Cihan Aydın
Namık Kemal University, Department of Cardiology, Faculty of Medicine, Tekirdağ, Turkey

Possible predictors of stroke in patients with atrial microfibrillation

Background	Very short-lasting episodes of AF-like activity (micro-AF) may be precursors of undiagnosed silent episodes of atrial fibrillation. In this study, we examined the relationship between increased left atrial sphericity index (LASI) and stroke in patients with micro-AF.
Material and Methods	A total of 100 consecutive patients with micro-AF enrolled in this study. The histories, cranial magnetic resonance, and computed tomography images of these patients were scanned from the hospital database. The patients were divided into two groups according to whether or not they had a stroke. LASI was calculated as a fraction of the left atrial maximum volume to the left atrial volume of the sphere in a 4-chamber view. Atrial electromechanical delay (AEMD) intervals were calculated from the atrial wall and atrioventricular valve annulus levels by using tissue Doppler imaging (TDI). These two groups were compared in terms of stroke predictors.
Results	A history of stroke was present in 25 (25%) patients diagnosed with micro-AF (Group 1). 75 patients did not have stroke (Group 2). There was a significant difference between the two groups in terms of left atrial lateral wall electromechanical delay (LA lateral AEMD) times, left atrial volume index (LAVI), and left atrial sphericity index (LASI). Findings: LAVI, 40.9±3.72 vs. 29.9±3.84, p<0.001; LASI, 0.84±0.07 vs. 0.66±0.07, p<0.001; LA lateral AEMD, 77.2±4.85 vs. 66.5±3.66, p<0.001.
Conclusions	Stroke precautions should be taken in patients with micro-AF. New predictive indexes should be given importance. Changes in LASI, LAVI and LA lateral AEMD values may be a predictor of stroke in patients with micro AF.

Keywords	Atrial fibrillation; left atrial sphericity index; micro-AF; electrocardiogram
For citations	Cihan Aydın. Possible predictors of stroke in patients with atrial microfibrillation. Kardiologiia. 2023;63(5):40–46. [Russian: Джихан Айдын. Возможные предикторы инсульта у пациентов с микрофибрилляцией предсердий. Кардиология. 2023;63(5):40–46].

Corresponding Author	Cihan Aydın. E-mail: drcihanaydin@hotmail.com

Introduction

Atrial fibrillation (AF) is the most common type of irregular heart rhythm without P waves and lasting a minimum of 30 sec. AF is associated with increased rates of stroke, death, thromboembolic events, heart failure, hospitalizations, impaired quality of life, reduced exercise capacity, and left ventricular (LV) dysfunction [1]. There are many causes of AF, including aging, hypertension, heart valve diseases, congenital heart defects, heart failure, chronic obstructive pulmonary disease, coronary artery disease, obesity, and thyroid hormone disorders.

Left atrial (LA) volume is usually assessed by measuring the LA volume with 2-dimensional transthoracic echocardiography (TTE), since determining LA volume using magnetic resonance imaging (MRI) and cardiac computed tomography (CCT) is time-consuming and limited due to kidney and radiation damage. Two-dimensional, linear measurements of LA do not accurately measure LA volumes because LA enlargement usually does not occur uniformly in all directions. Therefore, the LA sphericity index (LASI) has been found to reflect LA remodeling correctly and to accurately measure the spherical shape of the LA. Previous studies have suggested that a more spherical LA increases the risk of AF recurrence [2, 3].

Very short-lasting episodes of AF-like activity (micro- AF) may be precursors of undiagnosed silent, episodes of atrial fibrillation. In previous studies, sudden onset of irregular tachycardia with ≥5 consecutive supraventricular episodes and the total absence of pulses and P-waves and lasting less than 30 sec has been described as micro-AF [4]. We still have limited information about the risk of shorter episodes of atrial fibrillation-like activity. It has been reported that supraventricular ectopic beats and supraventricular tachycardias may be associated with an increased risk of AF and stroke over time [5, 6]. Currently, there are no recommendations on how micro-AF patients should be managed or whether to use oral anticoagulants.

In this study, we examined the relationship between increased sphericity index and stroke in patients with micro-AF. In patients with whom we can show this relationship, we may start oral anticoagulants early to prevent stroke.

Material and methods

Study population

Patients over 18 yrs of age, without heart failure or heart valve disease, and who were diagnosed with micro-AF by 24-hour rhythm Holter monitoring were included in

ISSN 0022-9040. Кардиология. 2023;63(5). DOI: 10.18087/cardio.2023.5.n2158

this study. The clinical data of the patients were obtained retrospectively by examining the hospital's database. All blood samples from patients diagnosed with micro-AF were taken after 12 hrs of fasting. Holter monitor records of patients who complained of palpitations were scanned. A total of 100 patients with micro-AF detected in 24-hour Holter recordings between June 2021 and October 2021were randomly included in the study.

Patients diagnosed with paroxysmal AF in Holter monitoring, using new oral anticoagulants or warfarin, with structural valve disease, heart failure, thyroid hormone disorder, or significant coronary artery disease were not included in the study. We calculated the CHA_2DS_2-VASc score for each patient. CHA_2DS_2-VASc score was calculated as: Congestive heart failure or left ventricular ejection fraction < 40%: 1 point, Age 65–75 years: 1 point, Hypertension: 1 point, DM: 1 point, Female sex: 1 point, Vascular disease (defined as prior myocardial infarction, carotid artery disease, peripheral artery disease including intermittent claudication, and previous surgical or percutaneous intervention for abdominal aorta or vessels of upper or lower extremities): 1 point, History of stroke or transient ischemic attack: 2 points, Age ≥75 years: 2 points. The study was conducted according to the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee.

Transthrocacic Echocardiography

All transthoracic echocardiography was performed with Vivid 5 (GE Healthcare, Wauwatosa, WI, USA) and with a M4S Matrix array adult cardiac (3.5MHz) probe in the lateral decubitus position. LA maximum volume (LAV) was calculated using the area-length technique. During endocardial tracing, the pulmonary veins and atrial appendage were not included in the measurement. The LV ejection fraction was calculated using the Teicholz formula applied from the parasternal long-axis view. The long axis of the LA was considered as the measurement from the mitral valve atrial face to the posterior wall level. LA maximum volume was calculated as follows:

$$\text{LA maximum volume} = (0.848 \times \text{LA area}^{4\text{chamber}} \times \text{LA area}^{2\text{chamber}}) / (\text{minimum LA length}/2).$$

LA spherical volume was calculated as in the formula:

$$^{4\pi}/_{3} \times (\text{Maximum LA length}/2)^3,$$

LASI was calculated as the ratio of these two values:

$$\text{LASI} = (\text{LA maximum volume}) / (\text{LA volume of sphere}),$$

(Figure 1, Figure 2) [7, 8]. In the apical 4-chamber view, pulse wave Doppler (PWD) with 3 mm sample volume was placed at the mitral leaflet tips, then the peak E and A waves were measured. Tissue Doppler imaging (TDI) was performed at the septal and lateral mitral, tricuspid

Figure 2. Measurements of LAVI and LASI

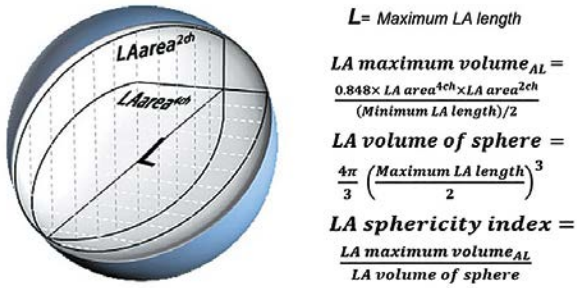
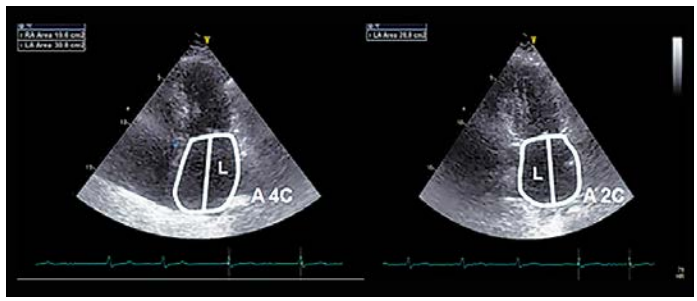
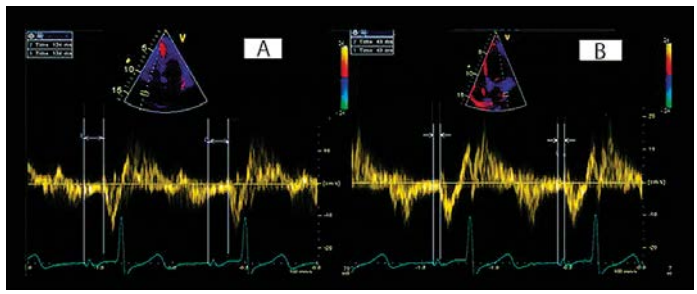


Figure 1. Left atrium area and volume measurement in 4 and 2 chambers view by bi-dimensional transthoracic echocardiography



A 4C: apical four chamber views;
A 2C: apical two chamber views; L: length.

Figure 3. A. Left atrium lateral atrial electromechanical delay (AEMD) duration. **B.** Right atrium lateral AEMD duration



valve annulus, and atrial walls in apical 4-chamber view. The time interval from the onset of the electrogram (ECG) P wave to the beginning of late diastolic wave (Am) was measured for atrial electromechanical delay (AEMD) from the atrial wall and valve annulus levels (Figure 3). The TE was defined as the time interval between the beginning of the ECG R wave to the beginning of the PWD E wave. The TEm was defined as the time interval between the beginning of the ECG R wave to the beginning of the TDI Em wave. The difference between these two times was calculated and named TEm-E.

Electromechanical time interval measurements

The time interval from the onset of the ECG P wave to the beginning of the late diastolic TDI wave (Am wave) was identified as AEMD (Figure 3A, 3B) [9].

Table 1. Characteristics of the patients

Characteristics	All patients (n=100)	Patients with stroke (n=25). Group 1	Patients without stroke (n=75). Group 2	p value
Age (yrs)	62.4±10.26	64.1±9.80	61.5±10.41	0.126†
Height (cm)	165.5±8.88	165.3±9.90	165.4±8.50	0.985#
Weight (kg)	80.7±13.87	80.4±13.12	81.4±14.14	0.516†
Male	39 (39)	11 (44)	28 (37.3)	0.554#
Female	61 (61)	14 (56)	47 (62.7)	0.554#
Smoking	39 (39)	8 (32)	31 (41.3)	0.407#
Diabetes	50 (50)	7 (28)	43 (57.3)	0.011#
Hypertension	56 (56)	17 (68)	39 (52)	0.163#
Coronary artery disease	21 (21)	3 (12)	18 (24)	0.202#
Chronic heart failure	8 (8)	1 (4)	7 (9.3)	0.729#
CHA_2DS_2-VASc Score	2.95±1.59	4.28±1.45	2.34±1.32	<0.001†
Laboratory Data				
BUN (mg/dl)	24.4±10.81	23.2±8.42	21.6±9.80	0.546†
Creatinine (mg/dl)	0.8±0.12	0.82±0.15	0.78±0.19	0.206†
Total cholesterol (mg/dl)	225 (33–446)	222 (117–260)	221 (133–446)	0.063*
Triglyceride (mg/dl) (min-max)	95.10 (31–339)	124.33 (71–322)	129.82 (31–274)	0.745*
HDL–C (mg/dl)	63 (31–166)	62 (31–82)	64 (33–66)	0.586*
LDL–C (mg/dl)	152.7±57.88	152.8±34.44	155.3±58.12	0.645†
Neutrophil ($\times 10^3$/μl)	5.1 (1.6–10.9)	5.3 (1.6–6.9)	5.5 (1.99–10.6)	0.874*
Lymphocyte ($\times 10^3$/μl)	3.59±1.39	3.77±0.49	3.2±1.36	0.647†
WBC ($\times 10^3$/μl) min-max)	11.60 (2.47–17.1)	11.40 (2.47–10.6)	12.21 (4.25–17.1)	0.746*
Platelet ($\times 10^3$/μl)	269.68±80.50	272.32±49.65	273±85.77	0.645†
Hemoglobin (g/dl)	13.28 (10.6–17.1)	13.38 (10.9–17.1)	13.27 (10.6–17.2)	0.949*
NT-proBNP (pg/ml)	129.60 (22.8–3463)	178.22 (22.8–1565)	124.42 (31.3–2134)	0.228*
Glucose (mg/dl)	111 (76–226)	104.54 (76–226)	114 (81–226)	0.481*
AST (IU/l)	16 (6–34)	18.52 (11–33)	16 (6–34)	0.946*
ALT (IU/l)	17.62 (6–41)	20.25 (13–31)	16 (6–41)	0.026*
Na (mEq/l)	140 (123-143)	139.51 (134–143)	140 (134–143)	0.383*
K (mEq/l)	4.41 (2.9–5.1)	4.62 (3.53–5.1)	4.45 (2.94–5.1)	0.347*
TSH (mIU/l)	1.57 (0.02–5.3)	1.13 (0.46–3.9)	1.27 (0.02–5.3)	0.428*
T_4 (ng/dl)	1.24 (0.02–5.3)	1.24 (0.92–1.8)	1.23 (0.02–4.1)	0.883*
Medications				
ACEI	20 (20)	4 (16)	16 (21.3)	0.729#
ARB	33 (33)	11 (44)	22 (29.3)	0.177#
β-Blocker	47 (47)	7 (28)	40 (53.3)	0.028#
Ca-channel blocker	31 (31)	2 (8)	29 (38.7)	0.004#
Diuretic	35 (35)	10 (40)	25 (33.3)	0.545#
Acetyl salicylic acid	8 (8)	2 (8)	6 (22.2)	0.252#
Clopidogrel	10 (10)	5 (5)	5 (6.6)	0.756#
Oral antidiabetic	37 (37)	7 (28)	30 (40)	0.282#
Insulin	22 (22)	6 (24)	16 (21.3)	0.780#
Statin	22 (22)	4 (16)	18 (24)	0.403#

Chi-square test. * Mann Whitney U test. † Student's t-test.
ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; HDL–C, high density lipoprotein-cholesterol; LDL–C, low-density lipoprotein cholesterol; WBC, white blood cell count; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TSH, thyroid stimulating hormone; T4, thyroxine; proBNP, N-terminal fragment of the B-type natriuretic peptide precursor, CHA_2DS_2-VASc score [C,congestive heart failure;H, hypertension; A,age≥75 years (doubled); D,diabetes; S, stroke (doubled) – V, vascular disease; 65–74 years of age, and sex category (female)].
Data are mean±standard deviation, median (minimum-maximum) or value (percentage).

AEMD intervals were defined as follows: lateral mitral annulus (mitral lateral AEMD), medial mitral annulus (mitral medial AEMD), lateral tricuspid annulus (tricuspid lateral AEMD), lateral LA wall (LA lateral AEMD), interatrial septum (LA medial AEMD), and lateral right atrium (RA) wall (RA lateral AEMD).

The differences between the following time intervals, respectively, were expressed as inter-atrial electromechanical

ISSN 0022-9040. Кардиология. 2023;63(5). DOI: 10.18087/cardio.2023.5.n2158

Table 2. Comparison of atrial electromechanical values

Ventricular annular measurements	Patients with stroke (n=25). Group 1	Patients without stroke (n=75). Group 2	p value
Mitral lateral AEMD (ms)	80.2±5.05	67.3±3.96	<0.001*
Mitral medial AEMD (ms)	75.8±5.38	63.7±4.54	<0.001*
Tricuspid lateral AEMD (ms)	72±5.69	59.7±4.88	<0.001*
Atrial wall measurements:			
LA lateral AEMD (ms)	77.2±4.85	66.5±3.66	<0.001*
LA medial AEMD (ms)	74±5.10	62.1±4.46	<0.001*
RA lateral AEMD (ms)	70.5±5.12	59±4.38	<0.001*
Inter-AEMD (min-max) (ms)	8.2 (4–16.1)	6.2 (3.4–13.6)	0.407†
Intra-AEMDLEFT (ms)	4.46±2.04	3.56±1.78	0.039*
Intra-AEMDRIGHT (ms)	3.8±2.62	3.97±1.92	0.740*

* Mann–Whitney U test. † Student's t test.
AEMD, atrial electromechanical delay; LA, left atrium; RA, right atrium. Data are mean±standard deviation or median (minimum-maximum).

delay (inter-AEMD); mitral lateral AEMD – tricuspid lateral AEMD, or LA lateral AEMD – RA lateral AEMD. Left intra-electromechanical delay (intra-AEMD LEFT) was defined as the difference between mitral lateral AEMD – mitral medial AEMD or LA lateral AEMD–LA medial AEMD. Right intra-electromechanical delay (intra-AEMDRIGHT) was defined as the difference between mitral medial AEMD – tricuspid lateral AEMD or LA medial AEMD – RA lateral AEMD.

Statistical Analysis

All data included were analyzed with the SPSS 22.0 statistics package (SPSS Inc, Chicago, Ill, USA). Continuous variables with normal distributions are reported as means± standard deviations; non-normally distributed, continuous variables are presented as medians (minimum-maximum). Categorical variables are reported as values (percentages). The student's t-test was used to compare normally distributed data, and the Mann–Whitney U test was used for non-normally distributed data. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. Univariate and multivariate logistic regression analyses were used to determine significant predictors of stroke in patients with micro-AF. The relationship between AEMD durations, left atrial volume index, and left atrial sphericity index was calculated using Pearson's correlation analysis. The sensitivity and specificity of the left atrial sphericity index to predict stroke in patients with micro-AF were analyzed by receiver operating characteristics (ROC) analysis. Values of p less than 0.05 were considered significant.

Table 3. Comparison of echocardiographic data

Variable	Patients with stroke (n=25). Group 1	Patients without stroke (n=75). Group 2	p value
LVEF (%)	60.3±4.91	59.5±4.66	0.456†
LAVI (ml/m²)	40.9±3.72	29.9±3.84	<0.001†
LASI	0.84±0.07	0.66±0.07	<0.001†
LV end-diastolic diameter [mm]	48.7±3.93	47.7±3.20	0.207†
LV end-systolic diameter [mm]	31±2.95	30±2.71	0.257†
LA diameter [mm]	41±3.05	35±2.10	<0.001†
Septum / Posterior wall thickness[mm]	13.5±0.40 / 12.7±0.30	13.8±0.70 / 12.4±0.20	0.456†
Mitral E velocity [m/s]	0.64±0.16	0.78±0.06	<0.001†
Mitral A velocity [m/s]	0.72±0.09	0.61±0.07	<0.001†
Mitral lateral Em velocity [cm/s]	0.10±0.03	0.1±0.02	0.138†
Mitral lateral Am velocity [m/s]	0.08±0.01	0.08±0.01	0.846†
Mitral medial Am velocity [m/s]	0.06±0.01	0.06±0.01	0.868†
Mitral lateral E/Em ratio	6.51±2.50	7.10±2.03	0.181†
Tricuspid lateral Em velocity [m/s]	0.12±0.03	0.12±0.03	0.990†
Tricuspid lateral Am velocity [m/s]	0.12±0.02	0.12±0.02	0.581†
Mitral lateral interval E–Em(ms)	48.50±5.11	46.30±5.50	0.083†
Tricuspid lateral interval E–Em(ms)	49.10±6.6	47.50±5.60	0.086†
LA lateral Sm velocity [m/s]	0.13±0.23	0.14±0.24	0.893†
LA lateral Em velocity [m/s]	0.09±0.01	0.08±0.01	0.609†
LA lateral Am velocity [m/s]	0.08±0.03	0.08±0.02	0.632†
LA medial Sm velocity [m/s]	0.07±0.01	0.07±0.01	0.486†
LA medial Em velocity [m/s]	0.06±0.01	0.06±0.01	0.561†
LA medial Am velocity [m/s]	0.05±0.01	0.05±0.02	0.928†
RA lateral Sm velocity [m/s]	0.12±0.02	0.12±0.02	0.896†
RA lateral Em velocity [m/s]	0.14±0.02	0.14±0.02	0.898†
Ra lateral Am velocity[m/s]	0.10±0.03	0.10±0.03	0.478†

† Student's t-test (mean ± standard deviation).
AEMD, atrial electromechanical delay; LA, left atrium; RA, right atrium; LAVI, left atrial volume index; LASI, left atrial sphericity index.
Data are mean±standard deviation.

Table 4. Correlation analysis between the left atrial sphericity index and atrial electromechanical delay variables and left atrial volume index variables

Variable	Durations or volume	Left atrial sphericity index	
		r	p
Mitral lateral AEMD (ms)	70.49±7.02	0.46	<0.001
Mitral medial AEMD (ms)	66.71±7.04	0.43	<0.001
Tricuspid lateral AEMD (ms)	62.72±7.30	0.41	<0.001
Inter-AEMD (ms)	7.77±2.62	0.09	0.367
Intra-AEMDLEFT (ms)	3.78±1.80	0.09	0.363
Intra-AEMDRIGHT (ms)	3.93±2.14	0.03	0.738
LA lateral AEMD (ms)	69.13±6.08	0.47	<0.001
LA medial AEMD (ms)	65±6.88	0.44	<0.001
RA lateral AEMD (ms)	63±7.20	0.57	<0.001
LAVI (ml/m²)	32.62±6.07	0.35	<0.001

AEMD, atrial electromechanical delay; LA, left atrium; RA, right atrium; LAVI, left atrial volume index; LASI, left atrial sphericity index.
Data are mean±standard deviation.

Figure 4. ROC analysis performed to assess the predictive power of the AEMD durations and LASI for stroke in patients with micro-AF

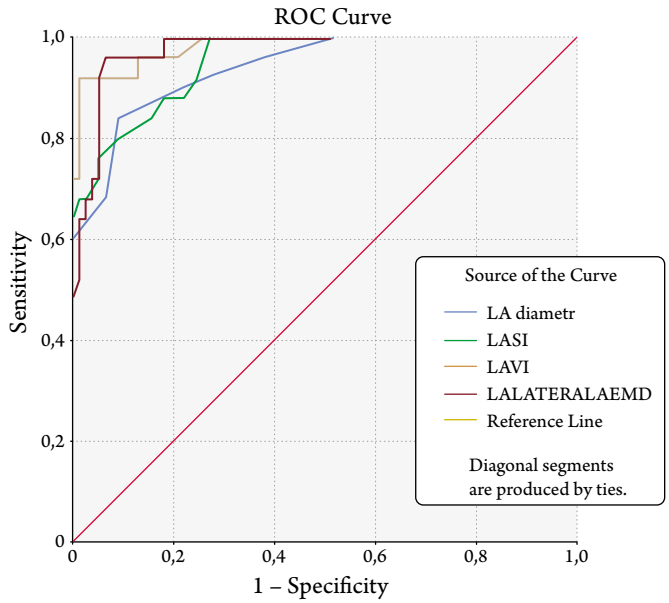


Table 5. Univariate and multivariate logistic regression analysis of predictors of stroke

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age	1.04 (0.989–1.096)	0.126	–	–
CHA2DS2-VASc Score	2.29 (1.558–3.373)	<0.001	2.05(0.802–5.284)	0.133
LAVI (ml/m²)	3.05 (1.672–5.591)	<0.001	2.20(1.113–4.353)	0.023
LASI	1.29 (1.01–7.12)	<0.001	7.45 (2.78–19.97)	0.027
LA diameter [mm]	2.15 (1.587–2.930)	<0.001	2.07(0.997–4.314)	0.051
LA lateral Am velocity[m/s]	0.02 (0.004–11.39)	0.628	–	–
LA lateral AEMD duration(ms)	1.84 (1.408–2.430)	<0.001	2.12(1.173-3.857)	0.013

AEMD, atrial electromechanical delay; LA, left atrium; RA, right atrium; LAVI, left atrial volume index; LASI, left atrial sphericity index; CHA2DS2-VASc score; C; congestive heart failure; H, hypertension; A2, age≥75 yrs; D, diabetes mellitus; S2, stroke; V, vascular disease; A, Age 65–74 yrs; Sc, sex category.

Table 6. ROC analysis performed to assess the predictive power of the AEMD durations and LASI for stroke in patients with micro-AF

Variable	AUC	p value	95% CI	
			Lower boundary	Upper boundary
LASI	0.95	<0.001	0.91	0.99
LAVI (ml/m2)	0.98	<0.001	0.96	1.00
LA diameter(mm)	0.94	<0.001	0.89	0.99
LA lateral AEMD (ms)	0.97	<0.001	0.95	1.00

AEMD, electromechanical delay; LA, left atrium; RA, right atrium; LAVI, left atrial volume index; LASI, left atrial sphericity index; AUC, area under the curve; CI, confidence interval.

Results

This retrospective study enrolled 100 consecutive micro-AF patients. In Table 1, baseline characteristics of the patients are summarized. The study group of 100 people was divided into Group 1 with stroke and Group 2 without stroke, according to the patients' history and the presence of infarct on cranial magnetic resonance imaging or cranial computed tomography. The CHA_2DS_2-VASc Score was significantly higher in Group 1 than in Group 2 (4.28±1.45 vs. 2.34±1.32; p<0.001).

In Group 2, the number of the diabetic patients, and the use of Ca-channel blockers and β-blocker drugs were higher than in Group 1 (28% vs. 57.3%; p=0.011), (8% vs. 38.7%; p=0.004), (28% vs.53.3%; p=0.028, respectively. The other parameters were similar between the groups (Table 1).

ISSN 0022-9040. Кардиология. 2023;63(5). DOI: 10.18087/cardio.2023.5.n2158

The times measured from both ventricular annular levels and atrial walls in Group 1 were longer (p<0.001). While the duration of Intra-AEMDLEFT was longer in Group 1 (4.46±2.04 vs. 3.56±1.78; p=0.039), Inter-AEMD and Intra-AEMDRIGHT times were similar in both groups (Table 2). LAVI (p<0.001), and LASI (p<0.001), and LA diameter (p<0.001) were significantly higher in Group 1. While mitral E velocities (p<0.001) were lower in Group 1, mitral A velocities (p<0.001) were higher. All other group echocardiographic measurements were similar. (Table 3). In the bivariate correlation analysis, significant, positive correlations were present between LASI and the following variables: Mitral lateral AEMD, Mitral medial AEMD, Tricuspid lateral AEMD, LA lateral AEMD, RA lateral AEMD, and LAVI (Table 4).

In the multivariate logistic regression analysis, LASI (odds ratio 7.450, p=0.027), LAVI (odds ratio 2.202, p=0.023), LA lateral AEMD duration (odds ratio 2.126, p=0.013) were significant predictors of stroke in micro-AF (Table 5).

A ROC analysis was performed to evaluate the predictive power of LASI and durations of AEMD for stroke in patients with micro-AF (Table 6, Figure 4). The area under the ROC curve was calculated for each parameter: LASI (0.95, p<0.001), LAVI (0.98, p<0.001), LA diameter (0.94, p<0.001), LA lateral AEMD (0.97, p<0.001). All these parameters were associated with stroke in patients with micro-AF (Figure 4). In the univariate analysis, CHA_2DS_2-VASc Score, LAVI, LASI, and LA diameter were significant predictors of stroke in patients with micro-AF.

Discussion

In this study, we aimed to investigate LA sphericity and atrial electromechanical delay time as stroke markers in patients with micro-AF. Previous studies related to LA sphericity have mainly focused only on AF patients. As far as we know, neither AEMD nor LASI have not been studied before in a patient group with micro-AF.

In a cohort study of 106 consecutive patients who underwent ablation for AF, LA sphericity index was found to be an independent risk factor for arrhythmia recurrence [2]. In previous studies, AF prevalence was reported to be more than four times higher in the micro-AF group compared to 3% in the control group [10]. Patients with a more spherical LA also more frequently had a history of a thromboembolic event [11]. In the current study, we investigated patients who had a stroke and were diagnosed with micro-AF.

LA pressure overload due to various reasons causes changes in LA shape. The easiest adaptation to increasing left atrial pressure may be the spherical shape of the atrium to achieve an optimal volume/surface ratio. In this way, wall stress of the LA reduces LA volume, so the sphericity index more accurately represents LA dimensions than LA linear measurements because the LA expands at different amounts in the three-dimensional plane. New methods, such as MRI and CCT, are highly successful in assess asymmetric changes in LA. However, exposure to radiation and its time-consuming nature reduces the usability of these processes. In this study, we used TTE, which we routinely use to calculate LASI.

We observed that a higher LASI, which means a more spherical LA, increases the risk of stroke. Binici et al. found that by the end of 6.3 yrs, in healthy patients with 30 or more supraventricular ectopic beats, the prevalence of AF increased 300% and the risk of stroke and death increased by 60% compared to the control group [5]. In a different study, it was found that 13% of patients with micro-AF were in AF after an average of 33 mos [7]. Therefore, close follow-up of patients with micro-AF and high LASI in terms of stroke is important. The importance of LASI in predicting AF recurrence in patients with a mild to moderate increase in LAVI has been demonstrated in previous studies [12]. Similarly, we found that LAVI and LASI values were higher in the stroke group with micro-AF in our study.

Before LA remodeling, electrical abnormality is first observed in the atrium. Electrical remodeling begins early in the process of atrial fibrillation, while structural remodeling is a late histopathological manifestation. The duration of AEMD is closely related to the histopathological changes in the atrium [13]. Atrial fibrosis, myocyte atrophy, and diffuse fibrotic foci in normal atrial tissue lead to non-homogeneous transmission of impulses in atriums. As shown in previous studies, the delay in this conduction is in the lateral walls of the LA and left ventricle, which is further away from the sinus node. In our study, LA lateral AEMD duration, LASI, and LAVI were found to be significant predictors of stroke in patients with micro-AF in multivariate logistic regression analysis. In support of the current findings, Park et al. found both left atrial volumes and AEMD durations to be longer in patients with AF recurrence [13].

When AF occurs, a gradual enlargement and remodeling is seen in the LA geometric dimensions, which causes worse LA remodeling. Increased LA pressure expands the atrium along the atrial orthogonal axis, causing the shape of the atrium to change from oval to spherical [14]. In the study of Armin Osmanagic et al., when LASI value was taken as 0.9 as the cut-off value in predicting AF recurrence, the specificity was 79.3% and the sensitivity was 51.8% [14]. In parallel with that study, LASI was significantly higher in stroke patients with micro AF in our study (0.84±0.07 vs. 0.66±0.07, p<0.001).

It is important to provide rhythm control in the early period to prevent LA geometric remodeling. Therefore, there is a need for indicators such as AEMD, LAVI, and

LASI that can help early diagnosis in AF, which is a cause of high morbidity and mortality. In a different study in which radiofrequency catheter ablation was applied to patients with AF, it was determined that the calculation of LASI together with LAVI would be a better indicator than left atrium diameter in predicting AF recurrence [7].

In the current study, we found that LAVI and LASI could predict the incidence of stroke in patients with micro-AF rather than a recurrence of AF. Stroke precautions should be taken in patients with micro-AF. New predictive indexes should be given importance. Oral anticoagulants may be given to this patient group, perhaps by considering LASI and LAVI values in the early period.

Study limitations

The study had some limitations. First, it was a single-center, retrospective study with a small number of patients. Patients with structural valve disease, heart failure, hormonal disorders, and significant coronary artery disease were not included in the study.

Apart from transthoracic echocardiography, cardiac magnetic resonance and computed tomography methods could be used in LAVI and LASI calculations in patients with poor image quality. Longer Holter monitoring could be performed in patients with micro-AF in 24-hour Holter recordings. In this way, paroxysmal AF attacks could be detected in these patients. Large-scale multicenter studies are needed to confirm the results of this study.

Conclusion

Although the term micro-AF is a new definition, it may herald an arrhythmia such as AF with high mortality and morbidity in the long term. Therefore, early diagnosis and treatment are important. We can predict patients at risk of stroke with indices that can be easily calculated by echocardiographic methods. Changes in LASI, LAVI and LA lateral AEMD values may be a predictor of stroke in patients with micro AF.

Funding

No funding was received for this study.

No conflict of interest is reported.

The article was received on 28/04/2022

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ISSN 0022-9040. Кардиология. 2023;63(5). DOI: 10.18087/cardio.2023.5.n2158