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Association of MAPH and CHA_2DS_2-VASc Scores with Left Atrial Thrombus in Atrial Fibrillation Patients Undergoing Ablation: A Comparative Evaluation

MAPH ve CHA_2DS_2-VASc Skorlarının Ablasyon Planlanan Atriyal Fibrilasyon Hastalarında Sol Atriyal Trombüs Varlığı ile İlişkisi: Karşılaştırmalı Bir Değerlendirme

ABSTRACT

Objective: This study aimed to compare the association of the MAPH score (Mean platelet volume–Age–Persistent atrial fibrillation–Hematocrit) and the CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack (2 points), Vascular disease, Age 65–74 years, and Sex category (female)) with the presence of left atrial thrombus in patients undergoing atrial fibrillation ablation.

Method: This retrospective cross-sectional study included 258 consecutive patients with atrial fibrillation (AF) who underwent transesophageal echocardiography to assess thrombus status prior to ablation. Based on these findings, patients were categorized according to the presence or absence of left atrial (LA) thrombus.

Results: The mean age of the study population was 55.2 ± 11.7 years, and 53.5% of the participants were female. Patients with LA thrombus were more likely to have ongoing AF during TEE, mild mitral stenosis, elevated C-reactive protein (CRP) and international normalized ratio (INR) levels, and reduced ejection fraction. The median MAPH score was significantly higher in the thrombus group ($P < 0.001$). In multivariable analysis, ongoing AF (odds ratio [OR]: 3.83), anticoagulant therapy (OR: 14.95), elevated albumin (OR: 1328.5), elevated CRP (OR: 1.38), and elevated INR (OR: 9.09) were independently associated with thrombus presence. The MAPH score demonstrated superior discriminative performance compared to the CHA_2DS_2-VASc score for identifying LA thrombus ($P = 0.014$).

Conclusion: The MAPH score was significantly associated with LA thrombus and demonstrated superior discriminative ability compared to the CHA_2DS_2-VASc score for detecting LA thrombus. These findings suggest that the MAPH score may serve as a useful marker for identifying existing LA thrombus in patients with AF undergoing pre-procedural evaluation.

Keywords: Atrial fibrillation, left atrial thrombus, MAPH score, risk assessment

ÖZET

Amaç: Atriyal fibrilasyon ablasyonu planlanan hastalarda MAPH skoru ile CHA_2DS_2-VASc skorunun sol atriyal trombüs varlığı ile ilişkisini karşılaştırmaktır.

Yöntem: Bu retrospektif kesitsel çalışmaya, ablasyon öncesinde trombüs durumunun değerlendirilmesi amacıyla transözofageal ekokardiyografi uygulanan, ardışık 258 AF hastası dahil edilmiştir. Bu inceleme temel alınarak hastalar, sol atriyal trombüs varlığına göre gruplandırılmıştır.

Bulgular: Çalışma popülasyonunun ortalama yaşı 55.2 ± 11.7 yıl olup, katılımcıların %53.5'i kadındı. Sol atriyal trombüsü olan hastalarda TEE sırasında devam eden AF, hafif mitral stenoz, artmış CRP ve INR düzeyleri ile daha düşük ejeksiyon fraksiyonu daha sık gözlenmiştir. Medyan MAPH skoru trombüs grubunda anlamlı olarak daha yüksekti ($P < 0.001$). Çok değişkenli analizde devam eden AF (OR: 3.83), antikoagülan kullanımı (OR: 14.95), yüksek albümin (OR: 1328.5), yüksek CRP (OR: 1.38) ve yüksek INR (OR: 9.09) trombüsün bağımsız belirleyicileri olarak bulunmuştur. MAPH skoru, sol atriyal trombüs varlığının belirlenmesinde CHA_2DS_2-VASc skoruna göre üstün ayırt edici performans göstermiştir ($P = 0.014$).

Sonuç: MAPH skoru, sol atriyal trombüs varlığı ile anlamlı şekilde ilişkili olup, LA trombüsünün belirlenmesinde CHA_2DS_2-VASc skorundan daha yüksek bir ayırt edici performans sergilemiştir. Bulgular, MAPH skorunun AF hastalarında işlem öncesi değerlendirmede mevcut LA trombüsünün saptanmasında yararlı bir belirteç olabileceğini düşündürmektedir.

Anahtar Kelimeler: Atriyal fibrilasyon, sol atriyal trombüs, MAPH skoru, risk değerlendirmesi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Atrial fibrillation (AF) is one of the most common sustained arrhythmias in the general population and is strongly associated with thromboembolic events. In patients with AF, thrombi most commonly form in the left atrial (LA) appendage, and evidence suggests that these patients are at risk for systemic embolism despite appropriate anticoagulant therapy. Detection of thrombus prior to therapeutic interventions is critical to ensuring procedural safety and preventing potential complications.[1,2]

Transesophageal echocardiography (TEE) is widely used to evaluate the LA and detect thrombus or dense spontaneous echocardiographic contrast (SEC). Although TEE remains the gold standard for thrombus detection due to its high sensitivity and specificity, it is a semi-invasive procedure requiring sedation, specialized equipment, and experienced operators. Therefore, complementary risk-stratification tools are valuable for identifying patients at higher risk who would benefit most from TEE.[3] The CHA_2DS_2-VASc score (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, prior Stroke/transient ischemic attack (2 points), Vascular disease, Age 65–74 years, and Sex category (female)) is one of the most widely used risk stratification systems in clinical practice for estimating thromboembolic risk. In patients with AF, it is the recommended tool for assessing thromboembolic risk and guiding anticoagulant therapy.[4,5] However, because the CHA_2DS_2-VASc score is based primarily on clinical characteristics and comorbidities, its specificity and sensitivity are limited, particularly for predicting left atrial appendage thrombus (LAAT). Many researchers have therefore been prompted to investigate novel biomarkers and scoring systems to improve LAAT detection.[6]

The MAPH score (Mean platelet volume–Age–Persistent atrial fibrillation–Hematocrit), which incorporates age and blood viscosity biomarkers such as mean platelet volume (MPV), total protein, and hematocrit (Htc), was introduced relatively recently into the literature and has been shown to predict thrombus burden in various clinical contexts.[7-10] However, the utility of the MAPH score in patients with AF remains understudied. In the present study, we aimed to evaluate the association between the MAPH score and the presence of LAAT in patients scheduled for AF ablation. A secondary objective was to assess clinical, laboratory, and echocardiographic parameters potentially associated with thrombotic properties and to identify factors independently associated with LAAT in AF.

Materials and Methods

Patients and Data Collection

This cross-sectional study was conducted at the Department of Cardiology of a tertiary center. The study protocol was approved by Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee (Approval Number: E-10840098-202.3.02-6131, Date: 15.09.2025), and was carried out in accordance with the ethical principles of the Declaration of Helsinki. All data were anonymized at the time of data recording and entry.

Patients scheduled for ablation due to AF between May 2022 and July 2024 were retrospectively screened. Of the 302 patients initially assessed, 44 were excluded for the following reasons: moderate-to-severe mitral stenosis (n = 16), prosthetic heart valves (n = 8), congenital heart disease (n = 7), prior left atrial appendage occlusion (n = 5), and hemodialysis-dependent renal failure (n = 8) (Figure 1). A total of 258 consecutive patients with non-valvular AF, defined as AF in the absence of mechanical prosthetic heart valves or moderate-to-severe mitral stenosis, either paroxysmal or persistent at presentation, were included in the analysis. The diagnosis of AF was confirmed by 12-lead surface electrocardiography (ECG) and/or 24-hour Holter monitoring.

ABBREVIATIONS

AF	Atrial fibrillation
aPTT	Activated partial thromboplastin time
CRP	C-reactive protein
HCT	Hematocrit
IAS	Interatrial septum thickness
INR	International normalized ratio
LA	Left atrial
LVEDD	Left ventricular end-diastolic diameter
LYMPH	Lymphocyte count
MPV	Mean platelet volume
ROC	Receiver operating characteristic
SEC	Spontaneous echocardiographic contrast
sPAP	Systolic pulmonary artery pressure
STEMI	ST-segment elevation myocardial infarction
TEE	Transesophageal echocardiography
TSH	Thyroid-stimulating hormone
TTE	Transthoracic echocardiography

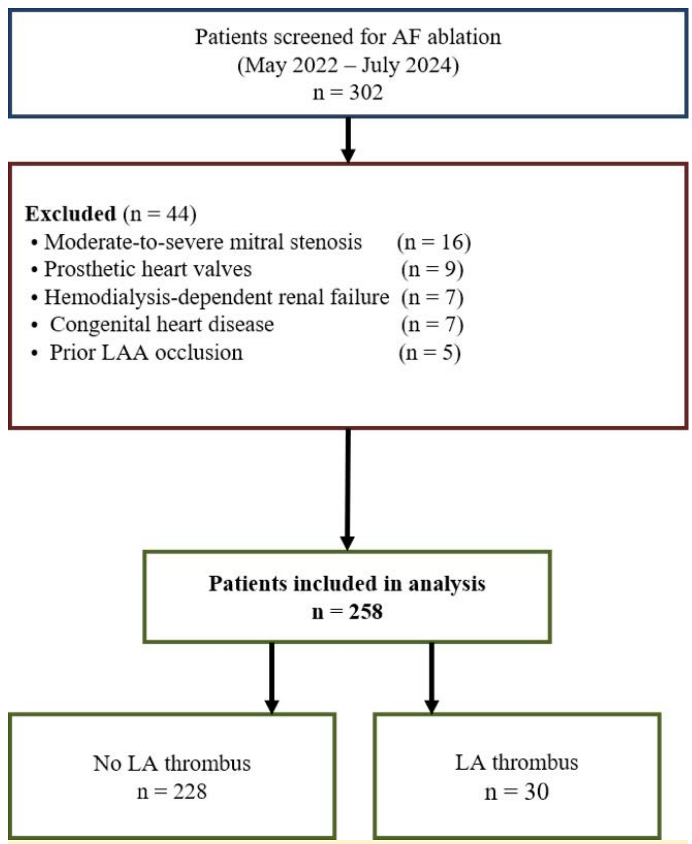

Figure 1. Patient flow diagram.

The inclusion criteria were as follows: age ≥ 18 years; availability of both transthoracic echocardiography (TTE) and TEE results performed within seven days prior to ablation; and complete clinical, laboratory, and echocardiographic data retrievable from the digital hospital records. Patients were excluded if they had moderate or severe rheumatic mitral stenosis, prosthetic heart valves, a history of congenital heart disease, prior left atrial appendage occlusion, or incomplete data. This exclusion criterion aligns with major direct oral anticoagulant trials,[11,12] which excluded only moderate-to-severe mitral stenosis and mechanical valves while including patients with other valvular diseases. In addition, patients with known active malignancies, hematologic disorders (e.g., myeloproliferative neoplasms or anemia requiring transfusion), acute infectious or inflammatory conditions at the time of blood sampling, advanced hepatic failure, or hemodialysis-dependent renal failure were excluded to minimize confounding effects on MAPH score components.

Demographic and clinical data were obtained from patient records and the electronic hospital system, including age, sex, AF type (paroxysmal, persistent, or permanent), comorbidities (hypertension, diabetes mellitus, coronary artery disease, heart failure, and history of stroke or transient ischemic attack), history of cardioversion or ablation, use of antiplatelet or anticoagulant medications (warfarin or direct oral anticoagulants), and heart rhythm at the time of TEE (AF or sinus rhythm).

The authors declare that no artificial intelligence tools were used in the conception, data analysis, drafting, or editing of this manuscript.

Sampling and Laboratory Measurements

Blood samples (collected into ethylenediaminetetraacetic acid [EDTA] and serum-separator tubes) were drawn from all patients in the morning hours (between 07:30 and 09:00) following at least 8 hours of fasting and 24–48 hours prior to TEE. Serum biochemistry and complete blood count parameters were analyzed in the hospital's central laboratory using automated analyzers. Measured parameters included albumin, C-reactive protein (CRP), international normalized ratio (INR), activated partial thromboplastin time (aPTT), thyroid-stimulating hormone (TSH), hemoglobin, hematocrit (Hct), and complete blood count indices.

Regarding anticoagulation management prior to TEE, patients receiving direct oral anticoagulants continued their medication without interruption, whereas those on warfarin were maintained on therapy with INR monitoring. Anticoagulant doses were not withheld prior to TEE, as the examination was performed under conscious sedation did not require interruption of therapeutic anticoagulation. All patients scheduled for ablation were required to have received at least three weeks of adequate anticoagulation or to have undergone TEE to exclude thrombus, in accordance with guideline recommendations.

Echocardiographic Evaluations

Transthoracic echocardiography was performed using a GE Vivid E9 system (General Electric, USA) equipped with a 3.5 MHz phased-array probe. All TTE examinations were conducted by experienced cardiologists certified in echocardiography who were blinded to thrombus status. Measurements, including left atrial diameter (parasternal long-axis view), left ventricular end-diastolic diameter (LVEDD), ejection fraction (Simpson's method), interatrial septum thickness (IAS), posterior wall thickness, and systolic pulmonary artery pressure (sPAP), were obtained in accordance with the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.

Transesophageal echocardiography was performed 48–72 hours prior to ablation under conscious sedation using a multiplane probe. The left atrial appendage was evaluated in at least four views (0°, 45°, 90°, and 135°), and the presence of LAAT and the severity of SEC were assessed. SEC was graded as absent, mild, moderate, or severe.[13] A thrombus was defined as a well-demarcated, echo-dense mass clearly separated from the endocardial surface and not confused with pectinate muscles or imaging artifacts. All TEE images were independently reviewed by two blinded cardiologists; in cases of disagreement, a third experienced cardiologist made the final decision. Formal inter-observer agreement statistics (e.g., Cohen's kappa) were not prospectively calculated. However, initial concordance between the two readers was high, with disagreement occurring in fewer than 5% of cases, all of which were resolved by the third adjudicator.

Score Calculation

All scoring systems were calculated individually by the investigators at the time of data collection.

The MAPH score was calculated according to its original definition,[7] based on four parameters: MPV, age, total protein level, and Hct. For each variable, a score of 1 was assigned if the value exceeded the predefined cutoff and 0 if it was below the cutoff. The total MAPH score for each individual was calculated by summing the scores of these four components. Possible scores ranged from 0 to 4, with higher values indicating greater thrombus risk.

The CHA_2DS_2-VASc score was calculated using the following criteria: congestive heart failure (1 point), hypertension (1 point), age ≥ 75 years (2 points), diabetes mellitus (1 point), prior stroke or transient ischemic attack (TIA) (2 points), vascular disease (1 point), age 65–74 years (1 point), and female sex (1 point). We used the CHA_2DS_2-VASc score rather than the sex-excluded CHA_2DS_2-VA formulation because CHA_2DS_2-VASc remains the most widely adopted scoring system in clinical practice and current guidelines, thereby facilitating comparability with existing literature. Additionally, our study population included both sexes, and excluding the sex component would have reduced consistency with standard clinical workflows.

We also assessed bleeding risk using the PRECISE-DAPT score (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy). This score was calculated using an online calculator by entering age, creatinine clearance (estimated using the Cockcroft-Gault formula), hemoglobin, white blood cell count, and history of significant bleeding.

Statistical Analysis

Sample size was calculated a priori using G*Power version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany). Based on expected sensitivities of 56.3% for the MAPH score and 40.0% for the CHA_2DS_2-VASc score, with $\alpha = 0.05$ (two-tailed), power = 0.80, and a 1:1 allocation ratio, the required sample size was 232 patients (effect size $|h| = 0.332$). Accounting for 10% incomplete data, we targeted 260 patients.

Table 1. Comparison of baseline demographic, clinical, echocardiographic, and laboratory characteristics between patients with and without left atrial appendage thrombus

		Thrombus status		***P***
	Total (n=258)	**No thrombus (n=228)**	**Thrombus present (n=30)**	
Age	55.25 ± 11.67	54.90 ± 11.80	57.93 ± 10.44	0.181†
Sex				0.831§
Female	138 (53.49%)	123 (53.95%)	15 (50.00%)	
Male	120 (46.51%)	105 (46.05%)	15 (50.00%)	
Comorbidities				
Coronary artery disease	29 (11.24%)	27 (11.84%)	2 (6.67%)	0.547#
Hypertension	96 (37.21%)	89 (39.04%)	7 (23.33%)	0.141§
Hyperlipidemia	37 (14.34%)	32 (14.04%)	5 (16.67%)	0.781#
Diabetes mellitus	17 (6.59%)	16 (7.02%)	1 (3.33%)	0.702#
Heart failure	13 (5.04%)	10 (4.39%)	3 (10.00%)	0.182#
Stroke/TIA	7 (2.71%)	4 (1.75%)	3 (10.00%)	**0.036#**
AF (at the time of TEE)	45 (17.44%)	27 (11.84%)	18 (60.00%)	**<0.001§**
Type of AF				**<0.001§**
Paroxysmal	195 (75.58%)	185 (81.14%)	10 (33.33%)*	
Persistent	43 (16.67%)	32 (14.04%)	11 (36.67%)*	
Permanent	20 (7.75%)	11 (4.82%)	9 (30.00%)*	
History of prior cardioversion	31 (12.02%)	28 (12.28%)	3 (10.00%)	1.000#
Receiving anticoagulant therapy	199 (77.13%)	170 (74.56%)	29 (96.67%)	**0.013§**
Warfarin	115 (44.57%)	89 (39.04%)	26 (86.67%)*	**<0.001¶**
Dabigatran	29 (11.24%)	27 (11.84%)	2 (6.67%)	
Rivaroxaban	10 (3.88%)	10 (4.39%)	0 (0.00%)	
Apixaban	45 (17.44%)	44 (19.30%)	1 (3.33%)*	
Antiplatelet therapy	50 (19.38%)	49 (21.49%)	1 (3.33%)	**0.034§**
ASA	39 (15.12%)	38 (16.67%)	1 (3.33%)	**0.154¶**
Clopidogrel	3 (1.16%)	3 (1.32%)	0 (0.00%)	
ASA + Clopidogrel	8 (3.10%)	8 (3.51%)	0 (0.00%)	
Intervention	176 (68.22%)	171 (75.00%)	5 (16.67%)	**<0.001§**
Cryoablation	160 (62.02%)	156 (68.42%)	3 (10.00%)*	
Radiofrequency	16 (6.20%)	15 (6.58%)	2 (6.67%)	
Thromboembolism after intervention	2 (0.78%)	1 (0.44%)	1 (3.33%)	0.219#
LVEDD, mm	46.18 ± 3.29	46.30 ± 3.26	45.27 ± 3.39	0.106†
IAS, cm	1 (1–1.1)	1 (1–1.1)	1 (1–1.15)	0.100‡
Posterior wall thickness, cm	0.98 ± 0.10	0.97 ± 0.10	1.01 ± 0.08	**0.049†**
Left atrial diameter, cm	4.02 ± 0.64	3.93 ± 0.59	4.63 ± 0.68	**<0.001†**
Ejection fraction, %	60 (60–61)	60 (60–61)	59.5 (55–60)	**<0.001‡**
Mitral stenosis	63 (24.42%)	45 (19.74%)	18 (60.00%)	**<0.001§**
Mitral regurgitation	257 (99.61%)	227 (99.56%)	30 (100.00%)	1.000#
Mild	247 (95.74%)	220 (96.49%)	27 (90.00%)	0.278¶
Moderate	9 (3.49%)	6 (2.63%)	3 (10.00%)	
Severe	1 (0.39%)	1 (0.44%)	0 (0.00%)	
sPAP	30 (25–38)	30 (25–35)	42 (35–45)	**<0.001‡**
Spontaneous echo contrast				**<0.001¶**
None	180 (69.77%)	178 (78.07%)	2 (6.67%)*	
Mild	36 (13.95%)	29 (12.72%)	7 (23.33%)	
Moderate	20 (7.75%)	14 (6.14%)	6 (20.00%)*	
Dense	22 (8.53%)	7 (3.07%)	15 (50.00%)*	

Table 1 (cont). Comparison of baseline demographic, clinical, echocardiographic, and laboratory characteristics between patients with and without left atrial appendage thrombus

		Thrombus status		***P***
	Total (n=258)	**No thrombus (n=228)**	**Thrombus present (n=30)**	
Albumin	4.22 ± 0.24	4.19 ± 0.24	4.44 ± 0.16	**<0.001†**
Total protein	7.19 ± 0.57	7.16 ± 0.57	7.38 ± 0.52	0.051†
TSH	1.7 (1.3–2.3)	1.7 (1.3–2.4)	1.3 (0.91–2.1)	**0.008‡**
Hemoglobin	14.13 ± 1.34	14.06 ± 1.35	14.61 ± 1.14	**0.034†**
Hematocrit	43.39 ± 3.95	43.01 ± 3.91	46.27 ± 2.98	**<0.001†**
CRP	1.1 (0.9–2.5)	1.01 (0.75–2.1)	3.05 (1.7–6.3)	**<0.001‡**
INR	1.1 (1.01–1.35)	1.1 (1.0–1.2)	2.0 (1.2–2.11)	**<0.001‡**
aPTT	31 (29–34.4)	31 (29–33.7)	37.5 (31–43)	**<0.001‡**
PRECISE-DAPT score	11.44 ± 4.45	11.43 ± 4.48	11.50 ± 4.33	0.935†
MAPH score	2 (2–3)	2 (2–3)	3 (2–4)	**<0.001‡**
CHA2DS2-VASc score	1 (0–2)	1 (0–2)	1 (0–3)	0.692‡

Descriptive statistics are presented as mean ± standard deviation for normally distributed continuous variables, median (25^{th}–75^{th} percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. †, Student's t test; ‡, Mann-Whitney U test; §, Chi-square test; #, Fisher's exact test; ¶, Fisher-Freeman-Halton test; *, Statistically significant category among variables with three or more categories; N/A, Not applicable. Statistically significant p values are shown in bold. AF, Atrial fibrillation; aPTT, Activated partial thromboplastin time; ASA, Acetylsalicylic acid; CRP, C-reactive protein; EF, Ejection fraction; IAS, Interatrial septum; INR, International normalized ratio; LA, Left atrium; LVEDD, Left ventricular end-diastolic diameter; sPAP, Systolic pulmonary artery pressure; TIA, Transient ischemic attack; TSH, Thyroid-stimulating hormone.

All analyses were conducted using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Two-tailed p-values < 0.05 were considered statistically significant. The assumption of normality was evaluated using histograms and Q-Q plots. Descriptive statistics are presented as mean ± standard deviation for normally distributed continuous variables, median (25^{th}–75^{th} percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Normally distributed continuous variables were analyzed using Student's t-test, whereas non-normally distributed continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test, Fisher's exact test, or the Fisher-Freeman-Halton test, as appropriate. The discriminative performance of the scores for identifying thrombus was evaluated using receiver operating characteristic (ROC) analysis. Optimal cutoff values for both scores were determined using Youden's index (sensitivity + specificity – 1). Comparison of area under the curve (AUC) values between the two scores was performed using the DeLong method. Multivariable logistic regression analysis was performed to identify factors independently associated with thrombus presence. Variables demonstrating statistical significance (P < 0.05) in univariate analysis were entered into the multivariable model using a forward conditional selection method. Before model construction, multicollinearity was assessed using variance inflation factors (VIF); all VIF values were below 5, indicating acceptable collinearity levels. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test.

Results

Thirty (11.6%) of the 258 patients undergoing AF ablation were found to have LAAT on TEE. Dense SEC was observed in 22 patients (8.53%). Patients with and without thrombi were similar in terms of age (57.9 ± 10.4 vs. 54.9 ± 11.8 years, P = 0.181) and sex (50.0% vs. 53.9%, P = 0.831). Clinical, echocardiographic, and laboratory parameters with group comparisons are comprehensively summarized in Table 1. Among anticoagulated patients, those with LA thrombus were more commonly treated with warfarin (76.2%) than non-vitamin K antagonist oral anticoagulants (NOACs) (11.9%), whereas the opposite pattern was observed in patients without thrombus (warfarin 35.0%, NOACs 58.4%, P < 0.001).

Patients with thrombi had a significantly higher frequency of AF at the time of evaluation (60.0% vs. 11.8%, P < 0.001) and were more likely to have persistent (36.7% vs. 14.0%) or permanent AF (30.0% vs. 4.8%) subtypes (P < 0.001). Anticoagulant treatment overall was significantly more prevalent in the thrombus group (96.7% vs. 74.6%, P = 0.013), particularly warfarin use (86.7% vs. 39.0%, P < 0.001). In contrast, apixaban was less frequently used among patients with thrombi (3.3% vs. 19.3%).

Spontaneous echo contrast was detected far more frequently in the LAAT group, with dense SEC observed in 50.0% versus 3.1% (P < 0.001). Other echocardiographic parameters also differed significantly: left atrial diameter was larger in patients with thrombi (4.63 ± 0.68 cm vs. 3.93 ± 0.59 cm, P < 0.001), systolic pulmonary artery pressure was higher (42 mmHg [interquartile range, IQR: 35–45] vs. 30 mmHg [25–35], P < 0.001), and ejection fraction was slightly lower (59.5% [55–60] vs. 60% [60–61], P < 0.001). Mitral stenosis was also significantly more prevalent in the thrombus group (60.0% vs. 19.7%, P < 0.001).

Laboratory analysis revealed significantly lower serum albumin levels in the LAAT group (4.44 ± 0.16 g/dL vs. 4.19 ± 0.24 g/dL, P < 0.001), along with higher levels of C-reactive protein (3.05 mg/L [1.7–6.3] vs. 1.01 mg/L [0.75–2.1], P < 0.001) and INR (2.0 [1.2–2.11] vs. 1.1 [1.0–1.2], P < 0.001). Hemoglobin (14.61 ± 1.14 g/dL vs. 14.06 ± 1.35 g/dL, P = 0.034) and Hct

Table 2. Discriminative performance of the MAPH and CHA_2DS_2-VASc scores for identifying left atrial appendage thrombus: receiver operating characteristic (ROC) curve analysis

	MAPH score	CHA_2DS_2-VASc score
Cutoff	>3.5	>2.5
Sensitivity	40.00%	30.00%
Specificity	89.04%	80.26%
Accuracy	83.33%	74.42%
PPV	32.43%	16.67%
NPV	91.86%	89.71%
AUC (95% CI)	0.679 (0.574–0.783)	0.478 (0.356–0.601)
P†	**0.001**	0.729
AUC difference (95% CI)		
P‡	0.200 (0.041–0.359)	
	0.014	

AUC, Area under the ROC curve; CI, Confidence interval; NPV, Negative predictive value; PPV, Positive predictive value; ROC, Receiver operating characteristic. Statistically significant p values are shown in bold; †, Significance of the AUC under the null hypothesis (H0: AUC = 0.500) for each score; ‡, Comparison of AUCs under the null hypothesis (H0: AUC difference = 0.000). Cutoff values were determined using Youden's index to maximize the sum of sensitivity and specificity.

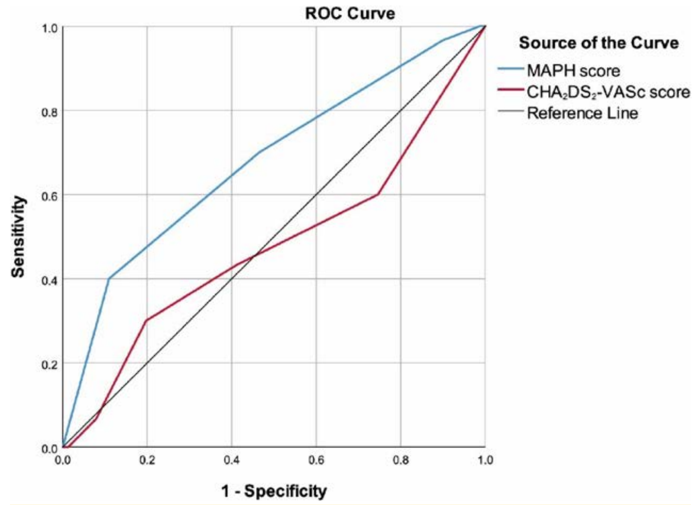

Figure 2. Receiver operating characteristic (ROC) curves of the MAPH score and the CHA_2DS_2-VASc scores for identifying left atrial appendage thrombus.

(46.27 ± 2.98% vs. 43.01 ± 3.91%, P < 0.001) values were also significantly higher in patients with thrombi. TSH levels showed a slight but statistically significant difference, with lower values in the LAAT group (1.3 mIU/L [0.91–2.1] vs. 1.7 mIU/L [1.3–2.4], P = 0.008). Importantly, MAPH scores were significantly higher in patients with thrombi compared to those without (median 3 [IQR 2–4] vs. 2 [2–3], P < 0.001). In contrast, CHA_2DS_2-VASc scores were similar between the two groups (median 1 [0–3] vs. 1 [0–2], P = 0.692).

Because CHA_2DS_2-VASc scores did not differ significantly between groups, ROC analysis was non-significant (AUC: 0.478, 95% confidence interval [CI]: 0.356–0.601; P = 0.729). In contrast, the MAPH score demonstrated significant discriminative ability for distinguishing patients with and without thrombi, with an AUC of 0.679 (95% CI: 0.574–0.783; P = 0.001). The difference between the AUCs was statistically significant (AUC difference: 0.200 [95% CI: 0.041–0.359], P = 0.014), indicating not only significant discriminatory power but also superior performance of the MAPH score in identifying thrombus presence. At the optimal cutoff value (> 3.5), as determined by Youden's index, the MAPH score yielded a sensitivity of 40.0%, specificity of 89.0%, and overall accuracy of 83.3%. Despite its non-significance, the discriminative performance of the CHA_2DS_2-VASc score was also evaluated. The best cutoff value was > 2.5, corresponding to a sensitivity of 30.0%, specificity of 80.3%, and accuracy of 74.4%. One subtle but important finding was that the MAPH score had a negative predictive value (NPV) of almost 92%, which was marginally higher than that of the CHA_2DS_2-VASc score (Table 2, Figure 2).

Our multivariable regression analysis identified several factors independently associated with the presence of thrombus. These included AF at the time of TEE (odds ratio [OR]: 3.834, 95% CI: 1.284–11.451; P = 0.016), anticoagulant treatment (OR: 14.954, 95% CI: 1.403–159.417; P = 0.025), high albumin levels (OR: 1328.499, 95% CI: 43.117–40933; P < 0.001), elevated CRP (OR: 1.381, 95% CI: 1.136–1.679; P = 0.001), and higher INR (OR: 9.093, 95% CI: 2.866–28.855; P < 0.001). Other variables included in the analysis, such as stroke/TIA (P = 0.695), AF type (P = 0.085), antiplatelet use (P = 0.390), posterior wall thickness (P = 0.145), left atrial diameter (P = 0.094), ejection fraction (P = 0.481), mitral stenosis (P = 0.160), sPAP (P = 0.098), TSH (P = 0.484), hemoglobin (P = 0.891), Hct (P = 0.231), aPTT (P = 0.836), and MAPH score (P = 0.146), were not independently associated with LAAT (Table 3).

Table 3. Factors independently associated with left atrial appendage thrombus: multivariable logistic regression analysis

	β coefficient	Standard error	*P*	Exp(β)	95% CI for Exp(β)	
AF present at the time of TEE	1.344	0.558	**0.016**	3.834	1.284	11.451
Anticoagulant therapy in use	2.705	1.207	**0.025**	14.954	1.403	159.417
Albumin	7.192	1.749	**<0.001**	1328.499	43.117	40933.511
CRP	0.323	0.100	**0.001**	1.381	1.136	1.679
INR	2.208	0.589	**<0.001**	9.093	2.866	28.855
Constant	-40.314	8.531	<0.001			

Nagelkerke R^2 = 0.594. Statistically significant p values are shown in bold. AUC, Area under the curve; CI, Confidence interval; CRP, C-reactive protein; Exp(β), Exponentiated beta coefficient (odds ratio); INR, International normalized ratio.

Discussion

We aimed to investigate the clinical, laboratory, and echocardiographic factors associated with LAAT in patients with AF and to determine whether the MAPH score could be used for this purpose and how it performs relative to the CHA_2DS_2-VASc score. Our findings demonstrate that inflammation (CRP), coagulation status (INR), heart rhythm at the time of imaging, and albumin levels were associated with the presence of LAAT. Although the CHA_2DS_2-VASc score is widely used for long-term thromboembolic risk stratification in cardiology, its association with existing LAAT was found to be limited. In contrast, the MAPH score showed a significantly stronger association with the presence of LAAT detected on TEE. Furthermore, our results demonstrate that LAAT is associated not only with conventional clinical risk factors but also with biochemical and rhythm-related parameters, indicating that comprehensive evaluation may improve patient risk stratification.

In our study, the prevalence of LAAT was 11.6% among patients with non-valvular AF scheduled for ablation. This finding indicates that LAAT may occur at a notable frequency even in a population receiving anticoagulant therapy. In contrast, a meta-analysis reported LAAT frequencies of 1.1% in pre-ablation TEE assessments and 4.0% in pre-cardioversion evaluations among patients with AF receiving oral anticoagulants.[14] Other series have reported LAAT prevalence ranging from 2.1% to 4.4%,[15-21] whereas some studies described rates exceeding 11% or reaching up to 15% patients with AF receiving oral anticoagulants.[22-25] This variability may be influenced by differences in patient clinical characteristics, duration and adequacy of anticoagulation, imaging modality, and study design. The relatively higher prevalence observed in our cohort may be partly explained by the greater proportion of patients in ongoing AF at the time of TEE and the overrepresentation of individuals with elevated thromboembolic risk among those referred for ablation. In addition, unlike many prior studies, our cohort included individuals who were not receiving anticoagulant therapy, which may also have contributed to the higher prevalence observed. We believe the present findings indicate the need for a multidimensional approach incorporating laboratory measurements to reliably assess LAAT presence, distinguishing the MAPH score from the CHA_2DS_2-VASc score.

An important methodological consideration is the timing of laboratory measurements relative to TEE. In our study, blood samples were obtained 24–48 hours prior to imaging. Therefore, the observed association between higher MAPH scores and LAAT presence likely reflects an ongoing thrombo-inflammatory state rather than the score's ability to predict future thrombus formation. The MAPH score should thus be interpreted primarily as a marker associated with existing thrombus at the time of evaluation, rather than as a tool for long-term thromboembolic risk prediction. It is also important to emphasize that the CHA_2DS_2-VASc and MAPH scores serve fundamentally different purposes. The CHA_2DS_2-VASc score is a validated clinical tool designed to estimate long-term stroke risk and guide anticoagulation decisions in patients with AF, incorporating demographic and comorbidity variables that reflect cumulative vascular burden. In contrast, the MAPH score is derived from contemporaneous hematological parameters that may reflect the current thrombogenic milieu. Therefore, our comparison should not be interpreted as suggesting that the MAPH score can replace the CHA_2DS_2-VASc score for long-term risk stratification. Rather, our findings indicate that the MAPH score may be more closely associated with the presence of an existing thrombus at a specific point in time, potentially complementing clinical risk assessment in the pre-procedural setting.

In our study, the presence of AF rhythm, receipt of anticoagulant therapy, elevated CRP and INR levels, and lower serum albumin concentration were independently associated with LAAT. The literature indicates that non-paroxysmal or persistent AF increases thrombus formation by impairing atrial contractility and promoting stasis. Additionally, electrocardiography-based interatrial block has been proposed as an independent marker of LAAT risk.[22,26] Structural and functional parameters, such as reduced left ventricular ejection fraction (LVEF), enlarged left atrial size, elevated N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels, and reduced left atrial appendage flow, have also been identified as predictors in previous studies.[2,21,27,28] Regarding systemic inflammation, elevated neutrophil-to-lymphocyte ratio, reduced lymphocyte-to-monocyte ratio, and increased fibrinogen and bilirubin levels are notable findings. In our cohort, the associations observed with CRP and INR further support the role of inflammation on endothelial dysfunction and circulation.[29-31] The type and adequacy of anticoagulation are also important considerations, as LAAT may still occur, particularly when dosing is inappropriately reduced.[24]

The MAPH score was initially introduced as a simple tool to estimate thrombus burden in patients with ST-segment elevation myocardial infarction (STEMI).[7] Subsequent studies have demonstrated its association with coronary thrombus burden in both STEMI and non-STEMI populations.[8-10] It has also been proposed as a useful marker for distinguishing central and peripheral subtypes of pulmonary embolism, and its association with the coronary slow-flow phenomenon has been reported.[32,33] In an analysis including patients with infective endocarditis, a strong correlation was observed between higher MAPH scores and the presence of vegetations larger than 10 mm.[34] A recent study also demonstrated a relationship between the MAPH score and the presence and severity of coronary artery disease, reporting that scores above 2 were associated with coronary artery disease, whereas scores above 3 were consistent with intermediate-to-high SYNTAX scores (Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery score).[35] In the field of neurovascular disease, the MAPH score has been shown to aid in differentiating acute ischemic stroke from transient ischemic attack and in identifying major vessel occlusion.[36] Taken together, these findings suggest that the MAPH score is a reliable inflammation-related marker capable of reflecting thrombotic processes across various clinical conditions. Our study extends this body of evidence by demonstrating that the MAPH score is significantly associated with the presence of LAAT. This may be particularly relevant for evaluating patients at increased risk of cardioembolic stroke, especially in cases where the CHA_2DS_2-VASc score may fail to identify risks. As such, the MAPH score represents a noninvasive and easily calculated tool that appears to be especially useful as a screening marker for thrombotic risk.

On the other hand, the CHA_2DS_2-VASc score is a widely validated clinical classification system for long-term stroke risk prediction in patients with AF and has been shown in some cohorts to correlate with thromboembolic risk markers identified by TEE.[37] It has also been suggested that its predictive accuracy may be enhanced by incorporating left atrial functional parameters.[38] Nevertheless, although certain studies have demonstrated an association between CHA_2DS_2-VASc and LAAT or have supported its role in risk stratification, its predictive performance has frequently been reported as limited.[21,25,29,37,39,40] This observation is consistent with our findings. The CHA_2DS_2-VASc score was originally designed to estimate long-term stroke risk and does not incorporate variables reflecting thrombogenic mechanisms such as inflammation, coagulation activity, or viscosity. In line with this, the higher specificity and negative predictive value observed for the MAPH score in our study suggest that supplementing clinical risk scores with biomarker-based parameters may provide a more reliable approach to assessing LAAT risk.

While the MAPH score demonstrated significantly better discriminative performance than the CHA_2DS_2-VASc score in our study, we must acknowledge that both scores showed only modest ability to identify LA thrombus. The MAPH score achieved an AUC of 0.683, which, although significantly higher than that of CHA_2DS_2-VASc (AUC: 0.486), still falls short of what is generally considered strong discrimination (typically AUC > 0.7). This finding underscores an important point: although these scores may assist in risk stratification, they cannot replace TEE when definitive exclusion of thrombus is required prior to a procedure. The moderate AUC values likely reflect the complexity of thrombus formation in AF, which involves hemodynamic alterations, blood clotting tendencies, and structural cardiac changes, processes that clinical scoring systems cannot fully capture.

An important finding that warrants careful interpretation is the association between anticoagulant treatment and LA thrombus in our study. Although anticoagulant therapy emerged as an independent predictor in multivariable analysis (OR: 14.95), subgroup analysis revealed that patients with thrombus were predominantly treated with warfarin (76.2%) rather than NOACs (11.9%), whereas the opposite pattern was observed among patients without thrombus. This apparent paradox likely reflects confounding by indication: patients prescribed anticoagulants, particularly warfarin, may have had inherently higher baseline thromboembolic risk, which prompted anticoagulation in the first place. The predominance of warfarin use in the thrombus group may also indicate inadequate anticoagulation control, as suggested by the elevated INR values observed in this group, or may reflect the tendency for warfarin to be prescribed to patients with more complex clinical profiles who are not suitable candidates for NOACs. Overall, this finding highlights that the mere prescription of anticoagulant therapy does not eliminate thrombus risk, particularly when anticoagulation intensity is suboptimal or when patients have particularly high-risk features.

Our findings have several practical implications, which should be interpreted within appropriate boundaries. First, the MAPH score—calculated from routine laboratory parameters— showed a stronger association with existing LA thrombus than the CHA_2DS_2-VASc score, potentially helping to guide decisions regarding which patients warrant TEE, even when CHA_2DS_2-VASc scores are low. Second, the MAPH score incorporates markers related to blood viscosity and prothrombotic status that are not included in traditional clinical risk scores. Third, although neither score can replace TEE for definitive thrombus exclusion, integrating the MAPH score into pre-procedural assessment may enhance risk stratification. Finally, our identification of AF at the time of TEE, elevated CRP levels, and suboptimal anticoagulation as independent predictors highlights potentially modifiable elements that warrant clinical attention. The potential clinical utility of the MAPH score may be particularly relevant in patients with CHA_2DS_2-VASc scores of 0 or 1, in whom anticoagulation decisions are often uncertain and the benefit-risk balance is less clear. In this subgroup, an elevated MAPH score might prompt consideration of TEE, even when conventional risk assessment suggests low thromboembolic risk. However, beyond this specific context, the current data do not support replacing validated thromboembolic risk scores with the MAPH score for broader clinical decision-making. Prospective validation studies evaluating the incremental value of MAPH in clearly defined risk subgroups are essential before clinical implementation can be recommended.

Limitations

This study has several limitations. First, its single-center retrospective design may limit generalizability. Second, although an a priori power calculation confirmed an adequate sample size (n = 258), the class imbalance (30 vs. 228 patients) may have affected the precision of performance estimates and regression coefficients. Third, biochemical parameters were assessed at a single time point without longitudinal follow-up, and TEE examinations and laboratory tests were not performed simultaneously, introducing the possibility of temporal variation not captured by the scores. Fourth, we did not include certain variables, such as body mass index, electrolyte levels, or hepatorenal function parameters, that may influence thrombogenesis.

Fifth, we lacked data on time in therapeutic range (TTR) for warfarin users. The predominance of warfarin use in the thrombus group (76.2% vs. 35.0%) may reflect suboptimal anticoagulation control, poor adherence, or preferential selection of higher-risk patients for vitamin K antagonist therapy. Sixth, formal inter-observer agreement statistics for TEE interpretation were not calculated, although the low frequency of disagreement suggests acceptable reliability. Seventh, the extreme odds ratio observed for albumin (OR: 1328.5) warrants careful interpretation. This implausibly large effect size likely reflects statistical artifacts related to the narrow distribution of albumin values within our cohort, potential quasi-complete separation in the logistic regression model, and the relatively small number of events (n = 30). Such extreme ORs may occur when a continuous variable shows limited variance between outcome groups or when the model approaches perfect classification across certain variable ranges. Therefore, this finding should be interpreted as indicating a strong statistical association rather than a clinically meaningful magnitude of effect. Eighth, the inclusion of INR in the multivariable analysis also warrants consideration. Given the unknown TTR for warfarin users and the predominance of warfarin use in the thrombus group, elevated INR may serve as a surrogate marker of inadequate anticoagulation control or selection bias rather than a true independent risk factor. Future studies incorporating detailed anticoagulation quality metrics are needed to clarify this relationship.

Conclusion

The MAPH score demonstrated a significantly stronger association with LA thrombus compared to the CHA_2DS_2-VASc score in patients with non-valvular AF undergoing pre-procedural TEE assessment. By incorporating hematological parameters that reflect blood viscosity and prothrombotic state, the MAPH score provided improved discriminative ability for detecting existing thrombus beyond traditional clinical risk factors. Although both scores exhibited moderate overall performance, and neither can replace TEE for definitive thrombus detection, the MAPH score may help identify patients with a higher likelihood of LA thrombus who could benefit most from TEE. These findings support further investigation of MAPH scoring as a complementary screening tool in the pre-procedural thrombus evaluation of AF patients scheduled for ablation, with the caveat that prospective validation is required before clinical implementation.

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