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The Relationship Between the CHA_2DS_2-VASc Score and Lesion Complexity and Long-Term Outcomes in Peripheral Arterial Disease

Periferik Arter Hastalığında CHA_2DS_2-VASc Skorunun Lezyon Karmaşıklığı ve Uzun Vadeli Sonuçlarla İlişkisi

ABSTRACT

Objective: Originally designed to evaluate stroke risk in individuals with atrial fibrillation unrelated to valvular disease, the CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack/systemic embolism, Vascular disease, Age 65–74 years, and Sex category – female) is now additionally utilized for the prognostic evaluation of cardiovascular diseases. This study aimed to evaluate the predictive role of the CHA_2DS_2-VASc score for lesion severity and long-term survival outcomes in individuals with peripheral artery disease (PAD).

Method: This retrospective analysis included 784 patients diagnosed with PAD via computed tomography (CT) angiography, consecutively enrolled from two medical centers. The CHA_2DS_2-VASc score was determined for all participants. Lesion severity was assessed according to the TASC II (Trans-Atlantic Inter-Society Consensus II) criteria, and patients were categorized into TASC-AB (simple) and TASC-CD (complex) lesion groups. Mortality data were obtained from hospital and social security records.

Results: The study included 784 patients (average age: 61.7 ± 9.9 years; 17.2% female). In the regression analysis performed to predict lesion severity, we found that the CHA_2DS_2-VASc score ($P < 0.007$) and left ventricular ejection fraction ($P = 0.009$) were independent predictors. The receiver operating characteristic (ROC) curve indicated that a CHA_2DS_2-VASc score threshold of 3.5 predicted long-term mortality with 70% sensitivity and 79% specificity ($P < 0.001$). Kaplan-Meier survival estimates indicated that patients with higher CHA_2DS_2-VASc scores had significantly lower survival rates over the 60-month follow-up period ($P < 0.001$).

Conclusion: The CHA_2DS_2-VASc score was independently associated with both lesion severity and adverse long-term outcomes in individuals with PAD.

Keywords: CHA_2DS_2-VASc score, lesion complexity, mortality, peripheral artery disease

ÖZET

Amaç: Başlangıçta kapak hastalığı ile ilişkili olmayan atriyal fibrilasyonu olan bireylerde inme riskini değerlendirmek için geliştirilen CHA_2DS_2-VASc skoru (Konjestif kalp yetmezliği, Hipertansiyon, Yaş ≥ 75, Diyabetes mellitus, daha önce inme/geçici iskemik atak/sistemik emboli, vasküler hastalık, yaş 65-74 ve cinsiyet kategorisi - kadın), günümüzde kardiyovasküler hastalıkların prognostik değerlendirmesi için de kullanılmaktadır. Bu çalışmanın amacı, periferik arter hastalığı (PAH) olan bireylerde lezyon şiddeti ve uzun dönem sağkalım sonuçları açısından CHA_2DS_2-VASc skorunun öngörücü rolünü değerlendirmektir.

Yöntem: Bu retrospektif analiz, bilgisayarlı tomografi (BT) anjiyografi ile PAH tanısı konulan ve iki tıp merkezinden ardışık olarak dahil edilen 784 hastayı içermektedir. Tüm katılımcılar için CHA_2DS_2-VASc skoru belirlendi, lezyon şiddeti TASC II kriterlerine göre değerlendirildi ve hastalar TASC-AB (basit) ve TASC-CD (kompleks) lezyon gruplarına ayrıldı. Mortalite verileri hastane ve sosyal güvenlik kayıtlarından elde edilmiştir.

Bulgular: Çalışmaya 784 hasta (ortalama yaş 61,7±9,9 yıl; %17,2 kadın) dahil edildi. Lezyon şiddetini öngörmek için yapılan regresyon analizinde, CHA_2DS_2-VASc skoru ($P < 0,007$) ve sol ventrikül ejeksiyon fraksiyonunun ($P = 0,009$) bağımsız öngörücüler olduğunu bulduk. ROC analizi, 3,5 CHA_2DS_2-VASc skoru eşiğinin uzun dönem mortaliteyi %70 duyarlılık ve %79 özgüllükle öngördüğünü göstermiştir ($P < 0,001$). Kaplan-Meier sağkalım tahminleri, daha yüksek CHA_2DS_2-VASc skorlarına sahip hastaların 60 aylık takip süresi boyunca anlamlı olarak daha düşük sağkalım oranlarına sahip olduğunu göstermiştir ($P < 0,001$).

Sonuç: CHA_2DS_2-VASc skoru, PAH'lı bireylerde hem lezyon şiddetiyle hem de olumsuz uzun dönem sonuçlarla bağımsız olarak ilişkili bulunmuştur.

Anahtar Kelimeler: CHA_2DS_2-VASc skoru, lezyon şiddeti, mortalite, periferik arter hastalığı

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Peripheral artery disease (PAD) predominantly results from atherosclerosis and manifests as a consequence of the systemic atherosclerotic process. Atherosclerosis-related risk factors, including hypertension (HT), hyperlipidemia (HL), diabetes mellitus (DM), and smoking, are frequently observed in individuals with PAD.[1] PAD has been linked to elevated risks of both cardiovascular events and overall mortality. With the aging of the global population, PAD continues to be a growing clinical problem and a significant cause of adverse outcomes and deaths, despite advances in modern treatment strategies.[2]

The CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack/systemic embolism, Vascular disease, Age 65–74 years, and Sex category – female) is a practical and easily applicable scoring system initially designed to assess the cardioembolic risk in individuals with atrial fibrillation (AF) not caused by valvular disease and to guide anticoagulation therapy decisions.[3]. The components of this scoring system—congestive heart failure (CHF), HT, stroke, advanced age, vascular disease, DM, and female sex—largely coincide with the key risk factors for PAD.[4] Initially designed as a risk assessment tool for AF, the CHA_2DS_2-VASc score has progressively been recognized for its prognostic value across various cardiovascular diseases.[5,6] It has been reported that this score can independently predict adverse outcomes, including both acute stent thrombosis and mortality, particularly in situations like stable and acute coronary artery disease (CAD).[7-13]

This study aimed to assess the predictive role of the CHA_2DS_2-VASc score, an established tool in cardiovascular risk assessment, for lesion complexity and prognosis in patients with PAD. Thus, we sought to evaluate the potential application of this scoring system in the context of PAD.

Materials and Methods

Study Methodology and Population

This observational, retrospective study, administered across two centers, included patients aged 18 to 95 years. A total of 784 consecutively selected patients with PAD who had been followed at the cardiology outpatient clinics between 2015 and 2020 were enrolled. The patients were followed for an average duration of 60 months.

Inclusion Criteria

All patients presented with symptoms of PAD, including intermittent claudication, ischemic rest pain, or non-healing ulcers. Patients who were found to have ≥ 50% luminal narrowing in the femoropopliteal or aortoiliac segments on computed tomography (CT) angiography were included in the study. These individuals subsequently underwent conventional peripheral angiographic evaluation for further assessment. Angiographic images were reviewed for lesion severity and classified into TASC-AB (simple lesions) and TASC-CD (complex lesions) groups based on the lesion classification criteria established in the TransAtlantic Inter-Society Consensus-II (TASC II), in accordance with the diagnostic and therapeutic recommendations of the European Society of Cardiology (ESC) (Figure 1).[14] Treatment strategies were determined by a specialized interventional cardiology team according to lesion complexity, patient comorbidities, and guideline-directed management protocols. The CHA_2DS_2-VASc score was calculated based on the presence of CHF, HT, age ≥65 years (with additional weighting for ≥ 75 years), DM, prior transient ischemic attack (TIA) or stroke, vascular disease (coronary or peripheral), and female gender, in accordance with established

ABBREVIATIONS

AF	Atrial fibrillation
AIP	Atherogenic index of plasma
AUC	Area under the curve
CAD	Coronary artery disease
CHF	Congestive heart failure
CKD	Chronic kidney disease
CLTI	Critical limb-threatening ischemia
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
DM	Diabetes mellitus
EF	Ejection fraction
ESC	European Society of Cardiology
ESVS	European Society for Vascular Surgery
GLASS	Global Limb Anatomic Staging System
HL	Hyperlipidemia
HT	Hypertension
IQR	Interquartile ranges
LVEF	Left ventricular ejection fraction
MALE	Major adverse limb events
PAD	Peripheral artery disease
ROC	Receiver operating characteristic
STEMI	ST-Elevation Myocardial Infarction
TASC II	Trans-Atlantic Inter-Society Consensus II
TIA	Transient ischemic attack
WIfI	Wound, Ischemia, and Foot Infection

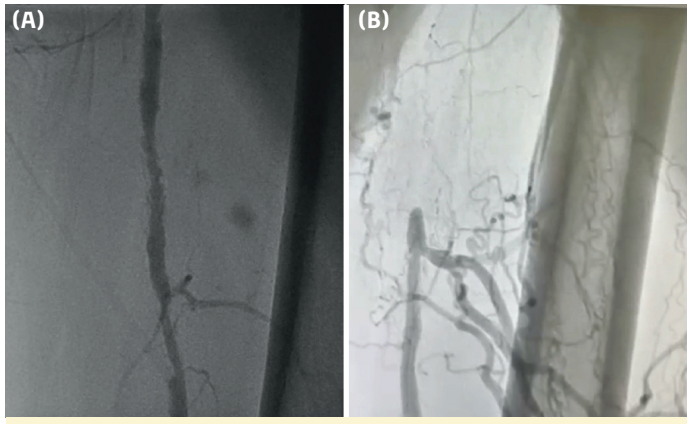

Figure 1. Angiographic images of simple and complex femoropopliteal lesions from patients included in the study. (A) Simple lesion: Angiographic image from a study patient demonstrating a short-segment, non-occlusive stenosis with preserved distal runoff in the superficial femoral artery. (B) Complex lesion: Angiographic image from another study patient showing a long-segment total occlusion of the femoropopliteal artery with extensive collateral circulation, consistent with a TASC-CD lesion. TASC-CD, TransAtlantic Inter-Society Consensus C–D

definitions.[13] Consistent with prior research, patients were categorized into two groups based on their CHA_2DS_2-VASc scores: low (< 3 points) and high (≥ 3 points). Although different threshold values (e.g., ≤ 2 and > 2) have been used in other studies,[11] we chose ≥ 3 points as the cut-off since this value has been associated with adverse cardiovascular outcomes in previous PAD-focused research. All patients had at least 1 point, as they were all affected by vascular atherosclerosis. The CHA_2DS_2-VASc score was calculated at the time of PAD diagnosis using the patients' demographic and comorbidity data as recorded in the hospital's electronic health records.

Exclusion Criteria

Individuals younger than 18 years, or those diagnosed with conditions such as familial hyperlipidemia, vasculitis, systemic inflammatory or autoimmune diseases, hematologic malignancies, end-stage heart failure (NYHA class IV), advanced chronic kidney disease (CKD) (glomerular filtration rate [GFR] < 30 mL/min/1.73 m²), severe liver diseases (e.g., cirrhosis, chronic hepatitis, hepatocellular carcinoma), Buerger's disease, those with a history of organ transplantation, patients with malignancies, and those who had recently received chemotherapy were not included in the analysis (Figure 2).

Data Collection

All demographic information regarding patient characteristics (age, gender), comorbid conditions such as DM, HT, AF, smoking, cerebrovascular diseases, CAD, HL, chronic obstructive pulmonary disease (COPD), CKD, physical condition, symptoms, clinical stages (Rutherford and Fontaine), and routine laboratory test results were extracted from hospital clinical documentation.

Blood tests were collected from the antecubital vein before the peripheral angiography, after a 12-hour fasting period in the morning, as well as following the procedure. Biochemical parameters were measured using a fully automated system (Roche Modular, Tokyo, Japan). All patients underwent transthoracic echocardiographic evaluation (Vivid S5; GE, Norway), with left ventricular ejection fraction (LVEF) calculated via the biplane Simpson's method.

Mortality Data

Death data were obtained from hospital and social security records. Patients were categorized based on survival upon completion of follow-up.

Endovascular Treatment Procedure

All procedures were conducted by a skilled team specializing in interventional cardiology, following standard protocols, including systemic heparinization. Depending on lesion characteristics, endovascular treatment involved the use of standard balloon dilation, balloons coated with antiproliferative agents, and stents with or without pharmacologic coatings. A procedure was considered successful if residual stenosis was reduced to below 20% in the absence of complications.

Clinical Outcomes

The clinical outcomes of the study included:

1. Lesion complexity, categorized as TASC-AB (simple) or TASC-CD (complex) based on the TASC II classification system;

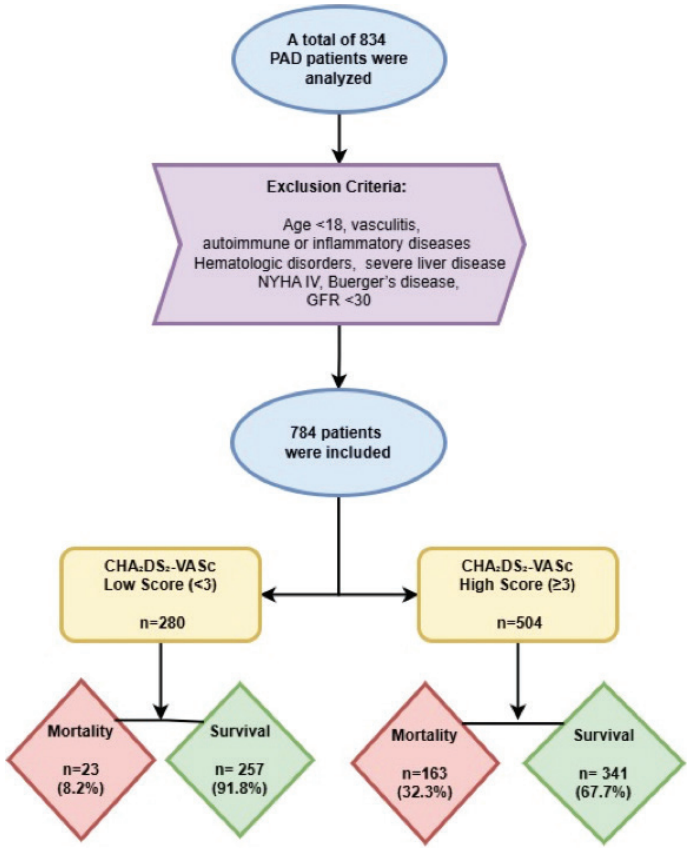

Figure 2. Study design flowchart.

2. Major amputations, defined as any limb amputation above the ankle level;
3. Minor amputations, defined as amputations at or below the ankle (e.g., toe or forefoot);
4. All-cause long-term mortality, obtained from hospital records and national social security system data.

Ethical Considerations

The study protocol was approved by Dicle University Medical Faculty Ethics Committee for Non-Interventional Studies (Approval Number: 2024-296, Date: 16.10.2024), and the research was carried out in accordance with the principles outlined in the Declaration of Helsinki.

Statistical Analysis

SPSS version 26.0 (IBM, Chicago, USA) was employed for data analysis. Demographic and clinical variables were outlined using descriptive statistical methods. Data distribution patterns were evaluated using histograms alongside appropriate statistical normality tests. Continuous variables were analyzed using the independent samples t-test or Mann-Whitney U test, depending on the distribution pattern. Categorical data were compared using either Pearson's chi-square or Fisher's exact test, as applicable. Variables exhibiting non-normal distributions were summarized by medians and interquartile ranges (IQR). In contrast, data with normal distribution were expressed as mean ± standard deviation. Categorical data were shown as percentages (%). All statistical tests were evaluated at a significance level of

P < 0.05. Survival outcomes were analyzed using Kaplan–Meier curves, and lesion complexity was further examined through Cox regression analysis. Receiver Operating Characteristic (ROC) curve analysis was performed to assess how well the CHA_2DS_2-VASc score could predict long-term outcomes.

Results

Patient Characteristics, Laboratory Findings, and Outcome Parameters

A total of 784 participants were included in the study, with a mean age of 61.7 ± 9.9 years. Of these patients, 135 (17.2%) were female, and the CHA_2DS_2-VASc score was calculated consistently for each participant. Patients were subsequently categorized into two groups based on their scores: the low score (< 3) group (n = 280, 36%) and the high score (≥ 3) group (n = 504, 64%) (Figure 1). Table 1 presents the demographic and procedural characteristics.

Age, female gender, TASC-CD, smoking, HT, DM, CAD, left ventricular hypertrophy (LVH), procedure duration, type of treatment, and CKD (all, P < 0.001) were substantially higher in the high score group. TASC-CD lesions were markedly more frequent in individuals with higher CHA_2DS_2-VASc scores in both the aortoiliac (P = 0.002) and femoropopliteal (P = 0.007) arterial segments. Consistently, analysis based on the Rutherford and Fontaine clinical classifications—used to evaluate the symptomatic severity of PAD—revealed that patients with higher CHA_2DS_2-VASc scores were more likely to present with advanced clinical stages (P = 0.001). Moreover, patients in the high-score group had importantly elevated levels of creatinine and fasting glucose (P < 0.001), systolic (P = 0.022) and diastolic blood pressure (P = 0.021), C-reactive protein (CRP) (P = 0.036), and leukocyte count (WBC) (P = 0.043). The high-score group demonstrated lower measurements of LVEF and hemoglobin compared to those with lower scores (P < 0.001).

In addition to the primary analysis based on CHA_2DS_2-VASc score groups, further subgroup analyses were conducted to enhance the depth of the study by addressing lesion complexity and clinical outcomes. Patients were categorized according to the severity of PAD (TASC-AB and TASC-CD) and survival status (survivor and non-survivor). The clinical, laboratory, and outcome characteristics of these additional subgroups are presented in Tables 2 and 3, respectively.

Follow-Up and Surveillance

The participants were retrospectively monitored over a mean period of 60 months. The average follow-up duration was similar in both low (< 3) and high (≥ 3) CHA_2DS_2-VASc score groups. Surveillance data were collected from hospital databases and Social Security records, including outpatient follow-up visits and rehospitalizations.

Major adverse limb events (MALE) were also assessed during follow-up. A total of 35 amputations were observed among 784 patients. When stratified, 23 were minor amputations and 12 were major amputations. Overall, the incidence of amputation was significantly higher in the high-score group (P < 0.007). Specifically, the rate of major amputation was significantly elevated in this group (P = 0.006), whereas the difference in minor amputation rates did not reach statistical significance (P = 0.156) (Table 1).

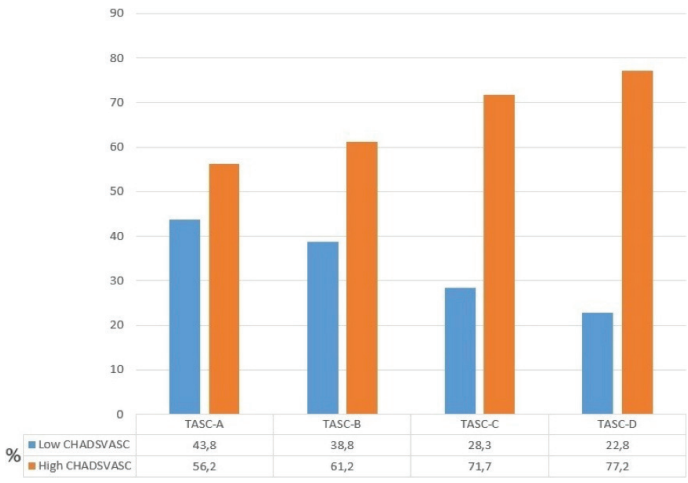

Figure 3. A bar graph showing that as lesion complexity increases, the proportion of high-scoring patients increases significantly.

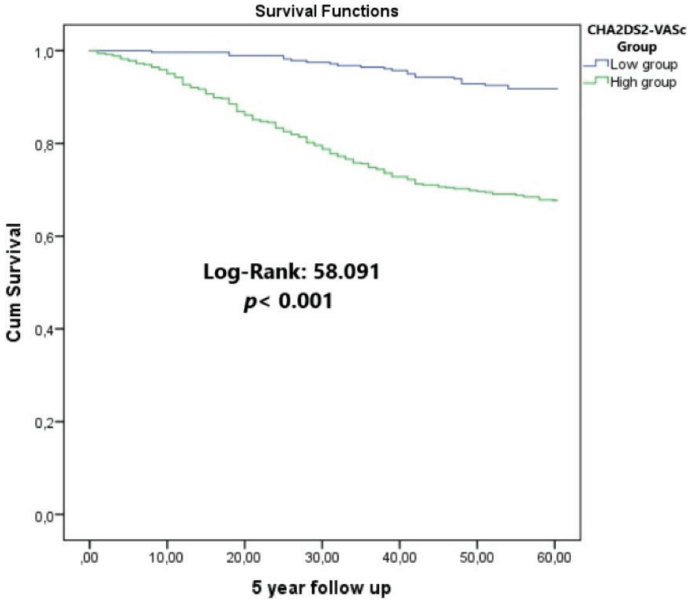

Figure 4. Kaplan–Meier survival curves demonstrating the association between CHA_2DS_2-VASc score and all-cause mortality during five-year follow-up. Patients were stratified into low and high CHA_2DS_2-VASc score groups. The high-score group exhibited significantly reduced cumulative survival (Log-rank = 58.091, P < 0.001). CHA_2DS_2-VASc score, Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack/systemic embolism, Vascular disease, Age 65–74 years, and Sex category – female.

Among the 784 patients, a total of 186 deaths were recorded during follow-up, with 163 occurring in the high CHA_2DS_2-VASc score group (P < 0.001).

Predictors of Lesion Severity

Univariate logistic regression revealed that the CHA_2DS_2-VASc score, LVEF, and CKD were considerably related to lesion severity (P

Table 1. Comparison of clinical, demographic, and outcome parameters between low and high CHA_2DS_2-VASc score groups

	All patients (n=784)	Low CHA_2DS_2-VASc score (n=280)	High CHA_2DS_2-VASc score (n=504)	P
Age, years	61.7 ± 9.9	56.5 ± 7.8	64.5 ± 9.8	**<0.001**
Gender (female), n (%)	135 (17.2)	13 (4.6)	122 (24.2)	**<0.001**
BMI, kg/m^2	26.9 ± 4.7	26.9 ± 4.7	26.9 ± 4.6	0.986
Heart rate (minute)	87.0 ± 17.9	88.2 ± 18.5	86.4 ± 17.5	0.188
Systolic blood pressure (mmHg)	129 ± 15.0	127.5 ± 14.0	130.1 ± 15.4	**0.022**
Diastolic blood pressure (mmHg)	79.7 ± 9.7	78.7 ± 9.3	80.3 ± 9.9	**0.021**
Smoking, n (%)	505 (64.7)	205 (73.5)	300 (59.9)	**<0.001**
Diabetes mellitus, n (%)	339 (43.2)	46 (16.4)	293 (58.1)	**<0.001**
Hypertension, n (%)	450 (57.4)	78 (27.9)	372 (73.8)	**<0.001**
CAD, n (%)	427 (54.5)	117 (41.8)	310 (61.5)	**<0.001**
Hyperlipidemia, n (%)	405 (51.7)	137 (48.9)	268 (53.2)	0.254
Cerebrovascular disease, n (%)	64 (8.2)	3 (1.1)	61 (12.1)	**<0.001**
CKD, n (%)	206 (26.3)	38 (13.6)	168 (33.3)	**<0.001**
LVEF, %	53.1 ± 11.1	57.9 ± 8.3	50.4 ± 11.6	**<0.001**
Creatinine, (mg/dL)	0.98 (0.82–1.20)	0.91 (0.81–1.10)	1.00 (0.84–1.23)	**<0.001**
Hemoglobin, g/L	13.48 ± 2.58	13.91 ± 2.46	13.24 ± 2.62	**<0.001**
Glucose (mg/dL)	147.4 ± 68.6	133.0 ± 64.2	154.6 ± 69.6	**<0.001**
WBC, 10^6/L	8.73 ± 1.40	8.60 ± 1.53	8.81 ± 1.32	**0.043**
Total cholesterol, mg/dL	198.3 ± 45.9	200.9 ± 46.6	196.8 ± 45.5	0.229
LDL-C, mg/dL	121.5 ± 39.4	123.4 ± 39.3	120.5 ± 39.5	0.323
HDL-C, mg/dL	38.5 ± 7.2	38.0 ± 6.9	38.8 ± 7.4	0.124
Triglyceride, mg/dL	156.5 (112.7–215.0)	161.5 (118.7–209.2)	156.0 (106.0–221.5)	0.172
CRP (mg/dL)	3.50 (1.26–9.76)	2.78 (1.08–6.46)	3.81 (1.31–11.28)	**0.036**
TASC, n (%)				**<0.001**
AB	510 (65.1)	208 (74.3)	302 (59.9)	
CD	274 (34.9)	72 (25.7)	202 (40.1)	
Aortoiliac TASC, n (%)				**0.002**
AB	250 (67.8)	100 (78.1)	150 (62.2)	
CD	119 (32.2)	28 (21.9)	91 (37.8)	
Femoro-popliteal TASC, n (%)				**0.007**
AB	260 (62.7)	108 (71.1)	152 (57.8)	
CD	155 (37.3)	44 (28.9)	111 (42.2)	
Contrast volume (mL)	162.7 ± 70.7	157.0 ± 80.9	165.8 ± 64.3	0.094
Procedure duration (min)	57.7 ± 20.8	53.3 ± 24.2	60.1 ± 18.3	**<0.001**
Rutherford, n (%)				**0.001**
1	54 (6.9)	27 (9.6)	27 (5.4)	
2	133 (17.0)	52 (18.6)	81 (16.1)	
3	362 (46.2)	142 (50.7)	220 (43.7)	
4	143 (18.2)	41 (14.6)	102 (20.2)	
5	73 (9.3)	15 (5.4)	58 (11.5)	
6	19 (2.4)	3 (1.1)	16 (3.2)	

Table 1 (cont). Comparison of clinical, demographic, and outcome parameters between low and high CHA_2DS_2-VASc score groups

	All patients (n=784)	Low CHA_2DS_2-VASc score (n=280)	High CHA_2DS_2-VASc score (n=504)	P
Fontaine, n (%)				**0.001**
I	72 (9.2)	30 (10.7)	42 (8.3)	
II	483 (61.6)	190 (67.9)	293 (58.1)	
III	144 (18.4)	45 (16.1)	99 (19.6)	
IV	85 (10.8)	15 (5.4)	70 (13.9)	
Type of treatment, n (%)				**<0.001**
Medical	122 (15.6)	23 (8.2)	99 (19.6)	
PTCA	352 (44.9)	109 (38.9)	243 (48.2)	
Stent	261 (33.3)	128 (45.7)	133 (26.4)	
Bypass	49 (6.3)	20 (7.1)	29 (5.8)	
Amputation, n (%)	35 (4.5)	5 (1.8)	30 (6.0)	**0.007**
Minor	23 (2.9)	5 (1.8)	18 (3.6)	0.156
Major	12 (1.5)	0 (0)	12 (2.4)	**0.006**
Mortality, n (%)	186 (23.7)	23 (8.2)	163 (32.3)	**<0.001**

BMI, Body Mass Index; CAD, Coronary Artery Disease; CKD, Chronic Kidney Disease; CRP, C-Reactive Protein; HDL-C, High-Density Lipoprotein Cholesterol (mg/dL); LDL-C, Low-Density Lipoprotein Cholesterol (mg/dL); LVEF, Left Ventricular Ejection Fraction; PTCA, Percutaneous Transluminal Coronary Angioplasty; TASC II, TransAtlantic Inter-Society Consensus-II; WBC, White Blood Cell Count (10^6/L). Data are presented as mean ± standard deviation (SD) or n (%). Statistical significance is considered at a P-value of less than 0.05.

< 0.001) (Table 2). According to the multivariate logistic regression model, the CHA_2DS_2-VASc score (odds ratio [OR] = 1.604; 95% confidence interval [CI]: 1.137–2.261; P = 0.007) and LVEF (OR = 0.982; 95% CI: 0.968–0.995; P = 0.009) were identified as independent determinants of lesion complexity (Table 4).

According to the TASC II classification, lesion complexity was evaluated according to CHA_2DS_2-VASc score groups. The proportion of high-scoring patients was found to increase significantly with greater lesion complexity (Figure 3).

Predictors of Long-Term Mortality

To determine independent predictors of long-term mortality, Cox proportional hazards regression analysis was performed. Variables that demonstrated a statistically significant association with mortality (Table 3) were included in both univariate and multivariate Cox regression models.

In the univariate Cox regression analysis, age, female sex, CHA_2DS_2-VASc score, DM, ejection fraction (EF), CAD, CKD, hemoglobin level, TASC classification, and amputation were all significantly associated with long-term mortality (all, P < 0.05). In the multivariate Cox regression model, age (hazard ratio [HR]: 1.062, 95% CI: 1.038–1.086, P < 0.001), CHA_2DS_2-VASc score (HR: 1.272, 95% CI: 1.040–1.555, P = 0.019), DM (HR: 1.589, 95% CI: 1.097–2.302, P = 0.014), lower EF (HR: 0.976, 95% CI: 0.962–0.991, P = 0.001), TASC classification (HR: 1.211, 95% CI: 1.034–1.418, P = 0.018), and amputation (HR: 2.450, 95% CI: 1.514–3.965, P < 0.001) emerged as independent predictors of long-term mortality (Table 5).

Survival Analysis

Kaplan-Meier survival analysis revealed that patients with higher CHA_2DS_2-VASc scores had significantly lower long-term survival, indicating a greater risk of all-cause mortality over the 60-month follow-up period (Log-rank = 58.091, P < 0.001) (Figure 4).

ROC Curve Analysis

Receiver operating characteristic curve analysis was conducted to evaluate the predictive performance of the CHA_2DS_2-VASc score for long-term mortality. The area under the curve (AUC) was 0.793 (95% CI: 0.755–0.832, P < 0.001), indicating good discriminative ability. The optimal cut-off value was identified as 3.5, yielding a sensitivity of 70% and a specificity of 79% (Figure 5).

Discussion

Our findings demonstrate that the CHA_2DS_2-VASc score, a widely used tool for cardiovascular risk grouping, may also serve as a practical and accessible prognostic indicator for evaluating lesion severity and predicting long-term outcomes in patients with PAD. The main findings are:

1. The CHA_2DS_2-VASc score was identified as an independent determinant of long-term mortality in patients with PAD, and higher scores were significantly associated with shorter survival times.
2. High CHA_2DS_2-VASc scores are associated with increased lesion severity in PAD.
3. Reduced LVEF was found to be an independent determinant of both lesion severity and long-term mortality.

PAD is becoming increasingly common, a trend largely driven by the rise in global life expectancy.[2] This growing prevalence has positioned PAD as a significant public health concern. In patients with PAD, advancing age was found to be an independent predictor of long-term mortality in our study, further emphasizing its prognostic importance in this high-risk population. In particular, the associated rise in major complications such as critical limb-threatening ischemia (CLTI) and limb amputations—both of which significantly impair quality of life—highlights the

Table 2. Comparison of clinical, laboratory, and outcome parameters between TASC-AB and TASC-CD groups

	All patients (n = 784)	Mild PAD (TASC-AB) (n = 510)	Severe PAD (TASC-CD) (n = 274)	P
Age, years	61.7 ± 9.9	60.7 ± 9.5	63.4 ± 10.5	**<0.001**
Gender (female), n (%)	135 (17.2)	74 (14.5)	61 (22.3)	**0.006**
BMI, kg/m^2	26.9 ± 4.7	26.8 ± 4.7	27.0 ± 4.7	0.493
CHA_2DS_2-VASc score	3.00 ± 1.25	2.75 ± 1.16	3.47 ± 1.29	**<0.001**
Heart rate (minute)	87.0 ± 17.9	86.7 ± 17.6	87.7 ± 18.3	0.429
Systolic blood pressure (mmHg)	129.2 ± 15.0	129.1 ± 14.7	129.3 ± 15.4	0.890
Diastolic blood pressure (mmHg)	79.7 ± 9.7	80.0 ± 9.6	79.2 ± 10.0	0.252
Smoking, n (%)	505 (64.7)	339 (66.7)	166 (61.0)	0.112
Diabetes mellitus, n (%)	339 (43.2)	201 (39.4)	138 (50.4)	**0.003**
Hypertension, n (%)	450 (57.4)	270 (52.9)	180 (65.7)	**0.001**
CAD, n (%)	427 (54.5)	259 (50.8)	168 (61.3)	**0.005**
Hyperlipidemia, n (%)	405 (51.7)	247 (48.4)	158 (57.7)	**0.014**
Cerebrovascular disease, n (%)	64 (8.2)	37 (7.3)	27 (9.9)	0.205
CKD, n (%)	206 (26.3)	119 (23.3)	87 (31.8)	**0.011**
LVEF, %	53.1 ± 11.1	54.2 ± 10.7	50.9 ± 11.6	**<0.001**
Creatinine, (mg/dL)	0.98 (0.82–1.20)	1.00 (0.83–1.18)	0.97 (0.82–1.28)	0.211
Hemoglobin, g/L	13.48 ± 2.58	13.53 ± 2.60	13.38 ± 2.56	0.453
Glucose (mg/dL)	147.4 ± 68.6	147.0 ± 65.1	148.0 ± 74.4	0.863
WBC, 10^6/L	8.73 ± 1.40	8.62 ± 1.29	8.93 ± 1.57	**0.003**
Total cholesterol, mg/dL	198.3 ± 45.9	197.0 ± 44.8	200.7 ± 48.0	0.279
LDL-C, mg/dL	121.5 ± 39.4	121.7 ± 38.7	121.3 ± 40.8	0.901
HDL-C, mg/dL	38.5 ± 7.2	38.0 ± 7.1	39.3 ± 7.4	**0.016**
Triglyceride, mg/dL	156 (112–215)	151 (110–215)	169 (116–223)	0.357
CRP (mg/dL)	3.50 (1.26–9.76)	3.59 (1.38–9.09)	3.34 (1.19–10.55)	0.543
Contrast volume (mL)	162.7 ± 70.7	161.2 ± 71.9	165.3 ± 68.6	0.445
Procedure duration (min)	57.7 ± 20.8	56.6 ± 21.1	59.6 ± 20.2	0.051
Rutherford, n (%)				**<0.001**
1	54 (6.9)	45 (8.8)	9 (3.3)	
2	133 (17.0)	100 (19.6)	33 (12.0)	
3	362 (46.2)	269 (52.7)	93 (33.9)	
4	143 (18.2)	57 (11.2)	86 (31.4)	
5	73 (9.3)	26 (5.1)	47 (17.2)	
6	19 (2.4)	13 (2.5)	6 (2.2)	
Fontaine, n (%)				**<0.001**
I	72 (9.2)	62 (12.2)	10 (3.6)	
II	483 (61.6)	354 (69.4)	129 (47.1)	
III	144 (18.4)	61 (12.0)	83 (30.3)	
IV	85 (10.8)	33 (6.5)	52 (19.0)	
Type of treatment, n (%)				**<0.001**
Medical	122 (15.6)	103 (20.2)	19 (6.9)	
PTCA	352 (44.9)	220 (43.1)	132 (48.2)	
Stent	261 (33.3)	165 (32.4)	96 (35.0)	
Bypass	49 (6.3)	22 (4.3)	27 (9.9)	
Amputation, n (%)	35 (4.5)	12 (2.4)	23 (8.4)	**<0.001**
Minor	23 (2.9)	11 (2.2)	12 (4.4)	0.079
Major	12 (1.5)	1 (0.2)	11 (4.0)	**<0.001**
Mortality, n (%)	186 (23.7)	86 (16.9)	100 (36.5)	**<0.001**

BMI, Body Mass Index; CAD, Coronary Artery Disease; CKD, Chronic Kidney Disease; CRP, C-Reactive Protein; HDL-C, High-Density Lipoprotein Cholesterol (mg/dL); LDL-C, Low-Density Lipoprotein Cholesterol (mg/dL); LVEF, Left Ventricular Ejection Fraction; PTCA, Percutaneous Transluminal Coronary Angioplasty; TASC II, TransAtlantic Inter-Society Consensus-II; WBC, White Blood Cell Count (10^6/L). Data are presented as mean ± standard deviation (SD) or n (%). Statistical significance is considered at a P-value of less than 0.05.

Table 3. Clinical, demographic, and outcome data by survival status

	All patients (n = 784)	Survivors (n = 598)	Non-survivors (n = 186)	P
Age, years	61.7 ± 9.9	59.6 ± 8.9	68.4 ± 10.1	**<0.001**
Gender (female), n (%)	135 (17.2)	76 (12.7)	59 (31.7)	**<0.001**
BMI, kg/m^2	26.9 ± 4.7	26.8 ± 4.5	27.0 ± 5.0	0.696
CHA_2DS_2-VASc score	3.00 ± 1.25	2.68 ± 1.07	4.06 ± 1.22	**<0.001**
Heart rate (minute)	87.0 ± 17.9	87.1 ± 17.8	86.6 ± 18.2	0.843
Systolic blood pressure (mmHg)	129.2 ± 15.0	129.1 ± 15.1	129.3 ± 14.5	0.878
Diastolic blood pressure (mmHg)	79.7 ± 9.7	79.5 ± 9.6	80.4 ± 10.1	0.269
Smoking, n (%)	505 (64.7)	382 (64.1)	123 (66.8)	0.494
Diabetes mellitus, n (%)	339 (43.2)	235 (39.3)	104 (55.9)	**<0.001**
Hypertension, n (%)	450 (57.4)	331 (55.4)	119 (64.0)	**0.038**
CAD, n (%)	427 (54.5)	306 (51.2)	121 (65.1)	**0.001**
Hyperlipidemia, n (%)	405 (51.7)	308 (51.5)	97 (52.2)	0.878
Cerebrovascular disease, n (%)	64 (8.2)	42 (7.0)	22 (11.8)	**0.037**
CKD, n (%)	206 (26.3)	118 (19.7)	88 (47.3)	**<0.001**
LVEF, %	53.1 ± 11.1	54.9 ± 10.0	47.3 ± 12.6	**<0.001**
Creatinine, (mg/dL)	0.98 (0.82–1.20)	0.94 (0.81–1.12)	1.13 (0.92–1.32)	**<0.001**
Hemoglobin, g/L	13.48 ± 2.58	13.64 ± 2.59	12.95 ± 2.49	**0.001**
Glucose (mg/dL)	147.4 ± 68.6	145.1 ± 68.0	153.9 ± 69.9	0.155
WBC, 106/L	8.73 ± 1.40	8.75 ± 1.42	8.69 ± 1.35	0.617
Total cholesterol, mg/dL	198.3 ± 45.9	198.0 ± 43.3	198.9 ± 45.0	0.821
LDL-C, mg/dL	121.5 ± 39.4	121.5 ± 39.8	121.5 ± 38.3	0.993
HDL-C, mg/dL	38.5 ± 7.2	38.4 ± 7.2	38.7 ± 7.2	0.599
Triglyceride, mg/dL	156 (112–215)	156 (110–210)	161 (117–224)	0.674
CRP (mg/dL)	3.50 (1.26–9.76)	2.95 (1.17–7.59)	4.70 (1.81–14.73)	**0.001**
Contrast volume (mL)	162.7 ± 70.7	161.6 ± 71.4	166.2 ± 68.6	0.437
Procedure duration (min)	57.7 ± 20.8	57.2 ± 21.2	59.2 ± 19.5	0.238
Rutherford, n (%)				**<0.001**
1	54 (6.9)	46 (7.7)	8 (4.3)	
2	133 (17.0)	117 (19.6)	16 (8.6)	
3	362 (46.2)	288 (48.2)	74 (39.8)	
4	143 (18.2)	99 (16.6)	44 (23.7)	
5	73 (9.3)	37 (6.2)	36 (19.4)	
6	19 (2.4)	11 (1.8)	8 (4.3)	
Fontaine, n (%)				**<0.001**
I	72 (9.2)	61 (10.2)	11 (5.9)	
II	483 (61.6)	393 (65.7)	90 (48.4)	
III	144 (18.4)	98 (16.4)	46 (24.7)	
IV	85 (10.8)	46 (7.7)	39 (21.0)	
Type of treatment, n (%)				**0.007**
Medical	122 (15.6)	85 (14.2)	37 (19.9)	
PTCA	352 (44.9)	257 (43.0)	95 (51.1)	
Stent	261 (33.3)	217 (36.3)	44 (23.7)	
Bypass	49 (6.3)	39 (6.5)	10 (5.4)	
TASC, n (%)				**<0.001**
AB	510 (65.1)	424 (70.9)	86 (46.2)	
CD	274 (34.9)	174 (29.1)	100 (53.8)	
Amputation, n (%)	35 (4.5)	15 (2.5)	20 (10.8)	**<0.001**
Minor	23 (2.9)	13 (2.2)	10 (5.4)	**0.024**
Major	12 (1.5)	2 (0.3)	10 (5.4)	**<0.001**

BMI, Body Mass Index; CAD, Coronary Artery Disease; CKD, Chronic Kidney Disease; CRP, C-Reactive Protein; HDL-C, High-Density Lipoprotein Cholesterol (mg/dL); LDL-C, Low-Density Lipoprotein Cholesterol (mg/dL); LVEF, Left Ventricular Ejection Fraction; PTCA, Percutaneous Transluminal Coronary Angioplasty; TASC II, TransAtlantic Inter-Society Consensus-II; WBC, White Blood Cell Count (10^6/L). Data are presented as mean ± standard deviation (SD) or n (%). Statistical significance is considered at a P-value of less than 0.05.

Table 4. Independent predictors of lesion severity in univariate and multivariate logistic regression analysis model

	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
Hemoglobin	0.979	0.925–1.036	0.453			
BMI	1.011	0.980–1.043	0.493			
CRP	0.994	0.986–1.001	0.097			
WBC	1.002	0.999–1.005	0.279			
LVEF	0.974	0.962–0.987	**<0.001**	0.982	0.968–0.995	**0.009**
Smoking	0.781	0.575–1.060	0.112			
CKD	1.529	1.102–2.120	**0.011**	1.287	0.917–1.806	0.144
Creatinine	1.029	0.877–1.208	0.725			
CHA_2DS_2-VASc group	1.932	1.401–2.666	**<0.001**	1.604	1.137–2.261	**0.007**

BMI, Body Mass Index; CI, Confidence Interval; CKD, Chronic Kidney Disease; CRP, C-Reactive Protein; LVEF, Left Ventricular Ejection Fraction; OR, Odds Ratio; WBC, White Blood Cell Count (106/L). Statistical significance is considered at a P-value of less than 0.05.

Table 5. Independent predictors of long-term mortality identified by univariate and multivariate cox regression analyses

	Univariate analysis			Multivariate analysis		
	HR	**95% CI**	**P**	**HR**	**95% CI**	**P**
Age	1.096	1.079–1.114	**<0.001**	**1.062**	**1.038–1.086**	**<0.001**
Gender	2.638	1.937–3.595	**<0.001**	1.258	0.881–1.797	0.207
CHA_2DS_2-VASc score	2.168	1.949–2.412	**<0.001**	1.272	1.040–1.555	**0.019**
DM	1.803	1.350–2.409	**<0.001**	1.589	1.097–2.302	**0.014**
LVEF	0.954	0.943–0.965	**<0.001**	0.976	0.962–0.991	**0.001**
CAD	1.622	1.200–2.192	**0.002**	1.137	0.830–1.557	0.424
CKD	3.027	2.269–4.038	**<0.001**	1.374	0.996–1.895	0.053
Hemoglobin	0.917	0.869–0.967	**0.001**	0.971	0.916–1.030	0.331
TASC	2.436	1.826–3.251	**<0.001**	1.211	1.034–1.418	**0.018**
Amputation	3.320	2.086–5.283	**<0.001**	2.450	1.514–3.965	**<0.001**

CAD, Coronary Artery Disease; CI, Confidence Interval; CKD, Chronic Kidney Disease; DM, Diabetes Mellitus; HR, Hazard Ratio; LVEF, Left Ventricular Ejection Fraction; TASC II, Transatlantic Inter-Society Consensus-II. Statistical significance is considered at a P-value of less than 0.05.

importance of early-stage classification and the development of effective treatment strategies. In this context, if risk stratification is performed early and high-risk patients are recognized, more effective interventions can be applied to improve the incidence and prognosis of PAD.[2,15] Although our study mainly focused on a non-invasive clinical risk score applicable to a broad PAD population, it is also important to consider advanced staging systems specifically developed for the management of CLTI. In recent years, classification systems such as WIfI (Wound, Ischemia, and Foot Infection) and GLASS (Global Limb Anatomic Staging System), supported by the European Society for Vascular Surgery (ESVS) guidelines, have been widely adopted, providing detailed anatomical and clinical risk stratification to guide revascularization strategies in CLTI patients.

Peripheral artery disease patients, particularly those classified as TASC-CD, demonstrated that higher WIfI clinical stages were associated with increased one-year amputation and mortality rates.[16] Similarly, in our study, when PAD patients were stratified according to lesion severity, those with TASC-CD lesions exhibited significantly higher rates of both amputation and long-term mortality.

These findings underscore the critical importance of evaluating wound infection and systemic comorbidities in the clinical decision-making process for TASC-CD patients. Although our study did not directly assess wound infection parameters, we believe that future research combining clinical risk scores such as CHA_2DS_2-VASc with wound-based or systemic comorbidity-based staging systems may offer a more comprehensive risk stratification for patients with advanced PAD.

With the rising prevalence of PAD, the importance given to this issue and the studies conducted have recently increased. Amputation rates also increase with the increasing incidence of PAD.[15] Interestingly, in our study, the overall rate of amputation—including among non-survivors—remained relatively low. This may be attributable to the advanced age, increased frailty, and higher burden of comorbidities in this population, which likely resulted in limited life expectancy and a greater emphasis on palliative care rather than limb salvage interventions. This has increased the use of various indices to evaluate the prognosis of PAD. Altunova et al.[17] analyzed the association between the atherogenic plasma index (AIP) and long-term consequences following endovascular treatment in patients with PAD. It was

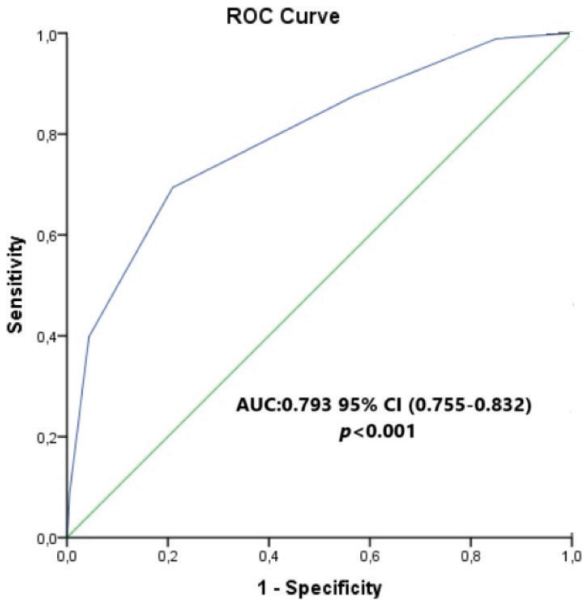

Figure 5. Receiver operating characteristic (ROC) curve demonstrating the predictive accuracy of the CHA_2DS_2-VASc score for long-term mortality. The score showed an area under the curve (AUC) of 0.793 (95% confidence interval [CI]: 0.755–0.832, P < 0.001), with an optimal cut-off value of 3.5, providing 70% sensitivity and 79% specificity. CHA_2DS_2-VASc score, Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack/ systemic embolism, Vascular disease, Age 65–74 years, and Sex category – female.

observed that long-term mortality and major adverse limb events increased as the AIP value increased. In that study, a rise in AIP was also associated with higher rates of amputation, suggesting that elevated AIP levels may contribute to both limb-related complications and overall mortality. In our study as well, both a high CHA_2DS_2-VASc score (≥ 3) and the presence of amputation were identified as independent predictors of long-term mortality. Notably, amputation was more frequently observed in patients with higher CHA_2DS_2-VASc scores, further emphasizing the close association between systemic cardiovascular risk burden and adverse limb outcomes in PAD. In a study by Duran Karaduman et al.,[18] which evaluated lesion severity in PAD, the relationship between the triglyceride-glucose index and PAD lesion severity was examined. It was observed that as the index increased, PAD lesion severity also increased. Consistently, we observed that lesion complexity increased in parallel with rising CHA_2DS_2-VASc scores, and the score was identified as an independent predictor of lesion severity in multivariate logistic regression analysis. An important distinction of our study from these others is the fact that indices like these may show dynamic changes during hospital admissions and follow-ups. However, the CHA_2DS_2-VASc score does not change before and after the procedure.

Recent literature suggests a link between the CHA_2DS_2-VASc score and the extent of CAD.[19] Given that both PAD and CAD share a common pathophysiological basis—namely, atherosclerosis—our findings support that higher CHA_2DS_2-VASc scores are significantly associated with greater lesion severity in PAD as well.

The CHA_2DS_2-VASc score was originally developed to stratify stroke risk in patients with non-valvular AF.[3] However, subsequent studies have demonstrated its prognostic utility beyond AF, particularly in patients with atherosclerotic cardiovascular disease. In this context, Goto et al.[20] reported that the CHADS2 score could predict cardiovascular mortality in high-risk atherosclerotic patients, even in the absence of atrial fibrillation. Bozbay et al.[11] indicated that a CHA_2DS_2-VASc score greater than 2 was connected with adverse clinical outcomes—including low LVEF, cardiogenic shock, reinfarction, and mortality—in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing percutaneous coronary revascularization. Similarly, in our study population, reduced LVEF was identified as an independent determinant of both lesion complexity and long-term mortality in patients with PAD. This parallel supports the broader applicability of a high CHA_2DS_2-VASc score in estimating unfavorable cardiovascular events across different patient populations.

One of the key advantages of the CHA_2DS_2-VASc score is its practicality. It is easy to apply at the bedside, does not require additional testing or incur extra costs, and remains stable regardless of pre- or post-procedural conditions. These features distinguish it from many other risk assessment tools. In patients with PAD, the use of the CHA_2DS_2-VASc score may support early risk stratification and subsequently aid in shaping treatment strategies. Specifically, patients with higher CHA_2DS_2-VASc scores were more likely to exhibit complex lesions according to TASC classification, potentially influencing therapeutic choices such as medical management, percutaneous transluminal angioplasty (PTCA), stenting, or surgical bypass. Furthermore, the score was identified as an independent predictor of long-term mortality in multivariate Cox regression analysis, highlighting its role in guiding clinical decision-making and demonstrating its prognostic utility during long-term follow-up in patients with PAD.

Several limitations should be considered. It is important to acknowledge that conducting the study retrospectively and within only two centers may constrain the external validity of the results. Furthermore, the relatively small cohort and the possibility of non-homogeneous patient distribution may also affect the robustness of the results. Due to the retrospective nature of the study and limitations in data availability, information regarding baseline medications could not be retrieved and was therefore not included. Additionally, although hypertension is incorporated as a binary parameter in the CHA_2DS_2-VASc score, the study design did not allow for distinguishing between controlled and uncontrolled hypertension, which may have differing prognostic implications. Propensity score matching or similar balancing techniques could not be performed, and this limitation may have introduced potential confounding related to baseline differences between groups. To confirm the prognostic findings, multicenter, long-term prospective studies with larger patient populations should be performed.

This study highlights the clinical utility of the CHA_2DS_2-VASc score in patients with PAD. Higher scores were significantly associated with increased lesion severity and reduced long-term survival. These findings indicate that the CHA_2DS_2-VASc score may serve as a practical and accessible prognostic tool in PAD, supporting risk stratification and potentially guiding treatment decisions.

Ethics Committee Approval: The study protocol has been approved by Dicle University Medical Faculty Ethics Committee for Non-Interventional Studies (Approval Number: 2024-296, Date: 16.10.2024).

Informed Consent: Written informed consent was not obtained due to the retrospective nature of the study.

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