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Original Article

Is Left Atrial Strain in Non-Valvular Atrial Fibrillation a Noninvasive Predictor of the Left Atrial Appendage Spontaneous Echo Contrast?

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ABSTRACT

Background: The left atrial appendage (LAA) spontaneous echo contrast (SEC) is a surrogate marker of thrombotic state in atrial fibrillation (AF). We investigated the correlation between LA speckle-tracking parameters and the LAA SEC or thrombosis.

Methods: This cross-sectional study evaluated 70 AF ablation candidates, irrespective of their rhythm. Complete 2D transthoracic and transesophageal echocardiographic examinations and LA speckle-tracking analyses were performed. Based on the presence of thrombosis and the severity of SEC in the LAA, the patients were divided into 3 groups.

Results: Seventy patients (mean age=54±13.6 y; 37 men) were evaluated. Sinus rhythm was reported in 41 patients and oral anticoagulant consumption in 51. The mean CHA2DS2-VASc score was 1.8±1.4, and the mean LVEF was 51.1±7.4%. The LASr in the 2- and 4-chamber views was lower in subjects with AF rhythm (P<0.0001). Patients with LAA thrombosis and moderate-to-severe SEC, all in AF rhythm, had lower LAA velocities (P<0.0001), LASr (4-chamber view=5.2±1% vs 9±2.7% vs 20.7±8.2%; P<0.0001), LAScd (P=0.003), and mean strain rates (P<0.0001) than patients with mild or no SEC. The best correlation with the LAA SEC was found for the LASr in the 4-chamber view (r= −0.58, P<0.0001). There were no differences in the time-to-peak velocities and the time delay of the opposite walls.

Conclusions: Patients in AF rhythm had remarkably lower LA strain values than those in sinus rhythm. Significantly lower LA emptying velocities and segmental and global speckle-tracking parameters were observed in patients with moderate-to-severe SEC or LAA thrombosis, and the best correlation was shown with the LASr. ***(Iranian Heart Journal 2021; 22(2): 83-95)***

KEYWORDS: Atrial fibrillation, Transesophageal echocardiography, Left atrial strain, Speckle-tracking echocardiography

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Atrial fibrillation (AF) is known as the most common sustained cardiac arrhythmia with up to 14% of prevalence in hospital-based studies. [1] It is estimated that the lifetime risk of AF development is 25% after the fourth decade of life. [2] AF in the absence of rheumatic mitral stenosis, mechanical or bioprosthetic heart valves, or mitral valve repair is termed "non-valvular atrial fibrillation (NVAF)". [3]
In a 14-year cohort of subjects with NVAF, an annual stroke risk of 3% was described. [4]
Multiple risk scores have been introduced for stroke risk stratification and anticoagulation in NVAF. The most useful scores are as follows: $CHADS_2$ "Congestive heart failure, Hypertension, Age of 75 years or higher, Diabetes mellitus, prior Stroke/transient ischemic attack"; CHA_2DS_2-VASc "Congestive heart failure, Hypertension, Age of 75 years or higher, Diabetes mellitus, Prior Stroke/transient ischemic attack, Vascular disease, Age between 65 and 74 years, Sex category"; and ATRIA "the same scores of CHADS2, renal function, proteinuria, and sex category". [4-6]
The left atrial appendage (LAA) is a finger-like projection in the anterolateral wall of the left atrium (LA) that shows the remodeling process, comprising dilation, patchy fibrosis, and reduced contractility, along with LA remodeling during AF rhythm. [7, 8] The contractions of the LAA could be assessed during transesophageal echocardiography (TEE) by measuring the LAA emptying velocity via pulsed-wave spectral Doppler study. [8] It is estimated that the prevalence of LAA thrombosis is 20% in patients with AF (either chronic or acute) and 14% in the acute setting (<3 d). [9] Swirling echo densities, composed of aggregated red blood cells and activated platelets and leukocytes, is termed "spontaneous echo contrast (SEC)" or "smoke". SEC is evaluated visually in the LAA as a marker of stasis and prothrombotic state. [8] It has been reported that dense LAA SEC in patients with NVAF is associated with an 18.2% rate of annual stroke risk (2.9 times that in patients without LAA SEC). [10]
Tissue Doppler studies on the LA volume, the mitral inflow pulsed-Doppler, and the mitral annulus are traditionally the main assessments for the evaluation of the LA function. The deformation parameters of the LA, especially the LA strain, are novel markers of LA mechanics. Having been introduced recently, these parameters confer invaluable information about all 3 phases of the LA function, comprising the reservoir, conduit, and booster pump phases, with large population studies having already defined cutoff values. [11, 12] The LA strain has been proposed to have an additive predictive role for stroke risk stratification in patients with AF. [13, 14]
There is still a dearth of validated data on the relationship between the LA strain and the LAA SEC and clots. In this study, we aimed to evaluate the correlation between LA speckle tracking, especially LA strain parameters, and the LAA SEC as a surrogate marker of thrombotic state in patients with NVAF who are candidates for AF ablation. The findings of such research could improve risk stratification in borderline stroke risk scores.

METHODS

Patient Population

This cross-sectional study was conducted at Rajaie Cardiovascular Medical and Research Center from April 2019 to December 2019. All patients with a history of NVAF who were referred by the expert team of electrophysiologists for pre-ablation TEE were evaluated as possible candidates for the study, irrespective of their rhythm at presentation. The exclusion criteria were defined as age under 18 or above 85 years, admission with acute coronary syndromes in recent months, any congenital heart disease, hypertrophic cardiomyopathy, left ventricular (LV) noncompaction cardiomyopathy, restrictive cardiomyopathy, more-than-mild mitral valve stenosis, more-than-moderate regurgitation or stenosis in other valves, prosthetic or repaired valves, heart transplantation, previous LAA closure, pregnancy, known malignancies, chronic liver disease, estimated glomerular filtration rates below 30 mL/min/1.73 m^2 and end-stage renal disease, known coagulopathies, any gastrointestinal diseases that precluded TEE, and refusal to participate in the study. Informed written consent was obtained from all the eligible patients.

The study population's demographic data, including weight and height, were recorded. Also recorded were the patients' clinical history, including congestive heart failure or a left ventricular ejection fraction (LVEF) of less than 40%, hypertension, diabetes mellitus, a history of transient ischemic attack or stroke, any atherosclerotic vascular disease, and the sex category for the calculation of the $CHADS_2$ and CHA_2DS_2-VASc scores. Additionally, a history of ablation or previous LAA thrombosis was noted. Further, the study population's drug history concerning the consumption of oral anticoagulants (vitamin K antagonists or new oral anticoagulants), antiplatelets, beta-blockers, statins, and anti-arrhythmic drugs was registered. Moreover, laboratory data regarding the complete blood count, the hematocrit concentration, the hemoglobin level, thyroid function tests, and coagulation factors (the prothrombin time, the international normalized ratio, and the activated partial thromboplastin time) were measured in keeping with the standard laboratory protocol at hospital admission.

Echocardiographic Evaluation

All the patients underwent complete electrocardiographically (ECG)-recorded 2D transthoracic echocardiography (TTE) and TEE using the Philips System (EPIQ or Affiniti 70 System, the S5-1 transducer for TTE and the X8-2t transducer for TEE). All the procedures and measurements were performed according to the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists guidelines for TTE and TEE. [15, 16] In TEE examinations, 3D studies were performed whenever it was necessary. All the basic measurements, including 2D-guided anteroposterior LV and LA volumes and diameters in 2 orthogonal views (apical 2- and 4-chamber views), were performed according to the American Society of Echocardiography and the European Association of Cardiovascular Imaging guideline for chamber quantification. [17] The diastolic function of the LV was evaluated in patients with sinus rhythm at presentation based on the last published guideline on diastolic function. [18] The body mass index was calculated as weight (kg) divided by height squared (m). The body surface area was calculated by entering the values of the patient's height (cm) and weight (kg) in the echocardiography system. The mean values of the 2- and 4-chamber LA and LV volumes and diameters were divided by the body surface area to calculate the LA volume index (LAVI), the left ventricular end-diastolic volume index (LVEDVI), and the left ventricular end-diastolic diameter index (LVEDDI), respectively.

During TEE, the presence of LAA thrombosis was carefully evaluated by using the X-plane method to examine the whole LAA cavity in multiple orthogonal views. The presence of SEC or smoke was evaluated at a standard gain of 50% to 55% while care was taken to avoid the misinterpretation of background noise as smoke. The severity of SEC was evaluated based on the grading system outlined by Fatkin et al. [19] The visual estimation of the SEC grading was done by 2 experienced echocardiologists. According to the presence and severity of SEC in the LAA, the patients were divided into 3 groups: Group I: no, mild, or mild-to-moderate SEC; Group II: moderate-to-severe SEC; and Group III: LAA thrombosis. Very dense, viscid smoke, known as “sludge”, was considered LAA thrombosis in this study. The pulsed-wave Doppler sample volume was placed at least 1 cm into the LAA cavity, and the left atrial appendage emptying velocity (LAAV, cm/s) at end-diastole was measured at 70° of the mid-esophageal TEE view. In patients with AF rhythm, the mean value of 10 consecutive velocities was recorded.

Speckle-Tracking Analysis

For speckle-tracking analysis, non-foreshortened apical 2- and 4-chamber LA-focused views were obtained at end-expiration in TTE examinations. Longitudinal strain analysis on the LA was performed off-line by using TOMTEC, version 4.6. Longitudinal LA speckle-tracking analysis was only defined for the 2-chamber view in the software. For the calculation of strain parameters in 2 orthogonal views, the 4-chamber views were inserted into the same software. The strain curves of the LA in this software were obtained through the manual selection of 3 reference points (2 at the mitral annulus and 1 at the LA roof); then, the software automatically traces the LA endocardial borders. After manual adjustments of the borders and definition of the time points of end-diastole and end-systole, the strain and strain rate curves were developed by the software. Longitudinal LA strain curves were automatically generated for 3 segments in each view (the lateral, septal, and roof segments in the apical 4-chamber view and the anterior, inferior, and roof segments in the apical 2-chamber view). All the measurements were performed based on the Consensus Document of the European Association of Cardiovascular Imaging/American Society of Echocardiography/Industry Task Force to Standardize Deformation Imaging. [20] For a more accurate analysis, the nadir of the LA strain curve at the mitral valve closure was considered end-diastole and the 0-reference point was set at this point. [20] The peak positive regional LA strain for each of the 3 segments in orthogonal views and strain values in the 3 phases of LA reservoir, conduit, and contraction in the cardiac cycle were measured (Fig. 1 & 2). The strain value of each phase was calculated as the difference of 2 points at the beginning and end of the phase on the strain curve. The reservoir phase begins at the end of the ventricular diastole and extends to the mitral valve opening. It is termed “LASr” and is considered a positive value (similar to the LA strain). The conduit phase starts at the mitral valve opening and terminates at the onset of LA contraction in sinus rhythm. It is termed “LAScd” and is considered a negative value. In patients with AF, it extends to the end of the ventricular diastole. The contraction phase starts at the onset of LA contraction and terminates at the end of the ventricular diastole in patients with sinus rhythm. It is termed “LASct” and is considered a negative value. The third phase is absent in patients with AF rhythm. [20] The present survey presents the negative values of LAScd and LASct as absolute numbers. For the evaluation of dyssynchrony between LA segments, the time delay between the peak positive strain (LASr) of the opposite walls (the time delay) and the time-to-peak of the positive strain (LASr) in each view were measured, and the latter was divided by the cycle length to adjust the measures for the heart rate (time-to-peak/cycle length) (Fig. 1 & 2).

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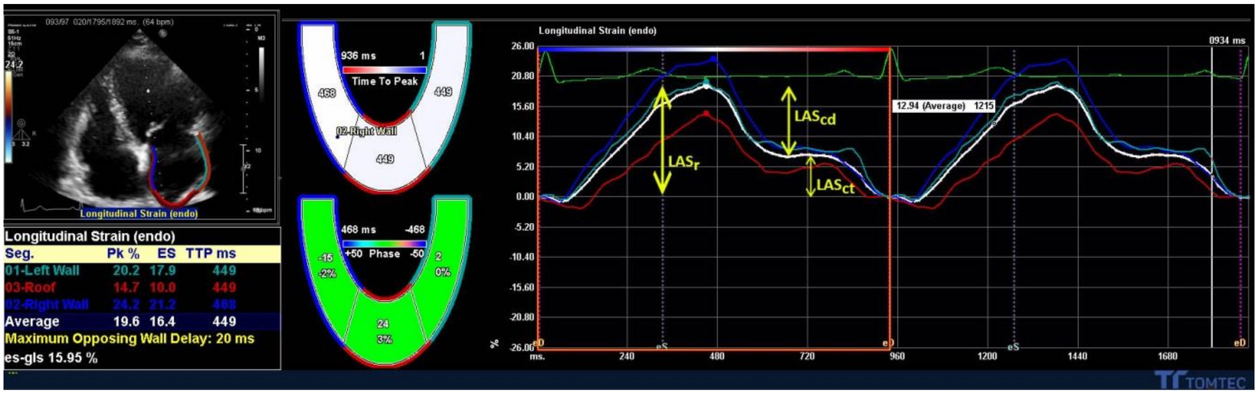

Figure 1.A

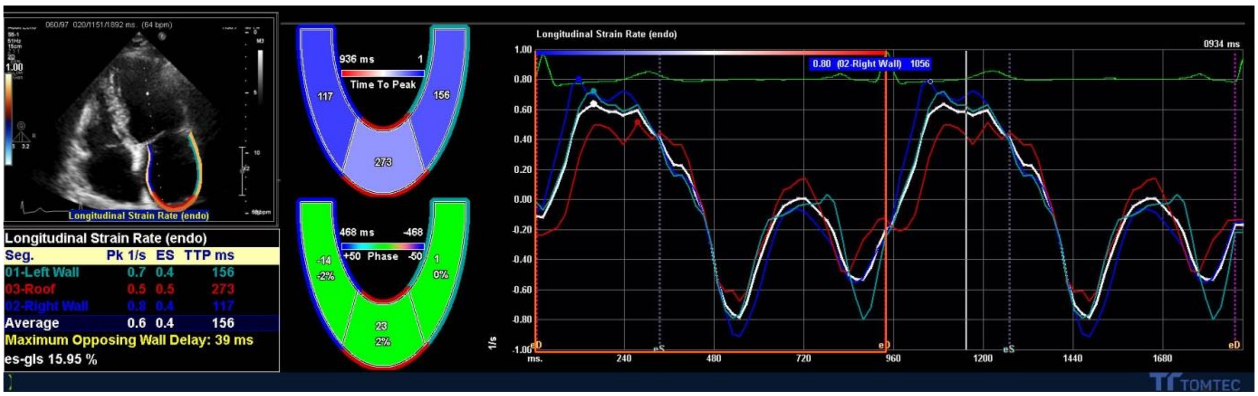

Figure 1.B

Figure 1: The image depicts the 4-chamber LA speckle-tracking analysis using TOMTEC software, featuring the LA strain and the components of 3 LA phases (1.A) and the LA strain rate (1.B) in a patient with sinus rhythm.
LA, Left atrium

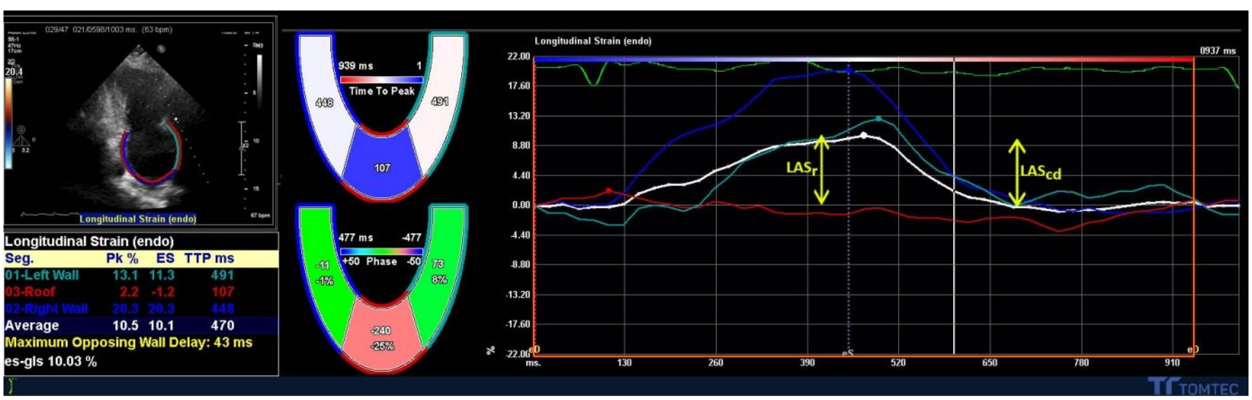

Figure 2.A

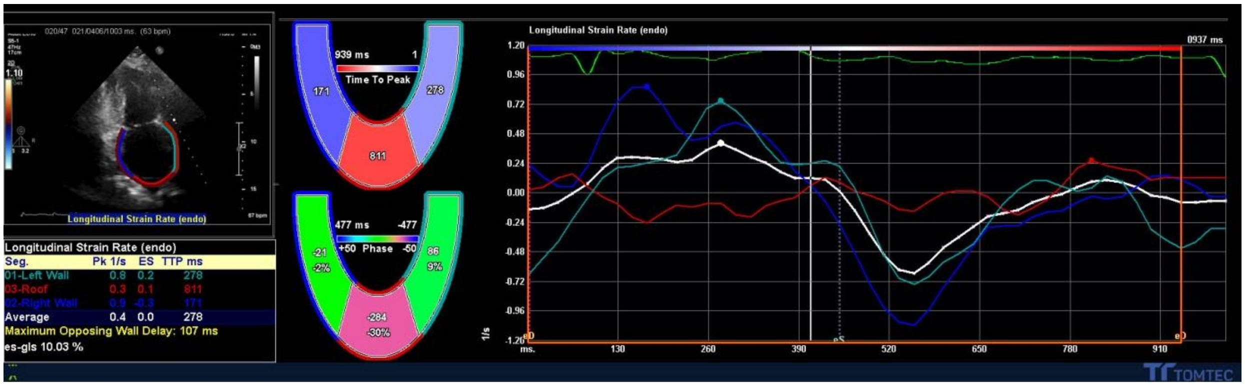

Figure 2.B

Figure 2: The image illustrates the 2-chamber LA speckle-tracking analysis using TOMTEC software, featuring the LA strain and the components of 2 LA phases (2.A) and the LA strain rate (2.B) in a patient with AF rhythm.
LA, Left atrium; AF, Atrial fibrillation

Statistical Analysis

The statistical analyses were performed with SPSS, version 15 (SPSS Inc, Chicago, IL, USA). Statistical significance was considered at a level of 0.05 (2-tailed). Qualitative variables were presented as frequencies (percentages), and the χ^2 test or the Fisher exact test was employed whenever appropriate. The normality of the distribution of quantitative variables was estimated by using the Kolmogorov–Smirnov test. Quantitative variables were expressed as the mean ± the standard deviation (SD) and analyzed via the independent Sample *t*-test or the Mann–Whitney *U* test. The one-way ANOVA test or the Kruskal–Wallis test was utilized to assess quantitative variables in the LAA SEC grading groups. The Pearson correlation coefficients were measured to evaluate the correlation between continuous variables.

RESULTS

During the study period, 70 patients with NVAF were selected based on the inclusion/exclusion criteria. The mean age of the patients was 54 13.6 years (range: 19–83 y). Thirty-seven patients (52.9%) were male, and 41 patients (58.6%) were in sinus rhythm at presentation. Normal diastolic function was observed in 51.7% of those with sinus rhythm, with Grade I diastolic dysfunction in the rest. Six patients (8%) had previous LA ablation procedures, and the same number had thyroid disorders. Three patients (4%), all with AF rhythm, had LAA thrombosis. Three patients (4%) had a history of LAA clots in the last TEE, and 1 of these patients showed LAA thrombosis in this evaluation. Oral anticoagulation was administered in 51 patients (73%), and 2 subjects did not receive any antithrombotic treatment.

The study populations' baseline demographic characteristics, history, and echocardiographic data, based on rhythm at presentation, are presented in Table 1. The patients in AF rhythm at presentation were older, had a significantly lower LVEF, a lower LVEDVI, a higher LA diameter, and a higher LAVI than the patients in sinus rhythm (*P*=0.04, *P*=0.02, *P*=0.009, *P*<0.0001, and *P*=0.003 respectively). The LAA velocity was significantly lower in the patients with AF (28.7±13 cm/s vs 65.5±24.6 cm/s; *P*<0.0001). The mean LASr in the 2- and 4-chamber views was remarkably lower among the patients in AF rhythm (*P*<0.0001). The patients' echocardiographic data, laboratory findings, and drug use based on the LAA SEC grading are listed in Table 2. All the patients in sinus rhythm had no or mild SEC. Among the patients in AF rhythm, 20 cases (69%) had no or mild SEC, 6 (20.7%) showed moderate-to-severe SEC, and 3 (10.3%) had LAA thrombosis (*P*=0.001). In the patients with LAA thrombosis and moderate-to-severe SEC, the LAA velocity was lower and the LA diameter and the LAVI were higher than those in the patients with no or mild SEC (*P*<0.0001, *P*<0.0001, and *P*=0.004, respectively). In this group, a trend toward a lower LVEF was observed (*P*=0.07). The CHA_2DS and CHA_2DS_2-VASc scores, as well as laboratory parameters, were not different between the SEC grading groups. Anticoagulation drug consumption had no meaningful relationship with the LAA SEC or thrombosis.

The associations between LA speckle-tracking measurements and the LAA SEC grading in the apical 4- and 2-chamber views are demonstrated in Table 3 and Table 4, respectively. The peak strain values of 3 cardiac phases, the segmental strain values, and the mean strain rates were significantly lower in the patients with LAA thrombosis and moderate-to-severe SEC than in the patients with no or mild SEC. No correlation was found between the time delay and the time-to-peak/cycle length and SEC severity.

The correlations between the LAA SEC grading and the LAAV, as markers of prothrombotic state, and echocardiographic parameters are represented in Table 5. The best correlation with both the LAA SEC and the LAAV was found for the LASr in the 4-chamber view (r= −0.58 and 0.69, respectively; *P* for both<0.0001).

Table 1: Baseline demographic, history, and echocardiographic data, as well as drug use, based on rhythm at presentation

	Total	Rhythm at Presentation		
N (%)	70 (100)	Sinus Rhythm 41 (58.6)	AF/AFL Rhythm 29 (42.4)	*P* value
Age (y)	54±13.6	51.2 ±13.8	57.9±12.5	0.04
Male sex, n (%)	37(52.9)	20(48.8)	17(58.6)	0.42
Height (cm)	168±9.2	168.2±8.6	167.6±10.2	0.79
Weight (Kg)	82±14.1	80.9± 13.7	83.6±14.7	0.45
BSA (m^2)	1.89±0.19	1.87±0.15	1.88±0.19	0.44
BMI (kg/m^2)	29.1± 5	29.1±4.5	30.6±6.5	0.27
Smoking, n (%)	8(11.4)	4(9.8)	4(14.8)	0.39
Alcohol, n (%)	2(2.9)	1(2.4)	1(3.6)	0.65
History of TIA/CVA, n (%)	5(7.1)	2(4.9)	3(10.3)	0.34
Diabetes mellitus, n (%)	12(17.1)	10(24.4)	2(7.4)	0.067
Hypertension, n (%)	34(48.6)	22(53.7)	12(42.9)	0.38
Ischemic heart disease, n (%)	13(18.6)	6(14.6%)	7(25)	0.28
History of heart failure, n (%)	11(15.7)	4(9.8)	7(24.1)	0.1
CHA_2DS_2-VaSc score	1.8±1.4	1.9±1.1	2±1.6	1
$CHADS_2$ score	1±1	1.2±0.8	1±0.9	0.99
LVEF (%)	51.1±7.4	51.9±8.3	46.9±8.8	0.02
LVEDDI (cm/m^2)	2.6±0.3	2.8±0.4	2.7±0.3	0.29
LVEDVI (cc/m^2)	51.6±11.8	57.6±7.1	52.1±9.5	0.009
LAD (cm)	3.9±0.6	3.8±0.3	4.3±0.9	<0.0001
LAVI (cc/m^2)	37.1±11.2	34.1±6.4	43.8±14.4	0.003
LAA velocity (cm/s)	53.2±28	65.5±24.6	28.7±13	<0.0001
LASr, 4C (%)	18.9±8.9	24.9±6	10.8±5	<0.0001
LASr, 2C (%)	19.4±9	25.4±6.4	11.6±5.3	<0.0001
Aspirin, n (%)	17(24.6)	11(26.8)	6(21.4)	0.6
Warfarin, n (%)	5(7.2)	1(2.4)	4(14.3)	0.08
NOAC, n (%)	46(66.7)	27(65.9)	19(67.9)	0.86
Beta-blocker, n (%)	55(79.7)	31(75.6)	24(85.7)	0.3
Anti-arrhythmic drug, n (%)	28(40.6)	18(43.9)	10(35.7)	0.49
Statin, n (%)	26(37.7)	15(36.6)	11(39.3)	0.82

AF, Atrial fibrillation; AFL, Atrial flutter; Antiarrhythmic drugs, flecainide, propafenone, amiodarone, or sotalol; BMI, Body mass index; BSA, Body surface area; CVA, Cerebrovascular accident; LAAV: Left atrial appendage emptying velocities; LAD, Left atrial diameter; LASr, Left atrial strain of reservoir phase; LAVI, Left atrial volume index; LVEDDI, Left ventricular end-diastolic diameter index; LVEDVI, Left ventricular end-diastolic volume index; LVEF, Left ventricular ejection fraction; NOAC, New oral anticoagulant; TIA, Transient ischemic attack; 4C, Four- chamber; 2C, Two-chamber

Bolded *P* values are statistically significant.

Table 2: Echocardiographic, laboratory data, and drug use based on the presence and severity of LAA SEC/thrombus

	No or Mild SEC	Moderate-to-Severe SEC	Thrombus	*P* value
AF Rhythm at presentation, n (%)	20(32.8)	6(100)	3(100)	0.001
LAA velocity (cm/s)	57.6±26	26.6±4.4	16.4±7.6	<0.0001
LVEF (%)	51.4±7.5	49±8.9	42.5±10.6	0.07
LVEDDI (cm/m^2)	2.65±0.37	2.61±0.29	2.7±0.14	0.35
LVEDVI (cc/m^2)	52.3±11.3	42.4±14.2	53.5±13.4	0.47
LVOT VTI (cm)	19.8±4.2	16.3±3.1	18±2.6	0.1
LAD (cm)	3.76±0.4	4.9±0.6	5±0.6	<0.0001
LAVI (cc/m^2)	34.1±7.3	45±16.5	67.5±2.1	0.004
Normal diastolic function	23(57.1)	-	-	-
CHA_2DS_2-VaSc	1.7±1.3	2±1	2±2.8	0.98
$CHADS_2$	0.9±0.9	1.6±1.1	1±1.4	0.36
NOAC use, n (%)	41(67.2)	5(83.3)	0	0.09
VKA use, n (%)	3(4.9)	1(16.7)	1(33)	0.03
Antiplatelet use, n (%)	14(23)	2(33.3)	1(33)	0.6
Leukocyte count (×10^9/L)	7.31±1.7	6.94±12.9	8.8±4.52	0.95
Hemoglobin (g/dL)	13.8±1.8	14.4±0.4	14.5±2.3	0.6
Hematocrit (%)	41.2±6.1	44.3±1.2	43.7±5.9	0.35
Platelet count (×10^9/L)	215.05	171.2	222.5	0.06
PT (seconds)	17±4.8	22.1±8.9	27.5±18	0.1
INR	1.3±0.4	1.7±0.6	2.2±1.6	0.16
aPTT (s)	35.8±7	35.8±6.8	40.4±17	0.98

AF, Atrial fibrillation; AFL, Atrial flutter; CVA, Cerebrovascular accident; INR, International normalized ratio; LAA SEC: Left atrial appendage spontaneous echo contrast; LAAV, Left atrial appendage emptying velocities; LAD, Left atrial diameter; LAVI, Left atrial volume index; LVEDDI, Left ventricular end-diastolic diameter index; LVEDVI, Left ventricular end-diastolic volume index; LVEF, Left ventricular ejection fraction; LVOT VTI, Left ventricular outflow tract velocity time integral; NOAC, New oral anticoagulant; PT, Prothrombin time; aPTT, Activated partial thromboplastin time; TIA, Transient ischemic attack; VKA, Vitamin K antagonist

Bolded *P* values are statistically significant.

Table 3: Associations between the 4-chamber speckle-tracking parameters and the LAA SEC grading

	No or Mild SEC	Moderate-to-Severe SEC	Thrombus	*P* value
LASr (%)	20.7±8.2	9±2.7	5.2±1	<0.0001
LAScd (%)	15.1±5.6	10.4±3.5	5.2±1	0.003
LASct (%)	11.4±3.8	-	-	-
Lateral wall LASr (%)	25.5±12.6	13.5±5.1	9±2.2	0.002
Septal wall LASr (%)	22.5±10.2	10.3±4.8	17.4±19.7	0.006
Roof LASr (%)	16.1±8.1	6.2±3.3	2±1.9	<0.0001
Time to peak/cycle length (%)	0.47±0.11	0.42±0.15	0.53±0.44	0.4
Time delay (ms)	42±52	65±48.8	53.3±11.5	0.3
Mean LA strain rate (1/s)	0.84±0.4	0.42±0.2	0.27±0.6	<0.0001

LAA SEC, Left atrial appendage spontaneous echo contrast; LASr, Left atrial strain of reservoir phase; LAScd, Left atrial strain of the conduit phase; LASct, Left atrial strain of atrial contraction phase

Bolded *P* values are statistically significant.

Table 4: Associations between the 2-chamber speckle-tracking parameters and the LAA SEC grading

	No or Mild SEC	Moderate-to-Severe SEC	Thrombus	*P* value
LASr (%)	21.8±8.7	10.7±5.7	5.8±1.4	<0.0001
LAScd (%)	15±5.3	10.9±5.2	7.1±0.8	0.01
LASct (%)	13.1±4.1	-	-	-
Anterior wall LASr (%)	24.7±12.6	12.1±6.6	8.7±1.5	0.007
Inferior wall LASr (%)	27.4±11.1	13±9.9	8.1±3.9	<0.0001
Roof LASr (%)	14.6±9	7.7±13.8	2.9±0.7	0.004
Time to peak/cycle length (%)	0.47±0.1	0.47±0.2	0.45±0.1	0.7
Time delay (ms)	32.5±34.3	41.8±18.2	50.3±17.9	0.2
Mean LA strain rate (1/s)	0.82±0.4	0.47±0.2	0.37±0.05	0.003

LAA SEC, Left atrial appendage spontaneous echo contrast; LASr, Left atrial strain of the reservoir phase; LAScd, Left atrial strain of the conduit phase; LASct, Left atrial strain of the atrial contraction phase

Bolded *P* values are statistically significant.

Table 5: Correlations between the echocardiographic parameters and the LAA SEC and the LAA velocity (prothrombotic markers)

	LAA SEC		LAA Velocity	
	Pearson Correlation	*P* value	Pearson Correlation	*P* value
LAD	0.48	<0.0001	-0.5	<0.0001
LAVI	0.39	0.001	0.57-	<0.0001
LASr, 4C	-0.58	<0.0001	0.69	<0.0001
LASr, 2C	-0.54	<0.0001	0.66	<0.0001
Mean strain rate	0.5-	<0.0001	0.64	<0.0001

LAA SEC, Left atrial appendage spontaneous echo contrast; LAAV, Left atrial appendage emptying velocities; LAD, Left atrial diameter; LAVI, Left atrial volume index; LASr, Left atrial strain of the reservoir phase; 4C, Four-chamber; 2C, Two-chamber

Bolded *P* values are statistically significant.

DISCUSSION

In this cross-sectional study on candidates for NVAF ablation, patients with more severe SEC in the LAA were all in AF rhythm at presentation, had a higher LA diameter, a higher LAVI, and a lower LAA velocity as well as a trend toward a lower LVEF. All segmental and global speckle-tracking parameters were significantly lower in patients with moderate-to-severe SEC or LAA thrombosis, and the best correlation was shown with the LASr. No relationship was found between LA dyssynchrony and SEC severity.

The prevalence rate of LAA thrombosis in NVAF has been reported as high as 20% in earlier and 12% in recent studies. [9, 21] LAA thrombosis was seen in only 3 patients (4% prevalence) in this survey. This low incidence of LAA thrombosis is related to the fact that the majority of our patients were candidates for AF ablation with a low overall stroke risk (the mean CHA_2DS_2-VASc score=1.8±1.4) and a history of adequate anticoagulation (73.9% of the study population).

A normal LAAV in sinus rhythm ranges from 50±6 cm/s to 83±25 cm/s in the literature, while in patients with NVAF, a velocity value of more than 25 cm/s with well-defined peak velocities is considered acceptable LAA function. [8, 22] In this study with a history of AF in all the patients, the mean LAAV in sinus rhythm was 65.5±24.6 cm/s, significantly higher than 28.7±13 cm/s in AF rhythm. Some authors have evaluated the relationship between the LAAV and the severity of SEC and have reported that velocities below 20 cm/s are associated with sludge formation and increased stroke risks, whereas values of 20 cm/s to 40 cm/s and 40 cm/s to 60 cm/s are linked to severe and mild-to-moderate SEC, respectively. [2, 7, 23] In the present study, the mean LAAV was 16.4±7.6 cm/s in patients with LAA thrombosis, all in AF rhythm, while the velocity was 26.6±4.4 cm/s in cases with moderate-to-severe SEC, all in AF rhythm too, whereas patients with no or mild SEC had near-normal velocities (57.6±26 cm/s). Zhao et al [24] proposed that a more severe LA SEC was an independent predictor of stroke at 2 years' follow-up of patients with NVAF.

Speckle-tracking echocardiography on the LA is a novel useful modality in the evaluation of LA mechanics that is load dependent and is affected by the LV function. [12] The normal value of the LA strain is dependent on the timing setting of the 0-reference point and is probably vender dependent too. According to a previous survey, LASr, LAScd, and LASct values of 46.8±7.7, 27.3±6.4, and 19.6±4.2% were reported in 121 healthy volunteers while ventricular end-diastole was set as the reference point. [25] The authors of the said study mentioned that the LA strain was age, but not gender, dependent. Liao et al [26] evaluated the LA strain among 2812 healthy individuals and reported higher LASr values in women (39.34±7.99% vs 37.95±7.96%; $P<0.001$) and concluded that it was dependent on age and blood pressure. In contrast, Saraiva et al [27] reported a mean value of 23.2±6.7% in 64 normal subjects while the reference point was set at the P-wave. Speckle-tracking echocardiography was performed by using EchoPAC, GE software, by all the last 3 mentioned studies. A value of the LA strain below 30% is considered significant reservoir dysfunction. [2] The mean LASr value in our study (25.15±6.2 in sinus rhythm vs 11.2±5.1 in AF rhythm) showed significant LA dysfunction even in patients with sinus rhythm at presentation.

The values of the LA strain and the LA strain rate have been reported to be predictive of cardiac events, heart failure, and stroke in NVAF. [28] Values of the LA strain below 24.5% have been proposed to be a predictor of AF recurrence in heart failure with a preserved LVEF. [29] Yasuda et al, [30] using EchoPAC, GE software, showed lower LASr values in patients with AF recurrence than in patients without AF recurrence after catheter ablation (12.0±4.3% vs 19.4±8.6%). They also reported a value of 23.0±5.8% for their normal control subjects. Another survey proposed values of the LA strain below 10% as a prognostic factor for AF recurrence after ablation. [31] In this study, the mean value of the LASr in cases with a history of AF ablation (6 patients) was 25.5±3.2%.

The associations between the LA strain and prothrombotic state and stasis in the LAA have been analyzed in multiple studies. Moderate positive correlations between the LAAV and the peak positive strain rate have been demonstrated. The peak negative strain rate and the time-to-peak strain were reported as independent predictors of LAA thrombosis or sludge by Providência et al. [32] In another study, lower LASr values were observed in patients with lower LAA velocities (<25 cm/s) and subjects with LAA thrombosis. [14] Cameli et al [33] proposed a cutoff value of the global LASr below 8.1% as a predictor for a reduced LAAV and LAA thrombosis. The authors reported a mean LASr of 7.9±3.2% in patients with LAAV values below 25 cm/s and a mean LASr of 28.5±6.1% in patients with LAAV values greater than 25 cm/s. In this study, the LASr, the LAScd, and the mean strain rate, as well as the regional strain values, in both orthogonal apical views, were significantly lower in patients with moderate-to-severe SEC and LAA thrombosis.

CONCLUSIONS

This survey was a well-defined quality-controlled investigation in an academic tertiary referral center. The present study indicates that among patients with a history of AF, who were candidates for AF ablation, patients who remained in AF rhythm had higher LVEDVI, LA diameter, and LAVI and remarkably lower LAA velocity and LVEF as well as LA strain values than patients in sinus rhythm. Furthermore, a higher LA diameter, a higher LAVI, a trend toward a lower LVEF, a significantly lower LAAV, and lower segmental and global speckle-tracking parameters were observed in patients with moderate-to-severe SEC or LAA thrombosis, all in AF rhythm at presentation. The best correlation between the LAA SEC and the LAAV was found for the LASr in the 4-chamber view. LA dyssynchrony had no correlation with the LAA SEC or LAA thrombosis.

Regarding the limitations of the survey, LA deformation imaging is difficult to perform due to the far-field structure in TTE, with thin walls and multiple entry sites of the pulmonary veins and the LAA. To the best of our knowledge, we are the first to use the TOMTEC software for LA speckle-tracking analysis. Hence, comparison with the values obtained via other vendors has an inherent error.

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