

Research Article

Association between Rutherford Classification and CHA₂DS₂-VASC, CHADS₂ and ASCVD Scores in Peripheral Artery Disease Patients

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ABSTRACT

Background and Aim: The classification system is important in assessing the severity of Peripheral Artery Disease (PAD) and making the treatment decision. However, classification systems may not be sufficient and scoring systems developed to predict cardiovascular and cerebrovascular events can also be useful to assess the severity of PAD. In this study, our aim was to investigate the association of the Rutherford classification and CHADS₂, CHA₂DS₂-VASC and ASCVD scores in PAD patients.

Method: A total of 65 consecutive patients with PAD (males 92.3%, mean age 63.0 ± 9.2 years), who underwent percutaneous peripheral intervention were included in our retrospective study.

Results: There were 16 patients in Category 2, 31 patients in Category 3, and 10 patients in Category 4 and eight patients in Category 5. The CHADS₂, CHA₂DS₂-VASC and ASCVD scores were found to be significantly different among the Rutherford categories and between each other. From Category 1 to 5, CHADS₂, CHA₂DS₂-VASC and ASCVD scores were significantly increased. When we grouped the scores as CHADS₂ <2 and ≥2 and CHA₂DS₂-VASC <4 and ≥4, it was determined that as the category increased the score group also increased. There was significantly correlation between CHADS₂, CHA₂DS₂-VASC and ASCVD scores with the Rutherford categories in correlation analyses.

Conclusion: As far as we know, in this study which is the first study about the association of Rutherford classification and scoring systems, the major finding of the present study is that the CHADS₂, CHA₂DS₂-VASC and ASCVD scores was independently correlated with the severity of Rutherford Category in patients with PAD.

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1. INTRODUCTION

Peripheral Artery Disease (PAD) secondary to atherosclerotic disease is currently the leading cause of morbidity and mortality in developed and developing countries. The frequency of PAD also increases with the increase of age. Risk factors for PAD are age, cigarette smoking, diabetes mellitus, hypertension, hyperlipidemia, Chronic Kidney Disease, obesity, and race similar to Coronary Artery Disease (CAD) and stroke [1,2]. The presentations of PAD are different, and these are; asymptomatic, intermittent claudication, Critical Limb Ischemia (CLI) or Acute Limb Ischemia (ALI). To date, many anatomical, clinical, or imaging-based classification systems have been used for PAD. Effective grading of patients provides physicians with objective criteria for patient assessment, treatment and clinical follow-up. Classification systems are also

important in determining medical, surgical and percutaneous treatment preferences [3].

Although the CHADS₂ scoring system was first used, after than the CHA₂DS₂-VASC scoring system which became standard, has been proven effective for assessing the prognostic risk of thromboembolism in nonvalvular Atrial Fibrillation (AF) patients [4]. Some scoring systems have been developed to evaluate and treat the risk of atherosclerotic Cardiovascular (CV) disease in adults without known cardiovascular disease. One of them is the atherosclerotic cardiovascular disease (x) Risk Estimator, which has been used frequently in recent years and is recommended by the American College of Cardiology and the American Heart Association [5].

These scoring systems and cardiovascular and cerebrovascular diseases have similar risk factors and may be useful even to assess the severity of atherosclerotic diseases. There is little and improper data on the relationship between PAD and risk scores. Rutherford classification is used to identify the severity of the clinical symptoms with objective findings in PAD. In this study, our aim was to investigate the association of the Rutherford classification and CHADS₂, CHA₂DS₂-VASC and ASCVD scores in PAD patients.

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Data availability statement: The data that support the findings of this study are available from the corresponding author (HA), upon reasonable request.

2. MATERIALS AND METHODS

A total of 65 consecutive patients with PAD (males 92.3%, mean age 63.0 ± 9.2 years), who underwent percutaneous peripheral intervention were included in our retrospective study. Detailed medical history [age, gender, Diabetes Mellitus (DM), Hypertension (HT), Hyperlipidemia (HL), current cigarette smoking, family history of premature CAD, chronic heart failure, previous ischemic stroke or TIA, and PAD] and physical, standard 12-lead electrocardiographic, and echocardiographic examinations were performed, and the Rutherford classification were obtained for each patient according to the current literature (Table 1) [6]. Thereafter, all the scores (CHADS₂, CHA₂DS₂-VASc and ASCVD) were calculated. Blood samples for fasting blood glucose, Total Cholesterol (TC), Low-density Lipoprotein Cholesterol (LDL-C), High-density Lipoprotein Cholesterol (HDL-C), Triglycerides (TG), and complete blood count were performed using standard laboratory methods. Type 2 DM was defined as a previous diagnosis and/or fasting blood glucose ≥ 126 mg/dl or the use of antidiabetic medications. HT was defined as repeated measurements of systolic blood pressure ≥ 140 mm Hg and/or diastolic ≥ 90 mm Hg, or chronic treatment with antihypertensive medications. HL was considered to be LDL-C above the target level according to the National Cholesterol Education Program-3 recommendations or the use of lipid-lowering medications. Cigarette smoking was defined as smoking ≥ 10 cigarettes a day for at least 1 year without a quit attempt. Transthoracic echocardiography was performed for each patient before intervention (Vivid 7 GE Medical System; GE Healthcare, Horten, Norway). Left Ventricular Ejection Fraction (LVEF) was measured using Simpson's method.

The CHADS₂ score was the total of one point each for Heart Failure (HF), HT, age ≥ 75 years, and DM and two points for prior stroke or TIA. The CHA₂DS₂-VASc score was the total of one point each for HF, HT, age 65–74 years, DM, vascular disease, and female gender and two points each for prior stroke or TIA and age ≥ 75 years. ASCVD score was calculated by using calculation tool of guideline (<http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/>). The study was approved by the local ethics committee and individual informed consent was obtained from all subjects.

2.1. Statistical Analysis

All analyses were performed using SPSS for Windows (version 22.0, SPSS, Chicago, IL, USA). Data are expressed as percentages or mean \pm standard deviation. Continuous variables were analyzed

Table 1 | Rutherford classification for chronic limb ischemia

Grade	Category	Clinical description
0	0	Asymptomatic—no hemodynamically significant occlusive disease
	1	Mild claudication
I	2	Moderate claudication
	3	Severe claudication
II	4	Ischemic rest pain
III	5	Minor tissue loss—non-healing ulcer, focal gangrene with diffuse pedal ischemia
	6	Major tissue loss—extending above TM level, functional foot no longer salvageable

for normal distribution using the Kolmogorov–Smirnov test. Categorical and continuous variables between groups were compared by independent Chi-square test and samples *t*-test, respectively. Categorical variables were presented as frequencies and percentages and compared using Pearson's and Fisher's Exact Test the Chi-square test. One-way repeated measures ANOVA was used for normally distributed continuous variables. A *p*-value < 0.05 was considered as significant.

3. RESULTS

Demographic and laboratory characteristics of patients were categorized by Rutherford Categories (1–5). There were 16 patients in Category 2 (100% men, with a mean age of 62.7 ± 7.9 years), 31 patients in Category 3 (96.8% men, with a mean age of 59.6 ± 8.9 years), and 10 patients in Category 4 (90.0% men, with a mean age of 71.8 ± 8.6 years) and eight patients in Category 5 (62.5% men, with a mean age of 64.8 ± 5.4 years). Table 2 shows the comparison of clinical characteristics between Rutherford classifications. Category 4 was older, Category 3 was younger and Category 5 has less male gender, and there was a significant difference between age and gender groups ($p = 0.004$ and 0.006 , respectively). While most of the patients in the categories presented with intermittent claudication symptoms, half of the patients in Category 5 consulted with rest pain. As the category stage increased, walking distance decreased significantly without intermittent claudication. DM and previous Percutaneous Coronary Intervention (PCI) were significantly different between the categories ($p = 0.007$ and 0.035 , respectively). In the majority of patients in all categories, the target vessels are iliac arteries and femoral arteries. Patients in the high category groups had significantly higher serum glucose, TC and LDL-C levels and HDL-C and TG levels were significantly lower compared with the other groups.

The CHADS₂, CHA₂DS₂-VASc and ASCVD scores were found to be significantly different among the Rutherford categories and between each other. From Category 1 to 5, CHADS₂, CHA₂DS₂-VASc and ASCVD scores were significantly increased. When we grouped the scores as CHADS₂ < 2 and ≥ 2 and CHA₂DS₂-VASc < 4 and ≥ 4 , it was determined that as the category increased the score group also increased. The CHADS₂, CHA₂DS₂-VASc and ASCVD scores of patients according to Rutherford categories are listed in Tables 3 and 4. The CHADS₂, CHA₂DS₂-VASc, and their groups correlated significantly with the Rutherford categories (Table 4). When we performed Rutherford staging instead of the category, the scores increased as the stage increased (Table 5). The association between the Rutherford Category and the CHADS₂, CHA₂DS₂-VASc and ASCVD scores was shown in Figure 1.

4. DISCUSSION

In this study, we evaluated the association of Rutherford classifications with CHADS₂, CHA₂DS₂-VASc and ASCVD scores. The major finding of the present study is that the CHADS₂, CHA₂DS₂-VASc and ASCVD scores was independently correlated with the severity of Rutherford Category in patients with PAD.

Peripheral artery disease often affects 13% of the population over 50 years of age with stenosis or occlusion due to atherosclerosis [7].

Table 2 | Baseline characteristics of the patients

Parameters	All patients (n = 65)	Rutherford Category 2 (n = 16)	Rutherford Category 3 (n = 31)	Rutherford Category 4 (n = 10)	Rutherford Category 5 (n = 8)	p-value
Age (years)	63.0 ± 9.2	62.7 ± 7.9	59.6 ± 8.9	71.8 ± 8.6	64.8 ± 5.4	0.004
Male, n (%)	60 (92.3)	16 (100.0)	30 (96.8)	9 (90.0)	5 (62.5)	0.006
Symptom, n (%)						<0.001
Intermittent claudication	53 (81.5)	14 (87.5)	31 (100.0)	6 (60.0)	2 (25.0)	
Rest pain	7 (10.7)	2 (12.6)	–	1 (10.0)	4 (50.0)	
Trophic changes	5 (7.8)	–	–	3 (30.0)	2 (25.0)	
Walking distance without claudication (mt)	74.0 ± 58.0	103.8 ± 51.8	79.3 ± 60.7	42.2 ± 38.2	26.0 ± 21.9	0.003
HT, n (%)	55 (84.6)	13 (81.3)	24 (77.4)	10 (100.0)	8 (100.0)	0.200
HL, n (%)	46 (70.7)	13 (81.3)	18 (58.1)	9 (90.0)	6 (75.0)	0.163
Current smoker, n (%)	33 (50.8)	7 (43.8)	18 (58.1)	5 (50.0)	3 (37.5)	0.174
DM, n (%)	34 (53.3)	8 (50.0)	10 (32.2)	8 (80.0)	8 (100.0)	0.007
AF, n (%)	4 (6.1)	1 (6.3)	1 (3.2)	–	2 (25.0)	0.110
Previous PCI, n (%)	27 (41.5)	9 (56.3)	12 (38.7)	6 (60.0)	–	0.035
Previous CABG, n (%)	14 (21.5)	5 (31.3)	7 (22.6)	1 (10.0)	1 (12.5)	0.554
Previous peripheral intervention, n (%)	9 (13.8)	3 (18.8)	5 (16.1)	1 (10.0)	–	0.600
Stenosis (%)	94.0 ± 7.2	94.6 ± 7.1	93.8 ± 6.9	92.0 ± 9.1	98.3 ± 4.1	0.242
CAD, n (%)						0.227
Normal	10 (15.4)	1 (6.3)	6 (19.3)	2 (20.0)	1 (12.5)	
1 vessel disease	22 (33.8)	8 (50.0)	7 (22.6)	4 (40.0)	3 (37.5)	
2 vessel disease	29 (44.6)	7 (43.8)	16 (51.6)	4 (40.0)	2 (25.0)	
3 vessel disease	4 (6.2)	–	2 (6.5)	–	2 (25.0)	
Target vessel, n (%)						0.829
CIA	24 (36.9)	6 (37.5)	10 (32.2)	5 (50.0)	3 (37.5)	
SFA	33 (50.8)	9 (56.4)	16 (51.6)	4 (40.0)	4 (50.0)	
Popliteal	5 (7.7)	1 (6.3)	2 (6.4)	1 (10.0)	1 (12.5)	
Below the knee	3 (4.6)	–	3 (9.7)	–	–	
CHA ₂ DS ₂ -VASc group, n (%)						0.002
<4	38 (58.5)	10 (62.5)	24 (77.4)	2 (20.0)	2 (25.0)	
≥4	27 (41.5)	6 (37.5)	7 (22.6)	8 (80.0)	6 (75.0)	
CHADS ₂ group, n (%)						0.003
<2	38 (58.5)	7 (43.8)	20 (64.5)	2 (20.0)	–	
≥2	27 (41.5)	9 (56.3)	11 (35.5)	8 (80.0)	8 (100.0)	
ASCVD score	22.9 ± 13.5	23.9 ± 15.5	17.0 ± 8.0	32.0 ± 14.7	30.4 ± 15.1	0.012
CHA ₂ DS ₂ -VASc	3.1 ± 1.1	3.0 ± 1.0	2.7 ± 1.0	4.1 ± 1.1	3.7 ± 0.6	0.001
CHADS ₂	1.6 ± 0.9	1.5 ± 0.8	1.3 ± 0.8	2.6 ± 0.8	2.1 ± 0.2	<0.001
Echocardiographic parameters						
LVEF (%)	51.2 ± 13.9	48.3 ± 15.6	52.9 ± 13.4	44.0 ± 15.7	56.8 ± 8.8	0.222
LVEDD (cm)	4.8 ± 0.6	5.3 ± 0.9	4.7 ± 0.5	4.8 ± 0.4	4.6 ± 0.2	0.435
LVESD (cm)	3.2 ± 0.7	3.7 ± 1.1	3.0 ± 0.7	3.3 ± 0.7	2.9 ± 0.1	0.623
LA (cm)	3.9 ± 0.5	4.0 ± 0.4	3.9 ± 0.5	3.9 ± 0.6	3.4 ± 0.2	0.033
sPAP (mm Hg)	23.8 ± 15.3	24.5 ± 16.1	21.0 ± 13.6	30.0 ± 19.5	23.7 ± 10.3	0.470
Laboratory parameters						
Serum glucose (mg/dl)	134.4 ± 70.0	139.7 ± 63.1	120.8 ± 68.3	115.3 ± 59.8	197.8 ± 76.2	0.019
HbA1c (%)	6.68 ± 1.66	6.54 ± 1.45	6.52 ± 2.04	6.32 ± 1.32	7.25 ± 0.82	0.080
Serum creatinine (mg/dl)	1.1 ± 0.9	1.2 ± 0.9	1.0 ± 0.3	1.1 ± 0.5	1.8 ± 1.1	0.208
Total cholesterol (mg/dl)	188.8 ± 41.9	185.9 ± 55.2	193.8 ± 35.7	149.4 ± 45.0	212.8 ± 35.9	0.004
Triglyceride (mg/dl)	192.7 ± 123.6	255.2 ± 201.8	188.9 ± 70.5	90.1 ± 19.4	193.5 ± 70.6	0.003
LDL cholesterol (mg/dl)	112.8 ± 33.3	105.6 ± 43.6	117.1 ± 28.5	85.2 ± 16.3	140.6 ± 24.6	0.002
HDL cholesterol (mg/dl)	39.9 ± 12.9	38.6 ± 9.5	40.7 ± 13.2	45.9 ± 17.0	33.0 ± 10.0	0.215
Hemoglobin (g/dl)	14.6 ± 2.1	14.1 ± 1.9	15.3 ± 1.6	13.7 ± 3.0	13.9 ± 2.2	0.346
Platelet (×10 ⁹ /L), mean ± SD	239.6 ± 61.8	229.5 ± 69.8	246.0 ± 46.0	215.3 ± 69.5	262.0 ± 74.2	0.261

CABG, coronary artery bypass grafting; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LA, left atrium; sPAP, systolic pulmonary artery pressure; CIA, common iliac artery; SFA, superficial femoral artery.

In our study, the mean age of the patients was 63.0 ± 9.2 years and the age increased as the category increased. A frequent symptom of PAD is painful pain in the leg muscles that pass through rest, triggered by walking, known as intermittent claudication. CLI is an

advanced stage of PAD and is manifested by rest pain, ulceration, gangrene and/or tissue loss in the extremities. The classification system is important in assessing the severity of PAD and making the treatment decision. Although there are many classification systems

Table 3 | Rutherford Category and scores

Parameters	Rutherford Category 2 (n = 16)	Rutherford Category 3 (n = 31)	Rutherford Category 4 (n = 10)	Rutherford Category 5 (n = 8)	p-value (2–3)	p-value (2–4)	p-value (2–5)	p-value (3–4)	p-value (3–5)	p-value (4–5)
CHA ₂ DS ₂ -VASc group, n (%)					0.279	0.034	0.083	0.001	0.005	0.800
<4	10 (62.5)	24 (77.4)	2 (20.0)	2 (25.0)						
≥4	6 (37.5)	7 (22.6)	8 (80.0)	6 (75.0)						
CHADS ₂ group, n (%)					0.172	0.216	0.026	0.014	0.001	0.180
<2	7 (43.8)	20 (64.5)	2 (20.0)	–						
≥2	9 (56.3)	11 (35.5)	8 (80.0)	8 (100.0)						
ASCVD score	23.9 ± 15.5	17.0 ± 8.0	32.0 ± 14.7	30.4 ± 15.1	0.049	0.202	0.345	< 0.001	0.001	0.821
CHA ₂ DS ₂ -VASc	3.0 ± 1.0	2.7 ± 1.0	4.1 ± 1.1	3.7 ± 0.6	0.250	0.025	0.097	0.001	0.010	0.414
CHADS ₂	1.5 ± 0.8	1.3 ± 0.8	2.6 ± 0.8	2.1 ± 0.2	0.420	0.003	0.101	< 0.001	0.027	0.063

Table 4 | Correlations of Rutherford Category and scores

Parameters	r	p-value
CHA ₂ DS ₂ -VASc group	0.308	0.012
CHADS ₂ group	0.270	0.030
ASCVD score	0.211	0.091
CHA ₂ DS ₂ -VASc score	0.300	0.015
CHADS ₂ score	0.325	0.008
Severity of stenosis	0.065	0.618
Gender	–0.343	0.005
DM	–0.299	0.015
Walking distance without claudication	–0.500	< 0.001

Table 5 | Rutherford stage and scores

Parameters	Rutherford stage I (n = 47)	Rutherford stage II (n = 10)	Rutherford stage III (n = 8)	p-value
CHA ₂ DS ₂ -VASc group, n (%)				0.001
<4	34 (72.3)	2 (20.0)	2 (25.0)	
≥4	13 (27.7)	8 (80.0)	6 (75.0)	
CHADS ₂ group, n (%)				0.002
<2	27 (57.4)	2 (20.0)	–	
≥2	20 (42.6)	8 (80.0)	8 (100.0)	
ASCVD score	19.4 ± 11.5	32.0 ± 14.7	30.4 ± 15.1	0.012
CHA ₂ DS ₂ -VASc	2.8 ± 1.0	4.1 ± 1.1	3.7 ± 0.6	0.001
CHADS ₂	1.3 ± 0.8	2.6 ± 0.8	2.1 ± 0.2	< 0.001

Rutherford Category and Scores

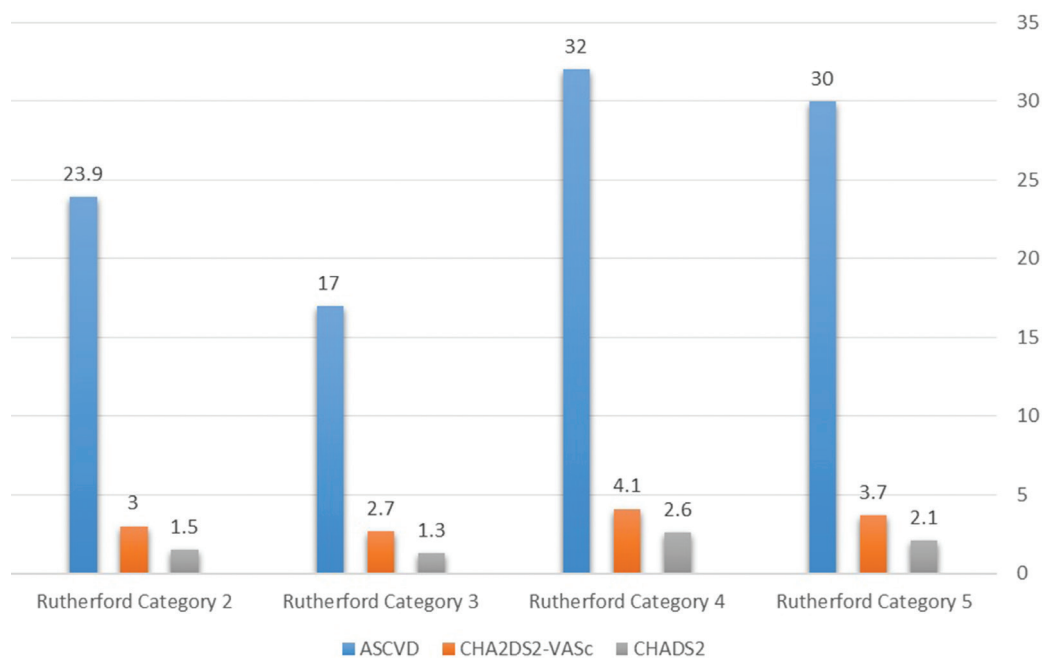


Figure 1 | The association between the Rutherford Category and the scores.

in this area, the most common and useful ones are Rutherford and Trans-Atlantic Inter-Society Consensus II (TASC) classifications. However, classification systems may not be sufficient and scoring systems developed to predict cardiovascular and cerebrovascular events can also be useful to assess the severity of PAD. Because having atherosclerosis in the extremities is not only associated with complications associated with it, but also carries a high risk of CV and cerebrovascular morbidity and mortality due to concomitant atherosclerotic disease and concomitant risk factors in other vascular beds [8,9].

In order to properly select prevention and treatment strategies, clinicians need viable, reliable, simple and objective tools to define patient risk limits. The CHADS₂, CHA₂DS₂-VASc and ASCVD scoring models are clinical predictors used to determine the risk of thromboembolism and CV risk estimate [4,5]. These risk scores are widely used in clinical practice and include similar risk factors for the development of PAD. A few observational and epidemiological studies have reported the association between PAD and scoring systems. CHADS₂ and CHA₂DS₂-VASc scores models were studied in non-AF patient groups and were found to be effective and usable [10–12]. In these four studies, these scoring models were shown to be associated with CAD severity and predicting events. However, data on PAD on this issue are limited in the literature. In the studies of Hsu et al. [13–15] evaluated the association between Ankle-Brachial Index (ABI) and CHADS₂ and modified CHA₂DS₂-VASc scores. In the first study, they showed that the association between CHADS₂ score and ABI < 0.9 and confirmed CHADS₂ score was significantly associated with ABI < 0.9 in non-AF patients [13]. After that they demonstrated that CHADS₂ score was useful in predicting the risk of new-onset PAD [14]. In their last study determined that modified CHA₂DS₂-VASc score was significantly associated with ABI < 0.9 and they argued that calculation of modified CHA₂DS₂-VASc score may be beneficial in recognizing patients with PAD and in graduating the risk of PAD [15]. In our study, the results are consistent with the results in these studies and as well as these scores, ASCVD score model has been shown to be related to the PAD stage. The CHADS₂ ≥ 2 and CHA₂DS₂-VASc ≥ 4 are well-known risk factor for other atherosclerotic disease and AF. Our present study in peripheral artery disease patients, similarly, found that the Rutherford Category was significantly high in the CHADS₂ ≥ 2 and CHA₂DS₂-VASc ≥ 4 groups. Based on these data, it is thought that the patient's Rutherford stage can be estimated according to the CHADS₂, CHA₂DS₂-VASc and ASCVD scores or CHADS₂ and CHA₂DS₂-VASc groups in patients with peripheral artery disease.

Several multivariable risk prediction algorithms incorporating major risk factors have been developed to assess the risk of atherosclerotic CVD, such as the European SCORE and ASCVD score systems [5,16]. The ASCVD, a gender-specific algorithm used to estimate the 10-year risk of developing CAD, was first developed based on data obtained from the Framingham Heart Study. In our study, we used the ASCVD scoring model, which was not previously studied in the literature, and showed that it is higher in the advanced Rutherford Category. While there is a statistically significant negative correlation between Rutherford Category level and gender, DM and walking distance without claudication, there is a statistically significant positive correlation with CHADS₂, CHA₂DS₂-VASc scores and CHADS₂ ≥ 2 and CHA₂DS₂-VASc ≥ 4 groups.

4.1. Study Limitations

There are several limitations of this study. First of all this study is a retrospective trial and the sample size is small. Another limitation of the study is the comparison according to the degree of Rutherford Classification and the absence of control group. Since our center is a reference center, as long-term follow-up data is limited, the effect on mortality is uncertain. The present our study was of a single-center retrospective design with a small sample size, and so the results might differ if a larger population were used.

5. CONCLUSION

According to the results obtained from our study, high CHADS₂, CHA₂DS₂-VASc and ASCVD scores have been shown to be associated with advanced Rutherford Classification. Further large randomized studies are needed in PAD patients and scoring systems.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

BDK and HA contributed in literature search, study conceptualization, study design, data collection, data analysis and manuscript writing. TK and EB contributed in curation and literature search.

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