

The Correlation between Left Atrial Deformation Indices and the CHA₂DS₂ - VASc Risk Score in Patients with Atrial Fibrillation

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Abstract

Objectives: To assess the relation between left atrial systolic strain and CHA₂DS₂ -VASc score in patients with non valvular atrial fibrillation and to assess whether it can be used in guiding the decision for oral anticoagulation.

Methods: The study included 100 patients with non- valvular persistent AF (group I) compared to 100 individuals with sinus rhythm of matching age and gender (group II). Standard two-dimensional echocardiography, PW Doppler and TDI derived velocity and strains were used to assess LA function then its correlation with CHA₂DS₂-VASc score in group I was evaluated.

Results: The prevalence of DM (P<0.001), HTN (P=0.001), prior stroke (P<0.001), heart failure (P < 0.001) and peripheral vascular disease (P < 0.001) was increased in patients in group I. Group I showed significant increase in LA diameters (anterio-posterior, transverse and longitudinal) P < 0.001, LA volumes (maximal and minimal P < 0.001 and mitral E/e" ratio P < 0.05). The correlation between LA emptying fraction and CHA₂DS₂ - VASc score was negative and significant (P < 0.05). Systolic LA strain was significantly reduced in patients with AF (P < 0.001) and it was negatively correlated to CHA₂DS₂ - VASc score but without statistical significance. There was no significant difference of LA systolic strain between the CHA₂DS₂ - VASc score of < 2 points and ≥ 2 points (P = 0.52). Systolic LA strain ≤ 17.44 was shown to have the best diagnostic accuracy (sensitivity = 42.11 %; specificity = 62.07%) in predicting CHA₂DS₂ - VASc ≥ 2.

Conclusion: LA systolic strain is significantly reduced in AF patients and negatively correlated to CHA₂DS₂-VASc score and no significant difference between LA systolic strain in patients with CHA₂DS₂ - VASc score of < 2 points and ≥ 2 points so LA strain may be a tool that helps in guiding the decision for oral anticoagulation.

Keywords: Atrial fibrillation; CHA₂DS₂ - VASc score; LA systolic strain

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia in the general population; its prevalence increases with age and is generally associated with increased mortality [1]. AF is associated with a five-fold risk of stroke and a three-fold incidence of congestive heart failure, and higher mortality. Hospitalization of patients with AF is also very common [2]. Notably, the risk for stroke is high irrespective of whether AF is paroxysmal, persistent, or permanent [3].

LA diameter enlargement carries a higher risk for CV death, especially in females. LA diameter was an independent predictor of CV death in female AF patients [4].

The CHADS₂ score does not include some common stroke risk factors. To complement the CHADS₂ score, by the inclusion of additional 'stroke risk modifier' risk factors, the CHA₂DS₂ -VASc score has been proposed [5]. The CHA₂DS₂ - VASc score has been used in the European Society of Cardiology guidelines for the management of AF [6]. The analysis of left atrial (LA) strain is a new tool that can be used to evaluate LA function [7].

The aim of the present study was to assess the relation between left atrial (LA) deformation using tissue Doppler image velocity and strain and CHA₂DS₂ -VASc score.

Patients and Methods

It was a single center, case control study that was conducted at cardiology department at "Benha University hospital" from March 2015 to January 2016. A total of 142 patients with atrial fibrillation were evaluated. Thirty-seven patients with valvular and coronary artery disease were excluded from the study. Also, five patients were excluded due to poor echogenicity.

The final study population comprised 100 patients with non valvular persistent AF (group I) who were compared with 100 control individuals presented to the outpatient clinic with sinus rhythm (group II) of matching age and gender.

Consent from the patients and the approval from the ethical committee was obtained.

Patients with primary valvular heart disease, mitral annular calcification, primary myocardial diseases, coronary artery disease, pericardial diseases, congenital heart diseases, a resting heart rate greater than 100 beats/min and any arrhythmia other than AF, poorly

echogenic patients, and patients refusing to participate in this study were excluded.

The following data were collected

Age, sex and the presence or absence of comorbid conditions as diabetes, hypertension, heart failure, a history of stroke and vascular diseases, including coronary artery disease, heart attack (myocardial infarction), peripheral arterial disease were taken into account to risk stratify the participants according to CHA₂DS₂ - VASc score.

Full clinical examination including heart rate & rhythm, systolic & diastolic blood pressure and chest & heart auscultation.

Electrocardiography: 12 lead resting surfaces ECG was done for each patient to confirm the presence of AF.

Echocardiography: Two-dimensional echocardiography and Doppler examination were performed with a GE Vivid 7 Ultrasound Machine (Echo Pac; GE Vingmed, Horten, Norway) with a multi frequency transducer equipped with DTI software and conducted to a single-lead ECG. All examinations were performed in the left lateral position.

LA dimensions: LA diameters were measured at the end-ventricular systole when the LA chamber is at its greatest dimension, in the parasternal long-axis view (antero-posterior diameter) and in the apical 4-chamber view (longitudinal and transverse diameters) [8].

LA volumes: Minimal LA volume (Vmin), measured just before the closure of the mitral valve in end-diastole; and maximal LA volume (Vmax), measured just before the opening of the mitral valve in end-systole [8]. The difference between maximum and minimum LA volume divided by the maximum LA volume is used to detect atrial emptying fraction.

LV volumes and left ventricular ejection fraction: Global LV function was assessed by measuring LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV) and LVEF from the apical 2- & 4-chamber views, using modified Simpson's method [9].

Pulsed Doppler trans-mitral flow: Mitral inflow patterns by pulsed wave Doppler examination demonstrate passive ventricular filling in early diastole (E wave) and late active filling phase during atrial contraction (A wave). The sample volume is placed at the tips of the mitral leaflets in the apical four-chamber view.

Doppler tissue imaging: Pulsed wave Doppler tissue imaging (DTI) is performed in the apical views to acquire mitral annular velocities. Measurements included the systolic (S), early diastolic (E'), and late diastolic (A') velocities [10]. The sample volume is placed on the mitral annulus in the apical four- and two-chamber views.

Color coded tissue doppler imaging: To detect the systolic and early diastolic LA myocardial velocities.

Strain doppler method: Real-time 2D color Doppler myocardial imaging data are recorded from the LA, using standard apical views at a high frame rate (>180 fps). The data are stored in digital format and analyzed offline by dedicated software that allows calculating local peak systolic strain [11].

Statistical analysis: The collected data were summarized in terms of mean ± standard deviation (SD) and range for quantitative data and frequency and percentage for qualitative data. Comparisons between the study groups were carried out using the Chi-square test (χ^2) and Fisher's Exact Test (FET) to compare proportions as appropriate.

The Student t-test (t) was used to detect mean difference between AF patients and controls regarding the normally distributed data. While the Mann Whitney test (z) was used to compare two non-normally distributed data. Pearson correlation coefficient (r) and Spearman correlation coefficient (rho; ρ) were used to test for the correlation between CHA₂DS₂ - VASc scores and normally and non-normally distributed echo parameters respectively. The receiver-operator characteristic (ROC) curve was used to test diagnostic value of various echocardiographic parameters models in predicting CHA₂DS₂ - VASc score equal to or more than 2. The best cutoff point and the corresponding sensitivity and specificity and area under the curve (AUC) were estimated. Stepwise multivariate regression analysis of LA strain conditioned on potential risk factors and echo parameters were carried to detect the most important predictors for LA strain in AF patients. After the calculation of each of the test statistics, the corresponding distribution tables were consulted to get the "P" (probability value). Statistical significance was accepted at P value < 0.05. A P value < 0.001 was considered highly significant while a P value > 0.05 was considered non-significant. The statistical analysis was conducted using STATA version 11 (STATA corporation, College Station, Texas).

Results

Both groups were of comparable age and gender, group I (46 males and 54 females with a mean age of 62 ± 9.26 years) and group II (53 males and 47 females with a mean age of 60.3 ± 7.88 years). DM (55% vs. 23%, p value < 0.001) and HTN (54% vs. 31%, p value = 0.001) were more prevalent in group I. Past history of stroke (55% vs. 25%, p value < 0.001), heart failure (36% vs. 0%, p value < 0.001) and peripheral vascular disease (43% vs. 1%, p value < 0.001) were significantly increased in group I (Table 1).

Variable	AF patients (n = 100)	Control group (n = 100)	P value
Age (Mean ± SD)	62 ± 9.26	60.3 ± 7.88	0.16
Gender			
Male	46 (46%)	53 (53%)	0.32
Female	54 (54%)	47 (47%)	
Cardiac risk factors:			
Diabetes mellitus	55 (55%)	23 (23%)	< 0.001
Hypertension	54 (54%)	31 (31%)	0.001
Past history			
Stroke	55 (55%)	23 (23%)	< 0.001
HF	36 (36%)	0 (0%)	< 0.001
PVD	43 (43%)	1 (1%)	< 0.001
Patients' clinical data:			
Heart rate	79.35 ± 9.5 bpm	71.94 ± 8.93 bpm	< 0.001
Systolic pressure	blood 117.8 ± 12.5 mm Hg	117.25 ± 10.4 mm Hg	0.73
Diastolic pressure	blood 73.1 ± 8.49 mm Hg	75.25 ± 8.74 mm Hg	0.08

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Diabetes mellitus	55 (55%)	23 (23%)	< 0.001
Hypertension	54 (54%)	31 (31%)	0.001
Past history			
Stroke	55 (55%)	23 (23%)	< 0.001
HF	36 (36%)	0 (0%)	< 0.001
PVD	43 (43%)	1 (1%)	< 0.001
Patients' clinical data			
Heart rate	79.35 ± 9.5 bpm	71.94 ± 8.93 bpm	< 0.001
Systolic blood pressure	117.8 ± 12.5 mm Hg	117.25 ± 10.4 mm Hg	0.73
Diastolic blood pressure	73.1 ± 8.49 mm Hg	75.25 ± 8.74 mm Hg	0.08

Table 1: Demographic & clinical data of the studied groups.

Conventional echocardiographic parameters

LA diameters (antero-posterior, transverse and longitudinal) were significantly increased in group I (3.84 ± 0.31 vs. 3.27 ± 0.35 cm, P < 0.001; 3.7 ± 0.52 vs. 3.54 ± 0.43 cm, p < 0.05 and 5.32 ± 0.73 vs. 4.8 ± 0.53 cm, p < 0.001, respectively). Also, the LA volumes (maximal and minimal) were significantly increased in group I (75.47 ± 21.88 vs. 50.77 ± 11.75 ml and 50.62 ± 17.92 vs. 29.06 ± 9.57 ml; respectively, P < 0.001). LA emptying fraction was significantly reduced in group I (33.12 ± 7.66 vs. 42.99 ± 12.39%, P < 0.001) (Table 2).

Left ventricular end diastolic volume (LVEDV) was significantly reduced in group I (60.53 ± 11.12 vs. 66.09 ± 14.46 ml, p < 0.05). Left ventricular end systolic volume (LVESV) was significantly increased in group I (27.95 ± 7.43 vs. 25.91 ± 6.86 ml, p < 0.05). Left ventricular ejection fraction (LVEF) was significantly reduced in group I (54.92 ± 4.23 vs. 63.19 ± 3.96%, p < 0.001) (Table 2).

Doppler tissue imaging

In group I, systolic mitral annular velocity (s) was significantly increased (0.15 ± 0.1 vs. 0.08 ± 0.03 m/s, p < 0.001). Also, the mitral

E/e' ratio was significantly increased (7.24 ± 5.03 vs 5.16 ± 2.11, p < 0.05). However there was no significant statistical difference between the 2 groups regarding peak E (0.75 ± 0.18 vs. 0.75 ± 0.14 m/s, p > 0.05) and early diastolic mitral annular velocity (E') (0.13 ± 0.06 vs. 0.14 ± 0.05 m/s, p > 0.05).

Systolic LA myocardial velocity (s) was significantly increased in group I (5.39 ± 0.8 vs. 5.06 ± 1.07 cm/s, p < 0.05). However there was no significant statistical difference between the 2 groups regarding early diastolic myocardial velocity (e) (-6.7 ± 0.84 vs. -6.49 ± 1.6 cm /s, p > 0.05).

Systolic LA strain was significantly reduced in group I (15.73 ± 3.0 vs.17.48 ± 1.46%, p < 0.001) (Table 2 and Figure 1).

Variable	AF patients (n = 100)	Control group (n = 100)	P value
Echocardiography:			
LA antero-posterior diameter	3.84 ± 0.31 cm	3.27 ± 0.35 cm	< 0.001
LA longitudinal diameter	5.32 ± 0.73 cm	4.8 ± 0.53 cm	< 0.001
LA transverse diameter	3.7 ± 0.52 cm	3.54 ± 0.43 cm	0.02
LA maximal volume	75.47 ± 21.88 ml	50.77 ± 11.75 ml	< 0.001
LA minimal volume	50.62 ± 17.92 ml	29.06 ± 9.57 ml	< 0.001
LA emptying fraction	33.12 ± 7.66%	42.99 ± 12.39%	< 0.001
LVESV	27.95 ± 7.43 ml	25.91 ± 6.86 ml	0.04
LVEDV	60.53 ± 11.12 ml	66.09 ± 14.46 ml	< 0.003
LV EF	54.92 ± 4.23%	63.19 ± 3.96%	< 0.001
Peak E	0.75 ± 0.18 m/s	0.75 ± 0.14 m/s	0.76
TDI:			
S	0.15 ± 0.1 m/s	0.08 ± 0.03 m/s	< 0.001
E'	0.13 ± 0.06	0.14 ± 0.05 m/s	0.22
E/e' ratio	7.24 ± 5.03	5.16 ± 2.11	0.03
Systolic LA myocardial velocity	5.39 ± 0.8 cm/s	5.06 ± 1.07 cm/s	0.01
Early diastolic myocardial velocity	-6.7 ± 0.84 cm/s	-6.49 ± 1.6 cm/s	0.23
Systolic LA strain	15.73 ± 3.0%	17.48 ± 1.46%	< 0.001

Table 2: Echocardiographic parameters of the studied groups.

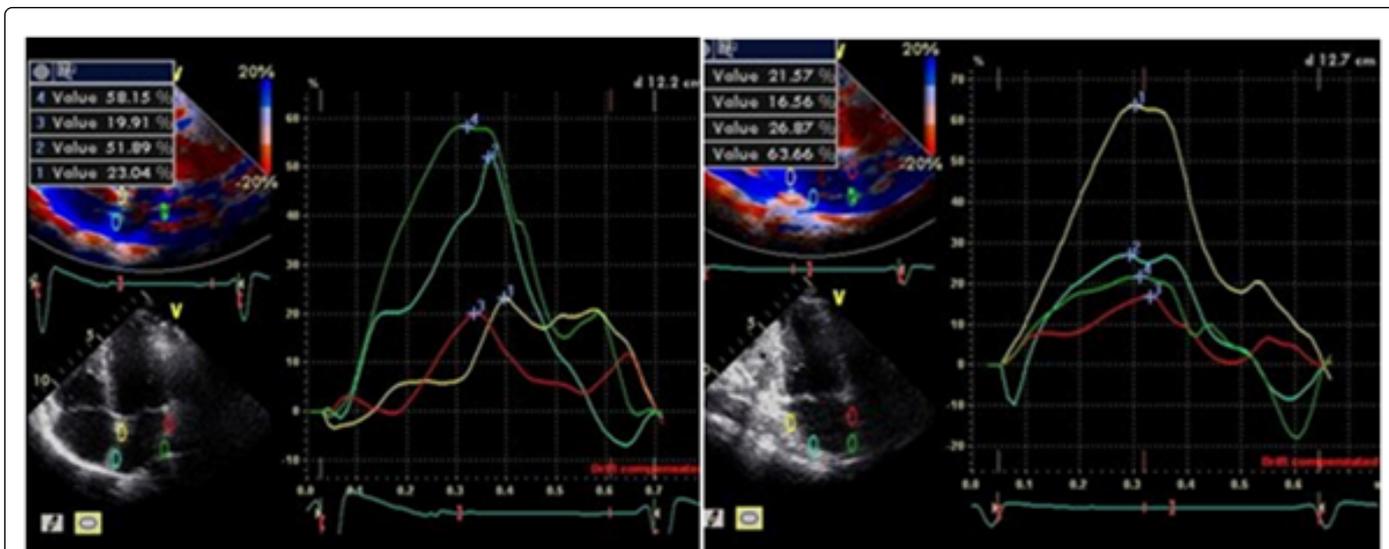


Figure 1: The LA systolic strain in the apical four- and two-chamber views.

Systolic LA strain, systolic (S) and early diastolic (E') mitral annular velocities, systolic LA myocardial velocity (s) and left ventricular EF were negatively correlated with the CHA₂DS₂-VASC score but without statistical significance ($P > 0.05$). The correlation between LA emptying fraction and CHA₂DS₂ - VASC score was significant and negative ($p < 0.05$) (Table 3).

The correlation between the CHA₂DS₂ - VASC score and LA diameters, LA volumes, Peak E, mitral E/e" ratio and early diastolic myocardial velocity (e) in patients with AF was positive, but it did not reach statistical significance ($P > 0.05$) (Table 3).

Variable (No = 100)	Correlation coefficient	P
LA antero-posterior diameter	$r = 0.03$	0.78
LA longitudinal diameter	$\rho = 0.01$	0.88
LA transverse diameter	$r = 0.09$	0.37
LA maximal volume	$\rho = 0.04$	0.68
LA minimal volume	$\rho = 0.12$	0.23
LA emptying fraction	$\rho = -0.24$	0.01

Peak E	$r = 0.10$	0.32
TDI S'	$\rho = (-) 0.14$	0.15
TDI E'	$r = (-) 0.15$	0.14
E/e'	$\rho = 0.14$	0.16
LA systolic strain (%)	$r = (-) 0.06$	0.54
Systolic LA myocardial velocity	$r = (-) 0.06$	0.56
Early diastolic LA myocardial velocity	$\rho = 0.15$	0.12
LVEF (%)	$r = -0.03$	0.74

Table 3: Correlation between CHA₂DS₂ - VASC score and echo parameters in AF patients.

The value of systolic LA strain ≤ 17.44 was shown to have the best diagnostic accuracy (sensitivity = 42.11%; specificity = 62.07%) in predicting the presence of CHA₂DS₂ - VASC ≥ 2 , with an AUC of 0.5062 (95% CI "0.43 to 0.58") (Figure 2).

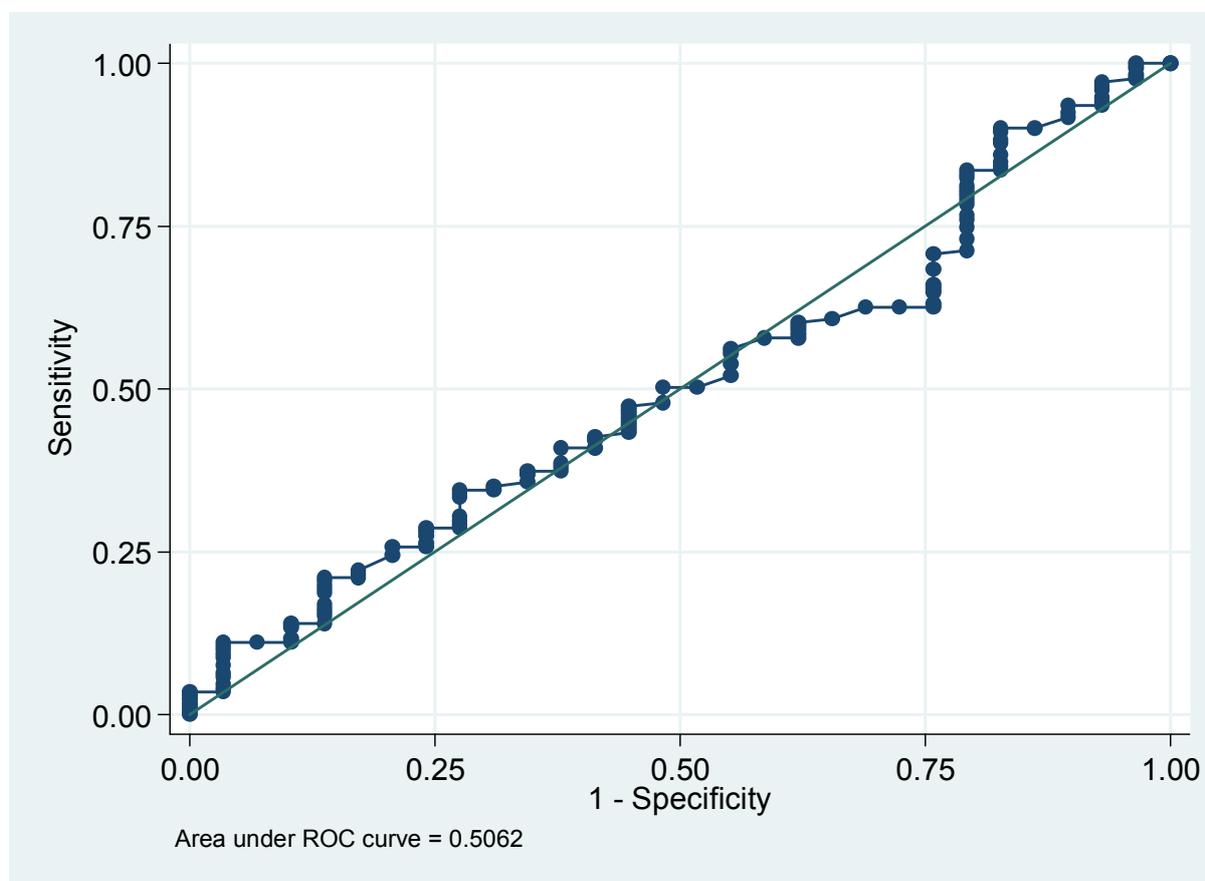


Figure 2: Roc curve of LA systolic strain.

Regarding each individual component of the CHA₂DS₂-VASc score, there was no significant statistical difference in LA systolic strain (p value > 0.05). In addition, the relationship between the age and LA systolic strain in patients with AF was evaluated. There was no significant difference in LA systolic strain among the different age groups (15.86 ± 2.91, 16.05 ± 3.16 and 13.99 ± 2.78 in patients < 65, 65-74 and ≥ 75 years old, respectively; p value = 0.15) (Table 4).

Variable	LA systolic strain		P value	
	No.	Mean ± SD		
Age (years)	< 65	60	15.86 ± 2.91	0.15
	65 - 74	30	16.05 ± 3.16	
	≥ 75	10	13.99 ± 2.78	
Gender	Males	46	15.92 ± 3.21	0.56
	Females	54	15.57 ± 2.84	
HF	Yes	36	15.75 ± 3.08	0.96
	No	64	15.72 ± 2.98	
HTN	Yes	54	15.5 ± 3.17	0.4
	No	46	16 ± 2.81	

DM	Yes	55	15.76 ± 2.61	0.9
	No	45	15.69 ± 3.46	
Stroke	Yes	55	15.89 ± 3.05	0.57
	No	45	15.54 ± 2.97	
PVD	Yes	43	15.67 ± 3.15	0.87
	No	57	15.77 ± 2.92	

Table 4: Relation of LA systolic strain and individual parameters of CHA₂DS₂-VASc score.

On categorizing AF patients based on the CHA₂DS₂-VASc score, no significant difference of LA systolic strain between the CHA₂DS₂-VASc score of < 2 points and ≥ 2 points could be shown (16.19 ± 3.1 vs. 15.65 ± 3, p = 0.52) (Table 5).

Discussion

The aim of the present study was to assess left atrial (LA) function using tissue Doppler and to study its correlation with the CHA₂DS₂-VASc score.

In the current study, DM and HTN were more prevalent in patients with AF, a finding consistent with previous reports by Abed Elaziz et al. [12]. In addition, past history of stroke, heart failure and peripheral vascular disease was significantly increased in patients with AF which was similar to those reported by Almendro-Delia et al. [13].

In the current study, regarding each individual component of the CHA₂DS₂-VASc scores, there was no significant statistical difference in LA systolic strain (p value > 0.05). In addition, the relationship between the age and LA systolic strain in patients with AF was evaluated. There was no significant difference in LA systolic strain among the different age groups (15.86 ± 2.91, 16.05 ± 3.16 and 13.99 ± 2.78 in patients < 65, 65 - 74 and ≥ 75 years old, respectively; p value = 0.15).

In the present study, patients with AF were more likely to have higher LA diameters (anteroposterior, longitudinal, transverse) and LA volumes (maximal and minimal). These finding are in agreement with Saha et al. [14] who reported that LA volumes (maximal and minimal) were significantly increased in patients with AF than those with sinus rhythm (p < 0.001). Similarly, Habibi et al. [15] found that LA diameters and volumes were significantly increased in patients with persistent AF.

CHA ₂ DS ₂ - VASc score	Systolic LA strain		P value
	No.	Mean ± SD	
< 2	15	16.19 ± 3.10	0.52
≥ 2	85	15.65 ± 3.0	

Table 5: LA systolic strain in patients with CHA₂DS₂-VASc score < 2 and ≥ 2.

LA remodeling occurs because of fibrotic changes in the atrial myocardium and is a hallmark of AF. Magnetic resonance imaging and electroanatomic mapping studies of the left atrium have shown presence of fibrosis and loss of electrical activity as an important influence in fibrillatory dynamics, including both the location and variability of wave-front breakthroughs [16].

In the current study, LA emptying fraction was significantly reduced in patients with AF and this was similar to Saha et al. [14]. Also, LVEF was significantly reduced in AF patients who were similar to Abed Elaziz et al. [12]. The impairment of LV systolic function in AF patients can be explained by tachycardia-induced heart failure as demonstrated by Umana et al. [17]; they found that 50% of the patients with AF and LV dysfunction have some degree of tachycardia-induced heart failure.

In the current study, systolic left atrial strain was significantly reduced in patients with AF than those with sinus rhythm (15.73% ± 3.0 vs. 17.84% ± 1.46, p < 0.001).

This was in agreement with Shaikh et al. [18] who found that systolic LA strain was significantly reduced in patients with AF compared with those of sinus rhythm.

Assessment of LA strain may add incremental information to that provided by LA volume assessment. Although LA volume reflects cumulative changes in LA remodeling occurring over time [19], the changes in LA strain reflect dynamic changes that may precede volumetric changes.

In the current study, Patients with AF had higher mitral E/e' ratio compared with those of sinus rhythm, a finding similar to Acar et al.

[1] who studied the prevalence and predictors of atrial fibrillation in hemodialysis patients.

In the current study, systolic LA strain, systolic (S) and early diastolic (E') mitral annular velocities, systolic LA myocardial velocity (s) and left ventricular EF were negatively correlated with the CHA₂DS₂-VASc score but without statistical significance. The correlation between LA emptying fraction and CHA₂DS₂-VASc score was significant and negative.

The correlation between the CHA₂DS₂-VASc score and LA diameters, LA volumes, Peak E, mitral E/e' ratio and early diastolic myocardial velocity (e) in patients with AF was positive, but it did not reach statistical significance.

These results was similar to Abed Elaziz et al. [12] who found that the correlation between the CHA₂DS₂-VASc score and the peak LA strain was negative correlation, but it did not reach statistical significance.

Also, Islas et al. [20] found that LA strain was correlated significantly and independently with CHA₂DS₂-VASc score. However, Kurosawa et al., [21] who studied the relationship between left atrial strain and CHA₂DS₂-VASc score compared to left atrial appendage emptying flow velocity found that the components of the score were not significantly correlated with LA strain except for age and CHF which were independently correlated with LA strain.

Current risk stratification scores as the CHADS₂ and the CHA₂DS₂-VASc scores are based on clinical risk factors and sub optimally weight the risk/benefit of anticoagulation [22]. These risk factors did not asses the LA contractility.

In the current study, the value of systolic LA strain ≤ 17.44 was shown to have the best diagnostic accuracy (sensitivity = 42.11%; specificity = 62.07%) in predicting the presence of CHA₂DS₂ - VASc ≥ 2. On categorizing AF patients based on the CHA₂DS₂ - VASc score, no significant difference of LA systolic strain between the CHA₂DS₂-VASc score of < 2 group and ≥ 2 group could be shown (16.19 ± 3.1 vs. 15.65 ± 3, p = 0.52).

Similarly, Azemi et al. [23] retrospectively studied patients with AF, stroke or transient ischemic attack, and CHADS₂ scores of ≤ 1 before their events from a large single-center stroke registry and compared it with age- and gender-matched controls regarding echocardiographic parameters including chamber volumes, the LV mass, the LA peak negative and positive strain, and the strain rate, and they reported that the peak positive LA strain (14 ± 11 vs. 25 ± 12%, P < 0.001) was significantly reduced in patients compared with controls. Even if the CHADS₂ score was 0, the LA mean strain was reduced as demonstrated by Li et al. [24], who found that the LA mean strain was 18.33 ± 8.57 in the patient group of CHADS₂ score 0.

Conclusion

LA systolic strain was significantly reduced in AF patients and negatively correlated to CHA₂DS₂-VASc score and there was no significant difference between LA systolic strain in patients with CHA₂DS₂-VASc score of < 2 points and ≥ 2 points. So LA strain may be a tool that helps in guiding the decision for oral anticoagulation.

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