

## ORIGINAL ARTICLE

### Measurement of Left Atrial Function by Speckle Tracking Echocardiography in Atrial Fibrillation.

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#### ABSTRACT

**Background:** Echocardiography can be used in estimation of thromboembolic risk in AF patients. There is direct relation between left atrial stasis and global LA strain which is superior to LA parameters of thromboembolic risk stratification of AF patients. The aim of this work is to demonstrate the importance of global LA Strain as predictor of stroke risk in patients with AF after PCI.

**Methods:** This work included 63 consecutive CAD patients who were admitted for elective PCI (42 with permanent AF as case group and 21 with sinus rhythm as control group) in Zagazig University Hospital and NHI. All patients were evaluated by history, clinical examination, echo-doppler study and 2D-speckle tracking echocardiography (2D STE). Patients with permanent AF only were evaluated by CHA<sub>2</sub>DS<sub>2</sub>-VASc Risk Score calculation, INR and TEE.

**Results:** The results showed that the global LA strain has high statistically significant lower value in case group than in control group ( $16.01 \pm 7.43$  vs.  $33.25 \pm 11.21$ ,  $P < 0.001$ ). 9 patients had abnormalities on TEE. The global LA strain has high statistically significant lower value in patients with high-risk features of stroke than patients without these features ( $6.8 \pm 1.1$  vs.  $18.2 \pm 6.5$ ,  $P < 0.001$ ). Areas under the ROC curve for identifying patients with high-risk features of stroke for global LA strain was 0.978. Cutoff value was  $\leq 7.5$ .

**Conclusions:** The addition of global LA strain as a marker of thromboembolic risk to current clinical classifications (e.g., CHA<sub>2</sub>DS<sub>2</sub>-VASc scores) will increase their accuracy as a guideline for anticoagulation by identification of patients with higher thromboembolic risk.

**Keywords:** Speckle Tracking Echocardiography, Percutaneous Coronary Intervention, Atrial Fibrillation, Left Atrial Function.



#### INTRODUCTION

AF is commonest arrhythmia seen in clinical practice. The risk of thromboembolic events in AF patients is affected by several risk factors. The CHA<sub>2</sub>DS<sub>2</sub>-VASc clinical risk score is recommended for assessment of thromboembolic risk in patients with AF in the new European Society of Cardiology guidelines for AF management. [1]

AF patients after PCI represent a risky population with a bad prognosis owing to several risk factors as age and presence of thromboembolic risk factors, also the high incidence of acute coronary syndromes in patients undergoing PCI. [2]

A management problem arises when patients with AF undergoing PCI are indicated for long-term anticoagulation with warfarin as thromboprophylaxis. [3]

Echocardiography can be used in estimation of thromboembolic risk in AF patients. [4]

The echocardiographic findings associated with high thromboembolic risk are large LA dimension, low LAAeV, and proof of thrombi or SEC during TEE. [5,6]

New technique to assess LA function from routine 2D echocardiographic images is known as 2D STE. [7]

Global PALS measured by 2D STE "is a strong and independent predictor of cardiovascular events and

appears to be superior to conventional parameters of LA analysis" [8]

Impaired LA function assessed by STE was associated with a higher risk of LA thromboembolism. These data suggest a possible application of global PALS measured by 2D STE in the context of risk stratification of AF. [9]

The addition of global LA strain as a thromboembolic risk factor to current clinical classifications (e.g., CHA<sub>2</sub>DS<sub>2</sub>-VASc scores) might increase their accuracy as a guideline for anticoagulation and especially in patients with low risk to improve decision making. [10]

Assessment of LA dysfunction by STE as LA stasis risk-prediction tool, in patients with AF after PCI was not studied yet. We aimed to study function of LA by 2D STE in a cohort of AF patients after PCI.

### METHODS

The study was accomplished prospectively in the period from July 2016 until June 2018 on 63 consecutive CAD patients after elective PCI (42 with permanent AF as case group and 21 with sinus rhythm as control group) in Zagazig University Hospital and NHI.

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients with valvular heart disease (> grade II), primary myocardial and pericardial diseases and Poor image quality were excluded from the study. All patients were evaluated by history, clinical examination, echo-doppler study, and 2D STE. Patients with permanent AF only were evaluated by CHA<sub>2</sub>DS<sub>2</sub>-VASc Risk Score calculation, INR and TEE to identify echocardiographic parameters of thromboembolic risk.

#### *Standard transthoracic echocardiography*

Complete standard TTE study was done using Philips EPIC 7 ultrasound machine (Q lab, 10.8; Andover, MA, USA) with a multi frequency transducer and conducted to 3 lead ECG. Standard echocardiographic views, including apical 4-, 3 and 2-chamber views and parasternal long and short axis with the patient in position of left lateral decubitus. Dimensions were measured as recommended by the American Society of Echocardiography. [11]

"Linear internal measurements of LV end diastolic diameter (LVEDD) and LV end systolic diameter (LVESD) were acquired in parasternal long-axis view perpendicular to the LV long axis, and measured at the level of the mitral valve leaflet tips. The LVEF was measured using commercially

available software program that applied the modified Simpson 's method on 4- and 2-chamber views. LA volume measured by biplane area-length method as the LA endocardial borders had been traced in both apical 4- and 2-chamber views to get the areas and LA length (L) was defined as the shorter of the two long axes measured in the apical two- and four-chamber views. Then LA volume was indexed by BSA to get LAVI. The maximal LA volume during LV systole (LAVs) and the minimal LV volume during LV diastole (LAVd) were obtained. LATEF was calculated as  $[(LAVs - LAVd)/LAVs] \times 100\%$  as total LA function. Measurements were repeated three times and the average was used" [11]

"Assessment of Mitral E velocity at Apical four-chamber with color flow imaging for optimal alignment of PW Doppler with blood flow between mitral leaflet tips with blood flow. At Apical four-chamber view: PW Doppler sample volume (usually 5–10 mm axial size) at lateral and septal basal regions so average early e' diastolic velocity was computed. Mitral E/e' ratio was also calculated" [11]

#### *Speckle tracking echocardiography*

Global LA strain was computed by 2D STE as shown in [Fig. 1]. ECG guided "apical 4- and 2-chamber view images were obtained using a conventional 2D grey scale echocardiography. The 2D strain was based on the frame-by-frame tracking of small rectangular image blocks with a stable speckle pattern. Three consecutive heart cycles were recorded and averaged for all patients. A minimum frame rate of 60 frames per second was required for the reliable operation of this program. Recordings were processed using acoustic-tracking software" [12] (QLAB 10.8, Andover, MA, USA) allowing offline, semi-automated analysis of speckle-based strain.

For 2D STE analysis, three points drew after contraction along the LA border endocardium of the Apical 4- and 2-chamber views. "An epicardial surface tracing were automatically generated by the system, creating region of interest (ROI) with default width of 15 mm. The tracking algorithm followed the endocardium from this single frame throughout the cardiac cycle. The software divided the ROI into 6 segments (annular, mid, and superior segments along the septal, lateral, anterior, and inferior LA walls using apical four-chamber and two-chamber images). To trace the ROI in the discontinuity of the LA wall corresponding to the pulmonary veins and LAA, the direction of the LA endocardial and epicardial surfaces at the junction with these structures was extrapolated" [12]

The software generated strain curves for each atrial segment. Global LA strain was considered

suboptimal if strain analysis cannot be performed for at least four of the six LA segments in each view. Data from all segments was averaged to calculate global LA strain.

### **Transesophageal Echocardiography**

TEE was used as a tool to identify echocardiographic parameters of thromboembolic risk which include complex aortic plaques and atrial stasis factors (SEC, low LAAeV and LA or LAA thrombus and increase IAS thickness) [13]. All TEEs were done by qualified cardiologists in a standard way, as recommended by the American Society of Echocardiography [14].

"TEE was performed with a 5-MHz transducer. The oropharynx was anaesthetized by use of topical lidocaine spray and viscous lidocaine solution prior to insertion of the probe. Assessment of LA and its appendage was obtained to delineate presence of thrombi and SEC by placing the probe at the level of mid-esophagus. The plane of multiplane probe was adjusted to achieve a short-axis view of the aortic valve (at 30°–60°); to obtain an optimal view of the LAA; the shaft of the scope was rotated anticlockwise in 5 to 10° increments from 0 to 180°. Multiple views of the LAA were then obtained; cine loops were acquired. The imaging plane and gain settings were adjusted for optimal visualization of thrombi and SEC in the LA and LAA" [14]

"For measurement of the blood flow velocities in LAA, the sample of pulsed wave Doppler was placed at the orifice of the LAA and profile of the velocities was recorded over at least five cardiac cycles. A maximum velocity was then calculated by averaging these five cardiac cycles. In order to image complex plaques, the thoracic aorta was carefully visualized by retracting and rotating the probe. The bicaval view was used (transverse mid-esophageal short-axis view at the level of the aortic valve with the transducer plane at 90°) to obtain maximal measurements of the interatrial septum (IAS) in end-diastole, one centimeter superior to the fossa ovalis" [14]

### **Echocardiographic parameters of thromboembolic risk were defined as follow:**

SEC was defined as "a persistent pattern of a slow swirling motion of intracavitary echo density throughout the LA and LAA" [15] imaged with gain settings will be adjusted to distinguish background noise. SEC was "classified into four groups (1+ to 4+, depending on the intensity, location, and presence of the swirling movement)" [15]

A thrombus "was defined as an intracavitary echo dense mass with sharp edges, echogenicity different from adjacent structures, some degree of mobility, and present in more than one plane" [16]

"Low blood flow velocity was defined as peak emptying velocity of less than 25 cm/s on TEE, measured at the orifice of the LAA" [13]

"Complex atheromatous plaque was defined as a mobile, pedunculated or ulcerated plaque, or plaque thickness  $\geq 4$  mm in the thoracic aorta" [17]

### **Statistical analysis:**

All results were collected in a specially designed database, tabulated and statistical analysis was performed using IBM compatible personal computer and by means of statistical software package namely statistical package for social science (SPSS).

*P*-value greater than 0.05 was considered as a nonsignificant result, *P*-value less than 0.05 was considered as a significant result, and *P*-value less than 0.01 was considered as a highly significant result.

## **RESULTS**

There were no statistically significant differences between patients and control subjects as regard demographic and clinical characteristics except for heart rate that was statistically high significant in case group [Table 1]. There was highly statistically significant reduction in case group as regarding LVEF and LATEF, whereas there was highly statistically significant increase in case group as regarding LAVI and E/e' ( $P < 0.05$ ) when compared to control group as shown in [Table 2]. As regard speckle tracking, global LA strain has statistically high significant lower values in case group than in control group ( $16.01 \pm 7.43$  vs.  $33.25 \pm 11.21$ ,  $p < 0.001$ ) as shown in [Table 2]. Also, global LA strain was statistically highly significantly reduced in patients with AF with stroke than those without stroke ( $7.2 \pm 2.8$  vs.  $17.8 \pm 6.5$ ,  $p < 0.001$ ). When values of the global LA strain correlated with the CHA2DS2VASc score, there was statistically significant negative correlation ( $P < 0.05$ ).

9 patients had high risk abnormalities of stroke on TEE; Thrombi were detected in one patient, low LAAeV were seen in 5 patients, SEC in 3 patients, and complex plaques in 1 patient. There were no statistically significant differences between patients with and without abnormalities as regard demographic and clinical characteristics except for incidence of previous episodes of stroke and/or TIA that was higher in patients with abnormalities. There was statistically highly significantly reduction in patients with high-risk features of stroke as regarding LVEF and LATEF, whereas there was highly statistically highly significantly increase in these patients as regarding LAVI and E/e' ( $P < 0.05$ ) when compared to patients without those abnormalities as shown in [Table 3]. As

regard speckle tracking, global LA strain was statistically highly significantly lower in patients in with high-risk features of stroke than patients without ( $18.2 \pm 6.5$  vs.  $6.8 \pm 1.1$ ,  $p < 0.001$ ) as shown in [Table 3]. A strong positive correlation was found between global LA strain and LAAeV [Fig. 2].

In univariate logistic regression analysis; LVEF, LAVI, global LA strain and CHA<sub>2</sub>DS<sub>2</sub>-VASc score were efficient for predicting high risk features of

stroke as shown in [Table 4]. While in multivariate logistic regression analysis only global LA strain was efficient as predictors of high-risk features of stroke as shown in [Table 5]. Areas under the ROC curve for identifying patients with high-risk features of stroke for global LA strain was 0.978. Cutoff value was  $\leq 7.5$ , with sensitivity of 87.5%, specificity of 97.1%, positive predictive value of 87.5%, negative predictive value of 97.1% and diagnostic accuracy of 95.2% as shown in [Fig. 3].

**Table (1):** Comparison between case group and control group regarding the baseline demographic & clinical characteristics.

Baseline clinical characteristics	Case group (N=42)	Control group (N=21)	P-value (Sig.)
Age (years)	$63.9 \pm 4.9$	$63.2 \pm 5.2$	$>0.05$ (NS)
BMI (kg/m <sup>2</sup> )	$29.9 \pm 1.5$	$29.3 \pm 2.1$	$>0.05$ (NS)
BSA (m <sup>2</sup> )	$1.92 \pm 0.13$	$1.91 \pm 0.13$	$>0.05$ (NS)
Male gender	22 (52.4%)	12 (57.1%)	$>0.05$ (NS)
DM	19 (45.2%)	6 (28.6%)	$>0.05$ (NS)
HTN	35 (83.3%)	16 (76.2%)	$>0.05$ (NS)
Smoking	14 (33.3%)	6 (28.6%)	$>0.05$ (NS)
Dyslipidemia	25 (59.5%)	12 (57.1%)	$>0.05$ (NS)
HF	21 (50%)	9 (42.9%)	$>0.05$ (NS)
Stroke/TIA	7 (16.7%)	1 (4.8%)	$>0.05$ (NS)
Vascular disease	21 (50%)	9 (42.9%)	$>0.05$ (NS)
HR (beat/min)	$86.1 \pm 8.0$	$79.5 \pm 8.5$	$<0.05$ (S)
SBP (mmHg)	$137.5 \pm 23.3$	$141.4 \pm 19.6$	$>0.05$ (NS)
DBP (mmHg)	$81.1 \pm 11.6$	$82.9 \pm 12.0$	$>0.05$ (NS)

BMI, Body mass index; BSA, Body surface area; DM, Diabetes mellitus; HTN, Hypertension; HF, Heart failure; TIA, Transient ischemic attack; HR, Heart rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure.  $P < 0.05$  is significant. Sig.: significance.

**Table (2):** Comparison between case group and control group regarding TTE data.

TTE data	Case group (N=42)	Control group (N=21)	P-value (Sig.)
LVEF (%)	$54.0 \pm 6.8$	$63.4 \pm 4.4$	$<0.001$ (HS)
LAVI (mL/m <sup>2</sup> )	$46.0 \pm 7.3$	$34.4 \pm 6.8$	$<0.001$ (HS)
LATEF (%)	$38.5 \pm 9.6$	$57.6 \pm 6.9$	$<0.001$ (HS)
E/e'	$12.8 \pm 2.5$	$9.2 \pm 2.3$	$<0.001$ (HS)
Global LA strain (%)	$16.01 \pm 7.43$	$33.25 \pm 11.21$	$<0.001$ (HS)

LVEF, left ventricular ejection fraction; LAVI, left atrial volume index; LATEF, left atrial total emptying fraction; E/e', the ratio of the early trans mitral flow velocity and the early mitral annular velocity.  $P < 0.05$  is significant. Sig.: significance.

**Table (3):** Comparison between the patients without and those with high-risk features of stroke regarding the TTE data (n=42).

TTE data	Without high stroke risk (N=33)	With high stroke risk (N=9)	P-value (Sig.)
LVEF (%)	$55.1 \pm 6.7$	$49.1 \pm 5.4$	$<0.05$ (S)
LAVI (mL/m <sup>2</sup> )	$43.9 \pm 6.4$	$55.0 \pm 5.2$	$<0.001$ (HS)
LATEF (%)	$41.3 \pm 8.6$	$26.9 \pm 1.5$	$<0.001$ (HS)
E/e'	$11.9 \pm 2.0$	$16.3 \pm 0.7$	$<0.001$ (HS)
Global LA strain (%)	$18.2 \pm 6.5$	$6.8 \pm 1.1$	$<0.001$ (HS)

LVEF, left ventricular ejection fraction; LAVI, left atrial volume index; LATEF, left atrial total emptying fraction; E/e', the ratio of the early trans mitral flow velocity and the early mitral annular velocity.  $P < 0.05$  is significant. Sig.: significance.



**Table (4):** Univariate regression analysis for high-risk stroke features (n=42).

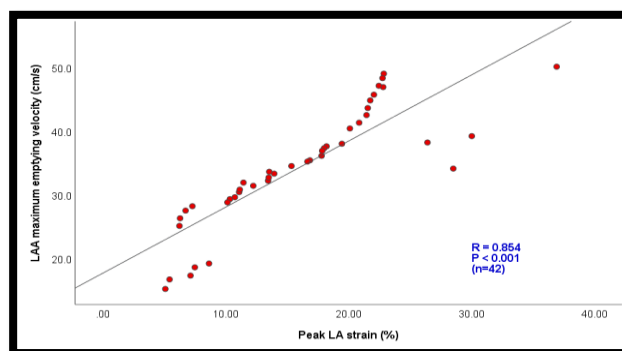
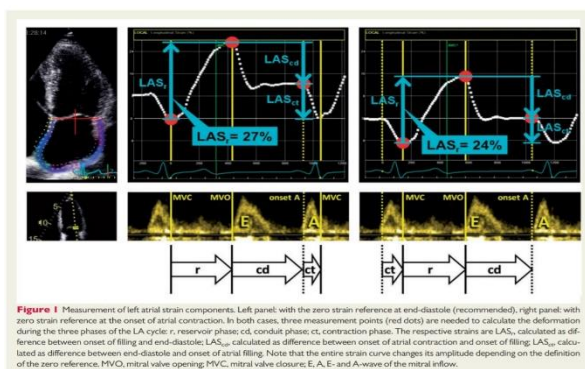
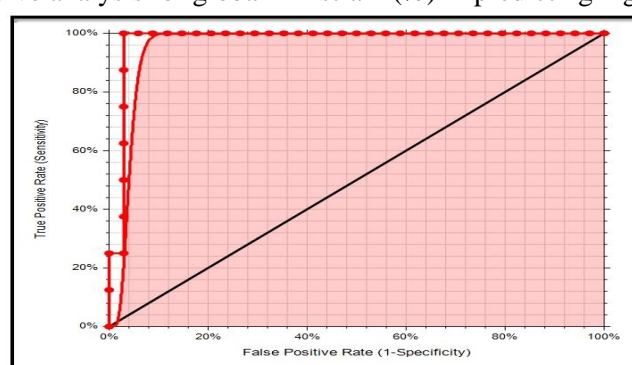
Variable	Unadjusted OR	95% Confidence Interval for OR		P-value (Sig.)
		Lower Bound	Upper Bound	
Global LA strain (%)	0.310	0.120	0.800	<0.05 (S)
IAS thickness (mm)	16.986	1.800	160.257	<0.05 (S)
LAVI (mL/m <sup>2</sup> )	2.281	1.178	4.416	<0.05 (S)
CHA <sub>2</sub> DS <sub>2</sub> -VASc	2.632	1.041	6.656	<0.05 (S)

IAS, inter atrial septum; LAVI, left atrial volume index; OR, odds ratio.  $P < 0.05$  is significant. Sig.: significance.

**Table (5):** Multivariate regression analysis for high-risk stroke features (n=42).

Variable	Adjusted OR	95% Confidence Interval for OR		P-value (Sig.)
		Lower Bound	Upper Bound	
Peak LA strain (%)	0.164	0.025	0.911	<0.05 (S)
IAS thickness (mm)	2.303	0.003	9.483	0.609 (NS)
LAVI (mL/m <sup>2</sup> )	2.552	0.084	2.467	0.535 (NS)
CHA <sub>2</sub> DS <sub>2</sub> -VASc	1.783	0.013	2.619	0.211 (NS)

IAS, inter atrial septum; LAVI, left atrial volume index; OR, odds ratio.  $P < 0.05$  is significant. Sig.: significance

**Figure 1:** Measurement of LA strain components. **Figure 2:** Correlation between LA AeV (cm/s) and global LA strain (%)

**Figure 3:** ROC curve analysis for global LA strain (%) in predicting high risk stroke features


## DISCUSSION

In this study, there were no statistically significant differences between patients and control subjects as regard demographic and clinical characteristics. This is consistent with the findings of numerous studies where the two groups were comparable as

regard demographic and clinical characteristics [18-21].

In this study, there was statistically highly significantly reduction in case group as regarding LVEF and LATEF, whereas there was statistically highly significantly increase in case group as regarding LAVI and E/e' ( $P < 0.05$ ) when compared to control group.

This is consistent with the findings of numerous studies who found that the AF patients exhibited a significantly higher LAVI and E/e' ratio and a smaller LATEF and LVEF compared with the controls [18, 20-25].

"The impairment of LV systolic function in AF patients can be attributed to tachycardia induced HF" as demonstrated by **Umana, E, et al. [26]**. They found that 50% of patients with AF and left ventricular dysfunction have some degree of tachycardia induced HF.

In this study, global LA strain was statistically highly significantly lower in case group than control group. Also, global LA strain was statistically highly significantly reduced in patients with AF with stroke than those without stroke and when values of the global LA strain correlated with the CHA2DS2VASc score, there was a negative significant correlation.

Previous studies had confirmed that global LA strain was reduced in AF patients and there was strong correlation between the global LA strain and stroke [6, 7, 18, 21-23, 25, 27-30].

Other studies had confirmed that there was strong correlation between the global LA strain and the CHA2DS2VASc score [6, 7, 31-34].

On the contrary, **Huaying et al. [19]** reported that the peak atrial longitudinal strain did not show statistically significant difference ( $p > 0.05$ ) between the 2 groups and was not significant predictor of the composite endpoint of death or hospitalization for ischemic stroke. Also, **Ahmed et al. [22]** reported that when values of peak LA strain correlated with CHA2DS2-VASc score, it did not reach statistical significance although it had a negative trend.

The reason for this discrepancy is not clear, but may be attributed to the patient selection criteria as patients with heart failure were included and small number of patients in the studies.

These results suggest that global LA strain may serve as additional risk marker for stroke and can be used to guide decisions for anticoagulation in AF patients.

In this study, 9 patients had high risk abnormalities of stroke on TEE. Thrombi were detected in one patient, low LAAeV were seen in 5 patients, SEC in 3 patients, and complex plaques in 1 patient. There was statistically highly significantly reduction in patients with high-risk features of stroke as regarding LVEF and LATEF, whereas there was statistically highly significantly increase in these patients as regarding LAVI and E/e' ( $P < 0.05$ ) when compared to patients without features. Several studies found similar results as regards echocardiographic parameters [9, 13, 35-36].

On the contrary, another study reported that no differences were found between the two groups as regards standard TTE parameters [4, 10]. This controversy may be explained by small number of patients in these studies compared to our study.

In current study, as regard speckle tracking, global LA strain was statistically highly significantly lower in patients in with high-risk features of stroke than patients without. A strong positive correlation was found between global LA strain and LAAeV.

The association between global LA strain and high-risk features of stroke may be attributed to increased dyssynchrony in LA and lower deformation (compromised contraction and relaxation) may lead to stasis) and subsequently increase severity of SEC and thrombus formation. This is consistent with the findings of numerous studies who found that global PALS was significantly lower in patients with reduced LAAeV and/ or LAAT [4, 6, 9, 10, 35, 36].

These results of previous trials demonstrate the importance of global LA strain as a risk of thromboembolism in AF patients. Finally, compared with number of patients in previous trials of stroke prevention in AF, the small number of patients in our study and infrequent LA thrombi events decreased our ability to analyze many covariates within a single regression model, and that mean our results should be interpreted with caution.

## CONCLUSIONS

A global LA strain obtained by 2D STE may be a reliable marker for LA dysfunction and thrombus formation. Reduction of A global LA strain is associated with increasing stasis risk Score. So, the addition of global LA strain as a marker of thromboembolic risk to current clinical classifications (e.g., CHA<sub>2</sub>DS<sub>2</sub>-VASc scores) might increase their robustness as a guideline for anticoagulation which improve their prognostic value by allowing the identification of patients with higher thromboembolic risk.

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