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The Association of CHA_2DS_2-VASc and CHA_2DS_2-VA Scores with Aortic Arch Calcification and Its Clinical Value in Individuals with Atrial Fibrillation

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ABSTRACT

Introduction: This study investigates the relationship between aortic arch calcification (AAC) and the stroke risk scores, CHA_2DS_2-VASc and CHA_2DS_2-VA, in patients with atrial fibrillation (AF). It aims to evaluate the association between AAC and these scores and to assess its potential as a marker for cardiovascular risk stratification.

Methods: This cross-sectional study included 492 participants stratified by AAC severity (Grades 0-3) based on standard chest X-rays. Stroke risk scores were calculated based on clinical data. Additional parameters, including renal function, inflammatory markers, and medication use, were recorded. Statistical analyses included univariate and multivariate regression analyses, as well as receiver operating characteristic (ROC) curve analysis, to evaluate the predictive value of stroke risk scores for AAC severity.

Results: Patients with higher AAC grades demonstrated significantly elevated CHA_2DS_2-VASc and CHA_2DS_2-VA scores ($p<0.001$). AAC severity correlated with advanced age, reduced glomerular filtration rate (GFR), lower serum albumin, and anemia. Logistic regression also identified GFR, beyond the stroke risk scores, as an independent predictor of AAC severity. ROC analysis demonstrated that CHA_2DS_2-VASc [area under the curve (AUC): 0.694] and CHA_2DS_2-VA (AUC: 0.688) scores significantly predicted AAC severity, with optimal cut-off values of >3 and >2, respectively ($p<0.001$).

Conclusion: AAC is significantly associated with higher stroke risk scores in patients with AF, and may serve as an additional tool for risk stratification. Incorporating the AAC assessment into current risk models could provide additional context for cardiovascular risk stratification in patients with AF; however, prospective validation with stroke outcomes is needed.

Keywords: Aortic arch calcification, CHA_2DS_2-VASc score, cardiovascular risk

Introduction

One important field of research in contemporary clinical practice is the prevention of cerebrovascular disorders. Thrombotic or embolic events that decrease blood supply to the brain are frequently implicated in the pathophysiology of ischemic stroke. The most prevalent cardiac arrhythmia associated with stroke etiology, especially when it comes to cardioembolic processes, is atrial fibrillation (AF) (1). As a result, AF diagnosis and treatment are crucial, particularly when it comes to detecting cardiac-origin thrombi and determining the etiology of the stroke. For risk assessment in clinical practice, numerous scoring systems have been created and are now in use. Initially, the $CHADS_2$ score was utilized, which was later updated to the CHA_2DS_2-VASc score by incorporating adjustments for gender, vascular disease, and age (2). Most recently, the scoring system was changed to the CHA_2DS_2-VA score because gender has declined in importance for risk weighting (3). These scoring systems provide clinicians with a convenient method for estimating the annual risk of embolic events. For example, an individual with a CHA_2DS_2-VASc score of 5 (or a CHA_2DS_2-VA score of 4) carries an approximate 7% annual risk of ischemic stroke (2,3).

Recent studies have made recommendations to enhance the relevance and accuracy of this scoring system. According to one study, adding creatinine clearance to mortality prediction data produced more reliable results, especially for those with low creatinine clearance (4). In addition, versions that modify the effectiveness of age have also been previously studied (5). In another study, the gender component score was reversed and it was suggested that the CHA_2DS_2-VASc score may be predictive as a mortality predictor during the pandemic period (6).

Aortic arch calcification (AAC) is a clinically significant characteristic in thrombotic events and has been linked to classic cardiovascular risk factors (7-9). Specifically, there are statistically significant correlations between the severity of cardiovascular illnesses and the degree of AAC

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(10,11). AAC has been thoroughly investigated in various studies as a significant indicator of active and progressive systemic atherosclerosis, rather than simply a manifestation of the aging process (7-11). Further advantages in risk assessment of patients with AF may arise from the correlation of CHA_2DS_2-VASc and CHA_2DS_2-VA scores with the extent of AAC. The aim of this study was to examine the severity of AAC in patients with AF and to evaluate a possible relationship with CHA_2DS_2-VASc and CHA_2DS_2-VA scores, which are used to predict the risk of cerebrovascular events.

Methods

This study was a cross-sectional observational study. Patients who presented to the outpatient clinic during a 6-month period were consecutively included in the study. The sample size required for inclusion in the study was calculated using the G*Power program. The study's primary variable is the degree of AAC. A sample size of at least 210 cases was determined, based on a paired Student's t-test with 95% power, an α error probability of 0.05, and a medium effect size according to Cohen.

All patients who presented to the cardiology outpatient clinic and provided consent to participate in the study underwent a comprehensive evaluation for inclusion. The exclusion criteria for the study were met if an active infection, an active malignancy, or pregnancy was detected.

A comprehensive medical history was obtained from all subjects included in the study, and comorbid cardiovascular, renal, and endocrinological conditions were documented. The body mass index [(BMI), kg/m^2] and the body surface area [(BSA), m^2] were calculated using the following formula: "weight/height²" and "SquareRoot ([height (cm) x weight (kg)]/3600)," respectively. Routine blood tests were performed on all individuals included in the study. The glomerular filtration rate (GFR) was calculated using the estimated GFR formula, and the modified Simpson method was used for the assessment of ejection fraction (12). CHA_2DS_2-VASc and CHA_2DS_2-VA scores were calculated based on the participants' data (2,3).

AACs and cardiac condition were assessed by cardiologists. At a focus-to-patient distance of 150 cm, standard chest X-rays were taken while the patient was upright. AAC received the following grade (13): There is no calcification apparent in Grade 0; there are thin calcifications or tiny calcification spots on the aortic knob in Grade 1; there are one or more thicker calcification areas in Grade 2; and there is circular calcification on the aortic knob in Grade 3 (Figure 1). Each participant's cardiothoracic index was determined using the same chest X-ray. The aorta/heart and aorta/lung ratios were also computed by dividing the aortic arch width by the heart and lung widths (as determined by the cardiothoracic index). Interobserver agreement, assessed by Cohen's kappa, was close to perfect (κ: 0.817, $p<0.001$).

For ethical compliance, approval was obtained from the Non-Interventional Ethics Committee of Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital (protocol number: 43, date: 12.05.2023). All individuals included in the study were informed about the research in accordance with the ethical principles outlined in the Second Declaration of Helsinki on research involving human subjects, and their written informed consent was obtained.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). The normality of continuous variables was assessed by visual inspection of histograms and Q-Q plots and by the Shapiro-Wilk test. Continuous variables following a normal distribution were presented as mean (± standard deviation), while non-normally distributed continuous variables were reported as median (interquartile range). Categorical variables were expressed as numbers and percentages. For group comparisons, continuous variables that were normally distributed were analyzed using Student's t-test, while continuous variables that were not normally distributed were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test or Fisher's exact test. Logistic regression analyses, both univariate and multivariate, were performed to identify predictors. Receiver operating characteristic (ROC) curve analysis was used to determine cut-off values and evaluate sensitivity and specificity. A two-sided p value <0.05 was considered statistically significant for all comparisons.

Results

A total of 492 consecutive individuals who provided consent to participate in the study were included in the analysis. First, participants were stratified into three groups based on AAC grade: absent (Grade 0, n=111), mild (Grade 1, n=211), and severe (Grade 2–3, n=170). Because clinical findings were prominent when AAC was present, significance tests were conducted on a binary basis according to the presence or absence of AAC (AAC absent, n=111; AAC present, n=381). The findings are detailed according to both AAC presence and category (Table 1).

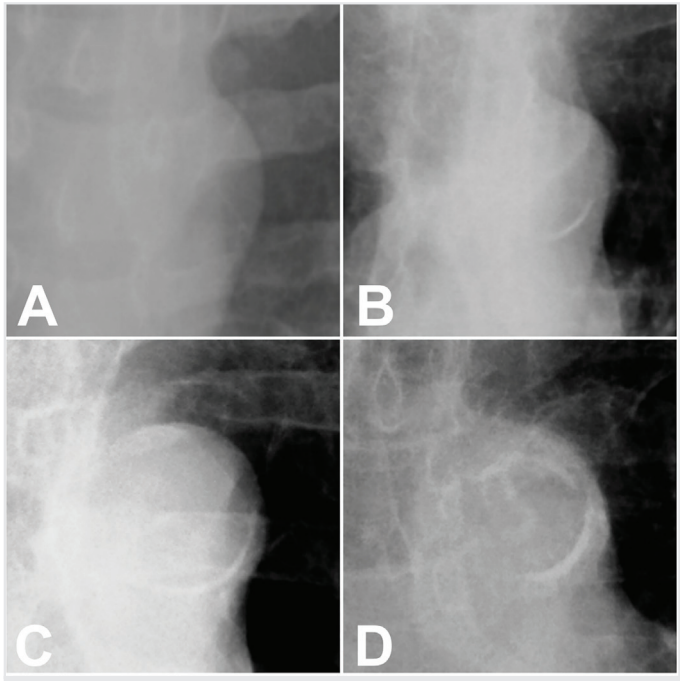

Figure 1. Aortic arch calcification grades. A) Grade 0: No calcification, B) Grade 1: Thin calcifications or tiny calcification spots, C) Grade 2: One or more thicker calcification areas, D) Grade 3: Circular calcification

Table 1. Demographic findings of study group

Parameters	Total n=492	AAC absent	AAC present			p value
		Grade 0 n=111	Mild (Grade 1) n=211	Severe (Grade 2-3) n=170	Total n=381	
Age, years	77.68±12.75	69.45±15.39	78.68±10.31	81.76±11.28	80.05±10.83	<0.001*
Gender (female)	282 (57.3%)	61 (54.9%)	117 (55.4%)	104 (61.2%)	221 (55.4%)	0.169
Body mass index, kg/m²	29.56±6.63	29.98±6.91	30.05±6.27	28.73±6.87	29.44±6.56	0.640
Body surface area, m²	1.41±0.82	1.50±0.83	1.36±0.86	1.44±0.78	1.39±0.83	0.390
Hypertension	420 (85.4%)	91 (82.0%)	179 (84.8%)	150 (88.2%)	329 (86.4%)	0.530
DM	132 (26.8%)	25 (22.5%)	54 (25.5%)	53 (31.2%)	107 (28.1%)	0.436
CAD	157 (31.9%)	27 (24.3%)	65 (30.8%)	65 (38.2%)	130 (34.1%)	0.172
CHF	65 (13.2%)	15 (13.5%)	27 (12.8%)	23 (13.5%)	50 (13.1%)	0.969
Stroke	123 (25.0%)	27 (24.3%)	52 (24.6%)	45 (26.4%)	96 (25.2%)	0.821
Hyperlipidaemia	161 (32.7%)	34 (30.9%)	64 (30.2%)	63 (37.0%)	127 (33.3%)	0.843
PAD	37 (7.7%)	8 (7.3%)	16 (7.5%)	13 (7.6%)	29 (7.6%)	0.975
CKD	51 (10.3%)	5 (4.5%)	30 (14.2%)	16 (9.4%)	46 (12.0%)	0.118
CHA_2DS_2-VASc	4.13±1.48	3.33±1.58	4.18±1.37	4.62±1.35	4.37±1.38	<0.001*
CHA_2DS_2-VA	3.56±1.41	2.78±1.56	3.63±1.26	4.00±1.29	3.79±1.28	<0.001*
RAAS blocker	280 (56.9%)	42 (37.8%)	132 (62.3%)	106 (62.4%)	238 (62.3%)	0.002*
Anti-hyperlipidaemic	146 (29.7%)	35 (31.5%)	44 (20.8%)	67 (39.4%)	111 (29.1%)	0.952
Calcium channel blocker	149 (30.3%)	24 (21.6%)	56 (26.4%)	69 (40.6%)	125 (33.6%)	0.156
Beta blocker	328 (66.7%)	76 (69.1%)	146 (68.9%)	106 (62.4%)	252 (66.0%)	0.787
Insulin	36 (7.3%)	4 (3.6%)	16 (7.5%)	18 (9.4%)	32 (8.4%)	0.370
Antiplatelet	50 (10.2%)	12 (10.9%)	18 (8.5%)	20 (11.8%)	38 (9.9%)	0.742
Digoxin	84 (17.1%)	22 (20.0%)	30 (14.2%)	32 (18.8%)	62(16.2%)	0.652
LT4	14 (2.8%)	2 (1.8%)	10 (4.7%)	2 (1.1%)	12 (3.1%)	0.511
Antithyroid	6 (1.2%)	2 (1.8%)	2 (0.9%)	2 (1.2%)	4 (1.0%)	0.890
Oral antidiabetic	114 (23.2%)	22 (20.0%)	46 (21.7%)	46 (27.1%)	92 (24.1%)	0.652
Diuretic	234 (47.6%)	38 (34.5%)	106 (50.0%)	90 (52.9%)	196 (51.3%)	0.041*
Amiodarone	28 (5.7%)	6 (5.5%)	14 (6.6%)	8 (4.7%)	22 (5.8%)	0.850
Anticoagulant						
Apixaban	144 (29.3%)	68 (30.9%)	68 (32.1%)	42 (24.7%)	110 (28.8%)	0.845
Dabigatran	12 (2.4%)	8 (3.6%)	6 (2.8%)	2 (1.2%)	8 (2.1%)	
Edoxaban	72 (14.6%)	28 (12.7%)	32 (15.1%)	26 (15.3%)	58 (15.2%)	
Rivaroxaban	234 (47.6%)	108 (49.1%)	92 (43.4%)	88 (51.8%)	180 (47.1%)	
Warfarin	30 (6.1%)	8 (3.6%)	14 (6.6%)	12 (7.1%)	26 (6.8%)	

*Statistically significant p values. AAC: Aortic arch calcification, DM: Diabetes mellitus, CAD: Coronary artery disease, CHF: Congestive heart failure, PAD: Peripheral artery disease, CKD: Chronic kidney disease, RAAS: Renin–angiotensin–aldosterone system, LT4: Levothyroxine

The cohort's average age was 77.68±12.75 years. The age difference between participants with severe AAC (81.76±11.28 years) and those without AAC (69.45±15.39 years, p<0.001) was significant. There was no discernible change in the gender distribution (p=0.169), despite a minor variation in the proportion of females between groups (56.3% in Grade 0 vs. 61.2% in Grades 2–3). Body composition measures showed no significant difference between groups (p=0.640 and p=0.390, respectively), with the mean BMI for the entire cohort being 29.56±6.63 kg/m² and the mean BSA being 1.41±0.82 m². Hypertension was the most prevalent comorbidity, affecting 85.4% of participants; however, the difference between the groups was not statistically significant (p=0.530). Diabetes mellitus was noted in 26.8% of participants; its prevalence increased with AAC severity (Grade 0: 21.8%; Grades 2–3: 31.8; p=0.436).

CHA_2DS_2-VASc and CHA_2DS_2-VA scores were significantly associated with AAC severity. The mean CHA_2DS_2-VASc score increased from 3.33±1.58 in the no AAC group to 4.62±1.35 in the severe group (p<0.001 for AAC presence). A similar pattern was observed for CHA_2DS_2-VA scores (Grade 0: 2.78±1.56 vs. Grades 2–3: 4.00±1.29, p<0.001 for AAC presence).

Laboratory parameters highlighted significant differences among AAC groups, particularly in markers of renal function, nutrition, and anemia (Table 2). GFR declined significantly with increasing AAC severity. The mean GFR was 83.80±14.75 mL/min in the absent AAC group compared to 69.79±18.79 mL/min in the AAC-present group (p<0.001). Serum albumin levels were lowest in patients with severe AAC (39.21±5.53 g/L) compared to those with no AAC (41.79±4.34 g/L, p=0.016). Haemoglobin levels showed a significant decline in patients with severe AAC (11.95±1.61 g/dL) compared to the no AAC group (13.05±1.74 g/dL, p<0.001). Lymphocyte counts were also significantly lower in AAC patients (p=0.028).

The groups were compared based on medication use. Renin–angiotensin–aldosterone system (RAAS) blockers were used by 56.9% of participants, with usage significantly lower in the absent AAC group (38.2%) compared with the mild AAC group (62.3%) and the severe AAC group (62.4%) (p=0.002). Similarly, diuretic use was higher in patients with mild AAC (50.0%) and severe AAC (52.9%) than in the absent AAC group (34.5%) (p=0.041). Other medications, including beta-blockers, oral antidiabetics, and anticoagulants, showed no significant variation across AAC groups (all p values>0.05).

Although inflammatory markers such as C-reactive protein (CRP) and lipid profiles (total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides) varied slightly across groups, these differences were not statistically significant. Glycated haemoglobin (HbA1c) levels, however, were significantly higher in AAC present patients (6.87±1.51%) than in the no AAC group (6.15±0.88%, p=0.031).

Univariate regression analysis identified several variables as significant predictors of AAC severity, including GFR, albumin, haemoglobin, lymphocyte count, and CHA_2DS_2-VASc score. Age was not included in the multivariate regression analysis as it was used to calculate CHA_2DS_2-VASc and CHA_2DS_2-VA scores. In the multivariate regression model, GFR emerged as an independent negative predictor of AAC severity [odds ratio (OR): 0.060, 95% confidence interval (CI): 0.010-0.362, p=0.009].

Table 2. Laboratory findings of study group

Parameters	Total	AAC absent	AAC present			p value
		Grade 0	Mild (Grade 1)	Severe (Grade 2-3)	Total	
Glucose, mg/dL	124.92±42.96	115.09±35.00	126.44±46.47	128.52±42.66	127.37±44.71	0.062
GFR, mL/min/1.73 m²	72.92±18.86	83.80±14.75	69.31±20.02	70.39±17.23	69.79±18.79	**<0.001**
ALT, IU/dL	18.71±12.31	21.09±13.16	17.47±8.92	18.73±15.02	18.03±12.01	0.105
AST, IU/dL	22.20±11.33	22.36±13.98	21.54±9.43	22.94±11.69	22.16±10.49	0.908
Sodium, mEq/L	140.46±2.97	140.48±2.29	140.55±3.11	140.35±3.21	140.46±3.15	0.961
Potassium, mEq/L	4.36±0.52	4.46±0.42	4.36±0.55	4.31±0.53	4.34±0.54	0.113
Albumin, g/L	40.16±5.19	41.79±4.34	40.13±5.15	39.21±5.53	39.71±5.33	**0.016**
C-reactive protein, mg/L	10.42±12.41	10.75±16.75	9.49±9.63	11.28±12.46	10.31±11.02	0.837
Haemoglobin, g/dL	12.32±1.76	13.05±1.74	12.25±1.80	11.95±1.61	12.12±1.72	**<0.001**
HbA1c, %	6.71±1.42	6.15±0.88	6.85±1.50	6.90±1.52	6.87±1.51	**0.031**
WBC, 10^3/µL	7.77±2.51	8.02±2.67	7.44±2.36	8.04±2.58	7.71±2.47	0.426
Neutrophils, 10^3/µL	5.07±2.19	5.11±2.45	4.83±2.05	5.37±2.18	5.07±2.12	0.908
Lymphocytes, 10^3/µL	1.89±0.95	2.14±0.74	1.82±0.70	1.83±1.28	1.82±1.00	**0.028**
Platelet, 10^3/µL	236.17±86.66	240.07±89.84	225.25±81.36	247.28±90.33	235.05±85.94	0.706
PDW, fL	16.01±2.87	16.37±2.82	16.15±3.08	15.58±2.60	15.90±2.89	0.279
RDW, %	15.69±2.39	15.33±2.35	15.60±2.33	16.06±2.47	15.80±2.40	0.192
Total cholesterol, mg/dL	179.71±42.74	187.37±44.81	179.09±41.40	175.37±42.81	177.42±41.96	0.141
Triglycerides, mg/dL	129.01±63.24	133.19±68.15	131.57±64.15	123.06±58.76	127.73±61.75	0.586
LDL, mg/dL	105.24±36.36	113.12±38.26	104.42±34.60	101.07±36.83	102.92±35.56	0.075
HDL, mg/dL	48.87±13.58	48.16±12.15	49.04±13.68	49.16±14.49	49.10±14.01	0.663
TSH, mIU/L	1.75±1.37	1.89±1.42	1.77±1.55	1.64±1.10	1.71±1.36	0.417
Aorta (mm)	40.76±5.98	40.10±5.52	41.43±6.02	40.36±6.19	40.95±6.11	0.354
CTI (fraction)	0.61±0.09	0.59±0.08	0.60±0.06	0.63±0.12	0.62±0.09	0.087
Aorta/heart (fraction)	0.23±0.03	0.24±0.03	0.23±0.03	0.23±0.03	0.23±0.03	0.488
Aorta/lung (fraction)	0.14±0.02	0.14±0.02	0.14±0.02	0.15±0.02	0.14±0.02	0.260
Ejection fraction (%)	54.37±9.5	55.20±8.65	54.52±10.33	53.64±8.99	54.13±9.74	0.463

*Statistically significant p values. AAC: Aortic arch calcification, GFR: Glomerular filtration rate, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, HbA1c: Glycated hemoglobin, WBC: White blood cells, PDW: Platelet distribution width, RDW: Red cell distribution width, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TSH: Thyroid-stimulating hormone, CTI: Cardiothoracic index

CHA_2DS_2-VA and CHA_2DS_2-VASc scores were strong positive predictors (OR: 4.763, 95% CI: 2.974-7.629, p=0.002; OR: 5.091, 95% CI: 3.039-8.527, p=0.007, respectively). Other parameters, such as haemoglobin and albumin, did not retain statistical significance in the adjusted model. Table 3 shows the univariate and multivariate regression analyses. Figure 2 shows the Forest plot of the multivariate regression analysis.

The predictive ability of CHA_2DS_2-VASc and CHA_2DS_2-VA scores for AAC severity was assessed using ROC curve analysis. For the CHA_2DS_2-VASc score, the area under the curve (AUC) was 0.694, with a sensitivity of 72.1% and a specificity of 63.6% at a cut-off score of >3. For the CHA_2DS_2-VA score, the AUC was 0.688, with higher sensitivity (83.2%) but lower specificity (45.5%) at a cut-off score of >2 (Table 4). Both scores demonstrated significant predictive value (p<0.001) for AAC severity (Figure 3).

Table 3. Regression analysis of possible variables for aortic arch calcification groups

Variable	Univariate regression analysis	Multivariate regression analysis			
	p value	p value	Odds ratio	CI lower	CI upper
Glomerular filtration rate	**<0.001**	**0.009**	0.060	0.010	0.362
Albumin	**0.016**	0.168	0.123	0.006	2.502
Haemoglobin	**<0.001**	0.218	0.119	0.004	3.511
Lymphocytes	**0.028**	0.256	0.433	0.019	9.885
HbA1c	**0.031**	0.372	0.447	0.026	7.673
Glucose	0.062				
LDL	0.075				
Cardio-thoracic index	0.087				
CHA_2DS_2-VA	**<0.001**[b]	**0.002**[b]	4.763	2.974	7.629
CHA_2DS_2-VASc	**<0.001**[b]	**0.007**[b]	5.091	3.039	8.527
Age	**<0.001**[a]				
RAAS blocker	0.179				
Diuretic	**0.030**	0.258	0.488	0.180	1.326

a: Age was not included in the analysis as it is a component of the scoring systems. b: Statistical p values were obtained from two separate multivariate models. CI: Confidence interval, HBA1c: Glycated haemoglobin, LDL: Low-density lipoprotein, RAAS: Renin–angiotensin–aldosterone system

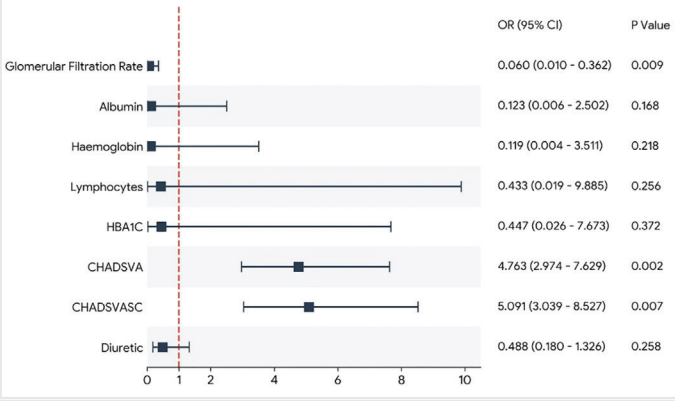

Figure 2. Forest plot of possible predictors for aortic arch calcification (multivariate analysis). OR: Odds ratio, CI: Confidence interval, HbA1c: Glycated haemoglobin

Discussion

The present study examined the association between AAC and stroke risk scores, specifically CHA_2DS_2-VASc and CHA_2DS_2-VA, in patients diagnosed with AF. Both scores demonstrated significant predictive ability, with cut-off scores of >3 and >2, respectively, showing reasonable sensitivity and specificity. The findings demonstrate a robust correlation between elevated stroke risk scores and the severity of AAC, suggesting that AAC may be used clinically as an adjunct tool for risk stratification in patients with AF. However, the moderate AUC values suggest that additional parameters, such as renal function, inflammatory markers, or imaging-based quantification of AAC, may improve predictive accuracy. This lends further support to the notion that a multi-faceted approach to risk assessment is imperative, particularly in high-risk populations such as AF patients.

The results demonstrated that individuals with prominent AAC had significantly higher CHA_2DS_2-VASc and CHA_2DS_2-VA scores compared with those without AAC. This finding aligns with previous research

Table 4. ROC curve findings for CHA_2DS_2-VASc and CHA_2DS_2-VA scores

Parameter	CHA_2DS_2-VASc	CHA_2DS_2-VA
Area under curve	0.694	0.688
Standard error	0.043	0.044
p value	<0.001	<0.001
Cut-off	3.5 (>3)	2.5 (>2)
Sensitivity	0.721	0.832
Specificity	0.636	0.455
Positive predictive value	87.3%	84.1%
Negative predictive value	39.8%	43.9%

ROC: Receiver operating characteristic

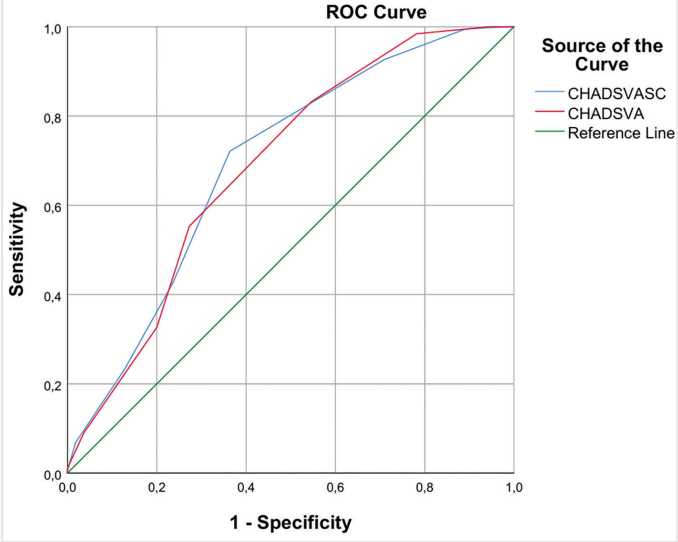

Figure 3. Receiver operating characteristic curve of aortic arch calcification for CHA_2DS_2-VASc and CHA_2DS_2-VA scores. ROC: Receiver operating characteristic

that has shown AAC as a reliable indicator of arterial stiffness, systemic atherosclerosis, and chronic inflammation, all of which have been linked to an increased risk of thromboembolism (8,9,14). The accuracy of stroke risk assessment could be enhanced by incorporating AAC assessment into existing risk prediction models, particularly for borderline or high-risk patients, for whom decisions regarding anticoagulant therapy are most challenging.

A CHA_2DS_2-VA score greater than 1 indicates an annual stroke risk of 1.5%. In light of the recent AF guidelines, this value is now considered the clinical threshold for initiating anticoagulation therapy (15). As stated in the guideline, anticoagulation therapy is recommended for patients with a score greater than 2, and this treatment has a class 1 level of evidence (15). As the score increases, so does the risk of thromboembolic events. Considering the findings of our study, the presence of AAC showed a difference of almost 1 point in the results of both scoring systems (4.37±1.38 vs. 3.33±1.58 and 3.79±1.28 vs. 2.78±1.56). This study suggests that the presence of AAC can be used as a logical indicator for initiating anticoagulation therapy, given that it can cause a 1-point difference in the scores of both scoring systems.

An important question is whether the positive correlation that AAC showed between high scores in both scoring systems can be used clinically. ROC cut-off values were considered high for both scores in clinical decision-making regarding anticoagulation. Considering the grey zone in current guidelines—such as a CHA_2DS_2-VASc score of 1 in males or 2 in females, or a score of 1 in the gender-neutral CHA_2DS_2-VA system—the clinical significance of AAC presence as an indication for initiating anticoagulation would be substantially greater. Therefore, we believe that the presence of AAC alone could be considered a tie-breaker for the use of anticoagulation.

Reduced GFR has been identified as a significant independent predictor and is strongly associated with higher AAC severity. This underscores the intricate relationship between vascular calcification and renal dysfunction (16). Chronic kidney disease (CKD) is known to accelerate vascular calcification, likely through pathways involving disturbances in calcium-phosphorus metabolism, elevated fibroblast growth factor 23 levels, and endothelial dysfunction (17). This study revealed a significant relationship between low GFR and both CHA_2DS_2-VASc and CHA_2DS_2-VA scores. These findings are consistent with prior research suggesting a strong association between declining renal function and accelerated cardiovascular calcification in AF patients (18,19).

Further clinical and laboratory findings provided valuable insights into the risk factors and systemic consequences of AAC. Patients with severe AAC exhibited lower serum albumin and haemoglobin levels, indicating the potential roles of malnutrition and anaemia in exacerbating vascular calcification (20,21). Albumin, a reliable marker of nutritional and inflammatory status, is frequently reduced in states of chronic disease and systemic inflammation, both of which may be implicated in AAC progression (20). Similarly, anaemia, a common occurrence in CKD and AF patients, has been observed to exacerbate hypoxic injury to vascular tissues, accelerating calcification (21). In the present study, univariate regression analysis revealed a significant association between hypoalbuminemia and low haemoglobin with CHA_2DS_2-VASc and CHA_2DS_2-VA scores. However, this significance was not sustained in multivariate regression analysis. The likely reasons for this are the number of study participants and selection imbalances. Given the combined roles of chronic inflammation, malnutrition, and renal failure in the progression of vascular calcification, these results are not surprising. AAC can emerge as an indicator of the cumulative burden of all these factors. We believe these findings demonstrate the clinical value of a holistic approach to AAC. Nevertheless, significant results in the initial analyses, which are in line with the literature, increase the consistency and value of this study.

It is interesting to note that higher HbA1c levels in patients with severe AAC suggest that poorly controlled diabetes is a key contributor to AAC progression (22). Persistent hyperglycaemia has been shown to exacerbate oxidative stress, promote vascular endothelial damage and accelerate calcification through non-enzymatic glycation of proteins and lipids (23). While there was no significant difference in inflammatory markers, such as CRP across AAC severity groups, the observed trend toward higher CRP levels in patients with severe AAC warrants further investigation. Chronic low-grade inflammation is a potential driver of both vascular calcification and systemic cardiovascular risk (24).

The study also explored medication use in relation to AAC severity, offering insights into current clinical management strategies. The significantly higher use of RAAS blockers and diuretics among patients with mild and severe AAC likely reflects their role in managing comorbid hypertension and heart failure. However, no significant differences in anticoagulant use were observed between AAC severity groups, suggesting that AAC is not currently considered in anticoagulation decision-making. These findings emphasise the necessity for future research to ascertain whether incorporating AAC into risk stratification tools could help guide anticoagulant therapy, particularly for intermediate-risk patients.

A potential source of confusion in this study pertains to the vascular disease component, denoted by the letter 'V' in these scoring systems. This component was defined as peripheral vascular disease, prior myocardial infarction, significant coronary artery lesion(s) with more than 50% stenosis on imaging, carotid disease and complex aortic plaque on computed tomography (CT) (25). The situation is characterised by a dichotomy. There is no ambiguity or overestimation. The definition of a complex aortic plaque is as follows: the presence of ≥4 mm in thickness, ulceration, or mobile thrombi (26). However, this study analysed the presence of any degree of AAC. Another point is that the presence of AAC could be included in this scoring system even in the absence of complex plaque. According to this study, the estimates show a difference of 1 point and the presence of AAC has been shown to be associated with recurrent ischaemic cerebral events (9,27).

The findings of this study have the potential to inform clinical practice in a number of ways. Incorporating AAC evaluation into routine risk assessment for AF patients could refine predictions of thromboembolic and cardiovascular events. This may be particularly valuable in patients with borderline or intermediate CHA_2DS_2-VASc scores, where the decision to initiate anticoagulation therapy often involves weighing the risks of thromboembolism against those of bleeding. In addition, these treatment plans have the potential to improve patient survival.

They may also generate economic, social, and psychological benefits by reducing the number of hospital admissions or shortening hospital stays. However, further studies are required to determine whether incorporating AAC into these risk scores is beneficial for calculating stroke risk in patients with AF. Furthermore, the observed associations between AAC and renal function, malnutrition, and glycemic control highlight the need for a holistic approach to managing AF patients that addresses both systemic and vascular risk factors.

Study Limitations

Despite the valuable insights this study provides, it is subject to several limitations. The study design initially included a longitudinal component; however, the current analysis focused on baseline clinical characteristics, stroke risk scores, and AAC severity and did not assess subsequent stroke incidence. This is a necessity rather than a limitation. Since the study population consisted of individuals diagnosed with AF and receiving anticoagulants for CVD prevention, minor modifications to the study cohort and a much longer follow-up are required to detect the effect of AAC in this population. Therefore, the findings should be interpreted as representing a cross-sectional association. Any assertion regarding the predictive value of AAC for stroke outcomes must be confirmed through longitudinal studies. Additionally, the number of patients included and the single-center nature of the study limit its generalizability and thus constitute significant limitations. Furthermore, the AAC grading was dependent on chest X-rays, which may understate the burden of calcification compared with more sophisticated imaging modalities such as CT, although it remains the standard criterion for aortic arch pathologies. Chest X-rays, on the other hand, are more useful and cost-effective in routine clinical practice. The relevance of the findings to other cardiovascular conditions is limited because the study population consisted exclusively of patients with AF. Additionally, bleeding, a significant endpoint of anticoagulant medications in AF patients, was not examined in the study. Should it be possible to infer an absence of a relationship with bleeding in this regard, it could further increase the diagnostic weight of AAC in CHA_2DS_2-VASc and CHA_2DS_2-VA scores.

Conclusion

This study demonstrates a substantial correlation between the severity of AAC and the stroke risk scores (CHA_2DS_2-VASc and CHA_2DS_2-VA) among individuals with AF. The results highlight the potential value of AAC as a supplementary risk stratification marker, providing a more sophisticated understanding of cardiovascular and thromboembolic risks. In addition, chest radiography offers clinicians a valuable and accessible tool for risk assessment without requiring additional radiation exposure or incurring additional cost. With a focus on enhancing patient outcomes through specialised therapy interventions, future research should seek to evaluate these findings and investigate the clinical implications of integrating AAC into risk prediction algorithms.

Ethics

Ethics Committee Approval: For ethical compliance, approval was obtained from the Non-Interventional Ethics Committee of Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital (protocol number: 43, date: 12.05.2023).

Informed Consent: All individuals included in the study were informed about the research in accordance with the ethical principles outlined in the Second Declaration of Helsinki on research involving human subjects, and their written informed consent was obtained.

Footnotes

Authorship Contributions: Surgical and Medical Practices - F.Ç.; Concept - F.Ç.; Design - F.Ç., U.K.; Data Collection or Processing - F.Ç., U.K.; Analysis or Interpretation - F.Ç., U.K.; Literature Search - F.Ç., U.K.; Writing - F.Ç.

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