow phenomenon. Circulation. 2002;105(5):656-62.

12. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach. Chest. 2010;137(2):263-72.

13. Katkat F, Karahan S, Varol S, Kalyoncuoglu M, Okuyan E. Mortality prediction with CHA2DS2-VASc, CHA2DS2-VASc-HS and R2CHA2DS2-VASc score in patients hospitalized due to COVID-19. Eur Rev Med Pharmacol Sci. 2021;25(21):6767-74.

14. Ipek G, Onuk T, Karatas MB, Gungor B, Osken A, Keskin M, et al. CHA2DS2-VASc score is a predictor of no-reflow in patients with ST-segment elevation myocardial infarction who underwent primary percutaneous intervention. Angiology. 2016;67(9):840-5.

15. Keskin K, Sezai Yildiz S, Cetinkal G, Aksan G, Kilci H, Cetin S, et al. The value of CHA2DS2-VASc score in predicting all-cause mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Acta Cardiol Sin. 2017;33(6):598-604.

16. Satilmis S, Durmus G. Predictive accuracy of CHA2DS2-VASc score in determining high thrombus burden in patients with non-ST-elevation myocardial infarction. Acta Cardiol. 2021;76(2):140-6.

17. Crea F, Camici PG, Bairey Merz CN. Coronary microvascular dysfunction: an update. Eur Heart J. 2014;35(17):1101-11.

18. Iwakura K, Ito H, Ikushima M, Kawano S, Okamura A, Asano K, et al. Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. J Am Coll Cardiol. 2003;41(1):1-7.

19. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Circulation. 2018;138(20):e618-e51.

20. Thrombolysis in Myocardial Infarction (TIMI) Trial. Phase I findings. N Engl J Med. 1985;312(14):932-6.

21. Gibson CM, de Lemos JA, Murphy SA, Marble SJ, McCabe CH, Cannon CP, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. Circulation. 2001;103(21):2550-4.

22. Parohan M, Yaghoubi S, Seraji A, Javanbakht MH, Sarraf P, Djalali M. Risk factors for mortality in patients with coronavirus disease 2019 infection: a systematic review and meta-analysis. Aging Male. 2020;23(5):1416-24.

23. Musher DM, Abers MS, Corrales-Medina VF. Acute infection and myocardial infarction. N Engl J Med. 2019;380(2):171-6.

24. Henry BM, Vikse J, Benoit S, Favaloro EJ, Lippi G. Hyperinflammation and derangement of the renin-angiotensin-aldosterone system in COVID-19. Clin Chim Acta. 2020;507:167-73.

25. Zuo Y, Estes SK, Ali RA, Gandhi AA, Yalavarthi S, Shi H, et al. Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19. Sci Transl Med. 2020;12(570).

26. Kuyumcu M, Ozen Y, Ozbay MJ. COVID-19 survivors may exhibit deterioration in frontal plane QRS-T angle and other electrocardiogram parameters. Eur Rev Med Pharmacol Sci. 2022;26(18):6879-84.

27. Srivastava S, Garg I, Bansal A, Kumar B. COVID-19 infection and thrombosis. Clin Chim Acta. 2020;510:344-6.

28. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with COVID-19. J Thromb Haemost. 2020;18(6):1324-9.

29. Toprak K, Kaplangoray M, Memioglu T, Inanir M, Omar B, Tascanov MB, et al. HbA1c/C-peptide ratio is associated with angiographic thrombus burden and short-term mortality in patients presenting with ST-elevation myocardial infarction. Blood Coagul Fibrinolysis. 2023;34(6):385-95.

30. Toprak K, Kaplangoray M, Palice A, Tascanov MB, Inanir M, Memioglu T, et al. SCUBE1 is associated with thrombotic complications, disease severity, and in-hospital mortality in COVID-19 patients. Thromb Res. 2022;220:100-6.

31. Kaplangoray M, Toprak K, Aslan R, Deveci E, Gunes A, Ardahanli I, et al. High CRP-albumin ratio is associated with high thrombus burden in patients with newly diagnosed STEMI. Angiology. 2023;74(41):e35363.

32. Kaplangoray M, Toprak K, Cekici Y, Yildirim A, Abacioglu OO. Relationship between blood viscosity and thrombus burden in ST-segment elevation myocardial infarction. J Clin Hemorheol Microcirc. 2023;Preprint:1-10.

33. Rozenbaum Z, Elis A, Shuvy M, Vorobeichik D, Shlomo N, Shlezinger M, et al. CHA2DS2-VASc score and clinical outcomes of patients with acute coronary syndrome. Eur J Intern Med. 2016;36:57-61.

34. Barman HA, Atici A, Alici G, Asoglu R, Aciksari G, Tugrul S, et al. The relationship between CHA2DS2-VASc score and isolated coronary artery ectasia. Am J Blood Res. 2021;11(4):391-8.

35. Seyis S, Kurmus O, Kilic S, Uzunget SB, Ercan EA. CHA2DS2-VASc score predicts intracoronary thrombus burden in patients with ST-elevation myocardial infarction. Angiology. 2017;68(5):354-60.

36. Unal S, Acar B, Yayla C, Balci MM, Ertem A, Kara M, et al. Importance and usage of the CHA2DS2-VASc score in predicting acute stent thrombosis. Coron Artery Dis. 2016;27(6):478-82.

37. Maden O, Cakmak Karaaslan O, Kanal Y, Yakut I, Yaman NM, Konte HC, et al. Association of CHA2DS2-VASc score with thrombus burden in patients with acute myocardial infarction undergoing SVG-PCI. Herz. 2022;47(5):456-64.

38. Ozen Y, Eftal Seyda K, Bilal O, Idris Y, Serdar K, Goktug E, et al. A new inflammatory marker of the no-reflow phenomenon after percutaneous coronary intervention (PCI) to saphenous venous in patients with coronary artery disease. Iran Red Crescent Med J. 2023;25(11):e.

39. Duman H, Cinier G, Bakirci EM, Duman H, Simsek Z, Hamur H, et al. Relationship between C-reactive protein to albumin ratio and thrombus burden in patients with acute coronary syndrome. Clin Appl Thromb Hemost. 2019;25:1076029618824418.

40. Kanal Y, Seyda Kanal HE, Yakut I, Ozen Y, Ozbay MB, Gulcihan Balci K, et al. CRP albumin ratio may predict no reflow in patients undergoing percutaneous coronary intervention for saphenous vein graft stenosis. Acta Cardiol. 2023;74(1):55-61.

41. Ertem AG, Ozen Y, Yuksekkaya B, Erdol MA, Erdogan M, Demirtas K, et al. Association of the novel inflammatory marker systemic immune-inflammation index and contrast-induced nephropathy in patients undergoing transcatheter aortic valve replacement for severe aortic stenosis. Angiology. 2022;73(5):422-30.

42. Rezkalla SH, Kloner RA. Coronary no-reflow phenomenon: from the experimental laboratory to the cardiac catheterization laboratory. Catheter Cardiovasc Interv. 2008;72(7):950-7.

43. Ozen Y, Ozbay MB, Yakut I, Kanal Y, Abdelmottaleb W, Nriagu B, et al. Atherogenic index of plasma and triglyceride-glucose index to predict more advanced coronary artery diseases in patients with first diagnosis of acute coronary syndrome. Eur Heart J Cardiovasc Pharmacother. 2023;27(9):XX-XX.

44. Ozen Y, Ozbay MB. Assessment of systemic immune-inflammation index as an independent surrogate biomarker of no-reflow phenomenon in acute coronary syndrome patients with CABG undergoing PCI of saphenous vein graft. Clin Res Cardiol. 2023;27(6):XX-XX.