Left Atrial Dysfunction and Deformation as Predictors of Recurrent Stroke in Patients with Atrial Fibrillation and First Acute Ischemic Stroke

Manar Al-zaky, Abdelsalam Sherif, Mohamed Emad El Deen Negm, Mohamed Abdelhady Mohamed, Mahmoud Abdelaziz

Cardiology Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding Author: Mohamed Emad El Deen Negm

Email: Dr.mohamednegm1988@gmail.com Tel: 00201220702170

Abstract:

Background: Although further research is necessary before adding LA strain to the present risk scheme, it may be a useful marker for stratifying stroke risk. Novel deformation imaging is becoming a widely used method for AF risk categorization at the moment. LA strain is the most widely utilised index for risk stratification among all LA deformation parameters, particularly for the course of AF. There aren't many investigations on the connection between AF-related stroke and LA distortion. Aim: To evaluate is relation between Left atrium deformation and dysfunction in AF patient and recurrent stroke. Materials and methods: This observational case control study was conducted at emergency room (ER), cardiac care units (CCU), ward and Echo cardiograph units of cardiology department, Zagazig university hospitals. This study included 92 patients with acute ischemic stroke. Left atrial function and deformation were assessed. Results: there was statistically significant difference between both subgroups with higher CHADSVASC score in the subgroup who developed recurrent stroke. There was statistically significant difference between both groups regarding all these parameters with better left ventricular and left atrial parameters in the subgroup who did not develop recurrent stroke. Conclusion: In conclusion, Patients with larger LA dimensions and impaired LA function assessed by strain and strain rate are more liable for recurrent stroke than those with normal dimensions and function. LA strain and strain rate outperformed the CHA2DS2-VASc score in predicting ischemic stroke in a broader and greater clinical risk cohort, independent of important AF baseline demographics and conventional echocardiography measures. LA strains could be used as possible risk stratification markers.

Keywords: Stroke, AF, Left Atrial Dysfunction.

Tob Regul Sci. ™ 2023; 9(1): 5830-5849

DOI: doi.org/10.18001 /TRS.9.1. 405

First Acute Ischemic Stroke

Introduction

One of the leading causes of death globally is stroke (**Peñafiel et al., 2021**). Finding the mortality risk variables would make it easier to identify high-risk groups that might profit from careful monitoring and a rigorous treatment plan. Therefore, despite great advancements in the diagnosis and treatment of stroke, subtype discrimination and mortality prediction remain difficult in clinical practise. This has an impact on the therapy of ischemic stroke (*Biteker et al., 2016*).

The most common adult cardiac arrhythmia in the world, atrial fibrillation (AF), is linked to a notably high rate of morbidity and death. An enlarged left atrium (LA), which creates anatomic substrates for repeated wavelet reentry, is a common characteristic of the pathophysiology of central AF (*Chao et al.*,2017).

Given that individuals with atrial fibrillation (AF) are susceptible to dynamic left ventricular (LA) function that is closely associated with LV filling conditions, evaluation of LA kinetics in this population may also incorporate mechanistic information that reflects the level of ventricular dysfunction and hypercoagulation status (*Thomas et al.*, 2017).

Participants with AF generally show worsened active booster pump and considerable deterioration in both reservoir and conduit phases when compared to non-AF participants, according to the phase-by-phase classification of dynamic LA mechanics (*Zhang et al.*, 2008).

A number of techniques have been developed to assess LA mechanics; Two-dimensional tracking of speckles Echocardiography: a trustworthy measurement Although primarily constrained by an irregular heart cycle in individuals with atrial fibrillation (AF), obviating angle dependency or load condition is developing as a novel and valuable method for detecting atrial mechanical dysfunction beyond anatomical information (*Marwick et al.*, 2019) and (*Cameli et al.*, 2016).

Subjects and Methods

This observational case control study was conducted in the period between November 2021 to January 2023 at emergency room (ER), cardiac care units (CCU), ward and Echo cardiograph units of cardiology department, Zagazig university hospitals. This study included 92 patients with acute ischemic stroke. A written consent was obtained from every patient after explanation of the procedure.

Inclusion criteria:

1-First attack of acute ischemic stroke defined as sudden loss of blood circulation to an area of the brain diagnosed radiologically either by MRI/MRA or CT scan, resulting a corresponding

loss of neurological function (Gallo et al., 2019).

2-Patients with atrial fibrillation: ECG documentation is required to establish the diagnosis of AF. A standard 12-lead ECG recording or a single-lead ECG tracing of \geq 30 s showing heart rhythm with no discernible repeating P waves and irregular RR intervals (**Steinberg et al., 2018**)

Exclusion criteria:

- 1- Dilated cardiomyopathy.
- 2- Severe mitral valve lesions.
- 3- Previous ischemic stroke, Non Ischemic stroke and a definite TIA (i.e., they returned entirely to normal within 24 hours)

All patients then were subjected to complete history taking, full clinical examination including: including resting blood pressure measurement, heart rate estimation body weight, height, body mass index and full cardiac exam, electrocardiographic examination: in order to find atrial fibrillation. An ECG trace that displays AF must be documented in rhythm for the diagnosis of AF to be made. For clinical AF EHRA 2020, chamber enlargement, and prior ischemia, a typical 12-lead ECG recording or a single-lead tracing of ≥30 of cardiac beat with no detectable recurring P waves and irregular R-R intervals (where atrioventricular conduction is not impeded) are diagnostic.

Transthoracic Echocardiography:

The SIEMENS ACUSON X300 was used to do echocardiography. A two-dimensional probe (M5S) is used in an echo cardiography equipment that operates at a frequency of two to four megahertz. Tissue Doppler imaging (TDI) is used to probe heart velocities while an ECG is being recorded simultaneously. The patient was examined while breathing quietly and in the decubitus left lateral posture. The left ventricular apical four-chamber view and two-chamber view were used to create 2D dynamic pictures.

The following parameters was calculated left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV) and Using the modified biplane method of Simpson and the following equation, the ejection fraction and fraction shortening was determined: LVEF= (LVEDV-LVESV)/LVEDV. (*Roberto et al.*,2015)

By tracing the motion of the LV wall frame by frame, the LV global longitudinal stresses (GLS) from the LV apical perspectives (4CH and 2CH) were automatically estimated.

Patients who may have myocarditis or CAD may find it very important to measure regional wall motion abnormalities.

Left Atrium Assessment:

LA size was assessed at end systole. The LA dimension was measured using its antero-posterior dimension obtained from the parasternal long axis view and LA volume (Biplane area-Length method) was measured from apical 4 and apical 2 views.

At end systole, the LA endocardial border was manually drawn in both the apical 4-chamber (4CH) and 2-chamber (2CH) views. After automatically creating an epicardial LA shape, which defines a zone of interest with six segments in each apical view, the software performs segmental tracking automatically. Following tracking, each atrial segment's LA strain and first derivation SR curves were produced, and average values from the apical 4CH and 2CH views were computed. (*Liao et al.*, 2020).

Follow up the patients for 6 months for monitoring for primary end Point recurrence of ischemic stroke upon course of follow up.

Statistical Analysis

All information was gathered, recorded, and subjected to statistical analysis utilising IBM SPSS Statistics for Windows, Version 20.0 (SPSS 20.0 for Windows). The mean \pm SD was used to show quantitative data, while absolute frequencies (number) and relative frequencies (%) were used to convey qualitative data. The student's t-test was utilised to compare two groups of regularly distributed data, while the Chi-square test was employed to assess the percentage of categorical variables. In order to define the link between the numerous study variables, Pearson's correlation coefficient was determined. Values close to 1 indicate strong correlation, while values close to 0 indicate weak correlation. The (+) sign denotes direct correlation and the (-) sign denotes inverse correlation. Every test had two sides. It was determined that a p-value of less than 0.05 was statistically significant (S), a p-value of less than 0.001 was highly statistically significant (HS), and a p-value greater than 0.05 was statistically insignificant (NS) (Armonk 2011).

Results

Table (1): Demographic and clinical data of recurrent and non recurrent stroke patients:

	Rec	current st	roke		Togtof	
	(yes) n	=16	(no) n	=76	Test of sig t=	p
	Mean ±SD		Mean	Mean ±SD		
Age (years)	77.88±7.8		64.53±15.47		3.351	0.001
BMI (Kg/m ²)	27.64	27.64±3.95		5±6.11	0.297	0.767
SBP(mmHg)	155.75	155.75±19.35 152.33±15.98		0.750	0.455	
DBP(mmHg)	85.44±7.56		86.14±9.06		-0.291	0.772
HR(beat/minute)	96.25	±7.48	96.25 ±8.99		0.000	1
	N.	%	N.	%	\mathbf{X}^2	
Sex						
Female	10	62.5	40	52.6	0.519	0.331
Male	6 37.5		36	47.4	0.319	0.331
HTN	16 100 54 71		6.087	0.008		
DM	14	87.5	43	56.6	5.36	0.017

BMI: body mass index, HTN: hypertension, Dm: diabetes mellitus, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR:heart rate, SD:standard deviation X2: Chi square coefficient, .P value<0.05 significant, p value>0.05 non-significant.

There were 16 patients who developed recurrent stroke in the follow up periods of them 6 male (37.5%) and 10 females (62.5%) the mean age was 77.88±7.8 years, 16patients (100%) were hypertensive and 14 patients (87.5%) were diabetic and the mean body mass index was 27.64±3.95 kg/M², The mean systolic blood pressure was 155.75±19.35 MMHG and the mean diastolic blood pressure was 85.44±7.56 MMHG the mean heart rate was 96.25±7.48 beat per minute. There were 76 patients who not readmitted to hospital in the follow up periods of them 36 male (47.4%) and 40 females (52.6%) the mean age was 64.53±15.47 years, 54 patients (71%) were hypertensive and 43 patients (56.6%) were diabetic and the mean body mass index was 27.165±6.11 kg/m² The mean systolic blood pressure was 152.33±15.98 MMHG, the mean diastolic blood pressure was 86.14±9.06 MMHG and the mean heart rate was 96.25±8.99 beat per minute. There was statistical significant diffrence between both subgroups regarding age, hypertension and diabetes mellitus (P value <0.05) but there was no statistical significant importance regarding sex ,body mass index, systolic ,diastolic blood pressure and heart rate (P value >0.05) (Table 1).

Table (2): CHADS₂VAS_C diference between two subgroups:

		Recu	2			
	(yes) n	=16	(no)	n =76	χ2	р
CHADS ₂ VAS _C	N.	%	N.	%		
2	0	0	1	1.32	22.81	0.000
3	0	0	26	34.21	22.01	0.000
4	1	6.25	6	7.89		
5	1	6.25	23	30.26		
6	9	56.3	15	19.73		
7	5	31.25	5	6.57		
	(mean± SD)			Test of sig	p	
CHADS ₂ VAS _C	6.125	±0.81	4.520	6±1.35	t=4.552	0.000

It was noticed that there was statistically significant difference between both subgroups with higher CHADSVASC score in the subgroup who developed recurrent stroke with P value<0.05. (Table 2)

Table (3):CHADsVASc as predictor of recurrent stroke:

	В	S.E.	Wald	df	Sig.	Exp(B)		C.I.for (P(B)
					~- g .		Lower	Upper
CHADS VASC score	1.232	.355	12.045	1	.001	3.429	1.710	6.878

By using logistic regression for prediction of adverse outcomes (recurrent stroke) in patients with atrial fibrillation and acute ischemic stroke through the 180 days follow up period it shows that CHADSVASC was statistically best fitted for such prediction with increasing score, probability of recurrent stroke increases (p value<0.05). (table 3)

Table (4): Echo cardiographic parameters of studied groups (recurrent and non recurrent):

	Recu	rrent stroke		
	(yes) n=16	(no) n =76	T	p- value
Left atrium diameter (mm)	42.63±3.6	37.12±3.4	5.77	0.000
LAVI (ml/m2)	47.88±8.94	32.54±7.05	7.54	0.000
LV EF (%)	54.8±3.1	58.9±5.84	-2.71	0.008
LV GLS (%)	-14.55±4.45	-20.63±3.79	5.65	0.000
LASr(%)	18.25±11.7	33.27±10.6	-5.07	0.000
LASRs(s-1)	1.12±0.51	1.91±0.77	-3.93	0.000
LASRe(s-1)	-1.45±0.38	-1.8±0.57	2.45	0.016

LV EF: left ventricular ejection fraction, LVGLS: left ventricular global strain, DD: diastolic dysfunction, LAVI: Left atrium volume index, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate (during Left ventricular systole), LASRe: Left atrium strain rate in early diastole, LASRa: Left atrium strain rate in late diastole.

Among patients with atrial fibrillation who developed recurrent stroke, the mean diameter of the left atrium was 42.63±3.6 mm, the mean left atrium volume index was 47.88±8.94 ml/m2. Regarding left ventricular systolic function the mean ejection fraction (EF) 54.8±3.1,Mean Global longitudinal strain (GLS) -14.55±4.45. Regarding left atrium function the mean left atrial peak strain (reservoir phase)(Sr) 18.25±11.7,Mean left atrium longitudinal systolic strain rate 1.12±0.51,left atrium longitudinal early diastolic strain rate -1.45±0.38 (Table 4).

Among patients with atrial fibrillation who did not develop recurrent stroke, the mean diameter of the left atrium was 37.12 ± 3.4 mm, the mean left atrium volume index was 32.54 ± 7.05 ml/m2. Regarding left ventricular systolic function the mean ejection fraction (EF) 58.9 ± 5.84 ,Mean Global longitudinal strain (GLS) -20.63 ± 3.79 . Regarding left atrium function the mean left atrial peak strain (reservoir phase)(Sr) 33.27 ± 10.6 ,Mean left atrium longitudinal systolic strain rate 1.91 ± 0.77 ,left atrium longitudinal early diastolic strain rate -1.8 ± 0.57 . There was statistically significant difference between both groups regarding all these parameters with better left ventricular and left atrial parameters in the subgroup who did not develop recurrent stroke. (p value <0.05) (table 4).

Table (5): Multivariate logistic regression of ECHO parameters for prediction of recurrent stroke between two subgroups:

	В	S.E.	Wald	df	Sig.	Exp(B)	95% (EXI	
							Lower	Upper
LVGLS (%)	0.123	0.245	0.251	1	0.616	1.131	0.699	1.829
LAVI (ml/m2)	1.214	0.428	8.015	1	.005	3.368	1.453	7.807
LASr(%)	0.813	0.305371	7.086	1	.008	2.254	1.239	4.102
LASRs(s-1)	-12.959	5.223	6.155	1	.013	.000	.000	0.066
LASRe(s-1)	-9.520	4.154	5.252	1	.022	.000	.000	.252

LVGLS: left ventricular global strain, DD: diastolic dysfunction, LAVI: Left atrium volume index, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate (during Left ventricular systole), LASRe: Left atrium strain rate in early diastole, LASRa: Left atrium strain rate in late diastole

By using Multivariate binary logistic regression for prediction of adverse outcomes (recurrent stroke) in patients with atrial fibrillation and acute ischaemic stroke through the 180 days follow up period the Echo parameters (LAVI, Reservoir Strain ,Reservoir Strain rate, Conduit Strain rate)were statistically best fitted for such prediction. (**Table 5**).

Table (6): Multivariate logistic regression of ECHO parameters and CHADSVAS score for prediction of adverse outcomes (recurrent stroke) in both subgroups:

	В	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
					8		Lower	Upper
LV GLS (%)	.309	.348	.790	1	.374	1.362	.689	2.691
LAVI (ml/m ²)	1.518	.659	5.298	1	.021	4.563	1.253	16.619
LASr(%)	1.011	.454	4.973	1	.026	2.749	1.130	6.687
LASRs(s-1)	-15.693	8.034	3.815	1	.051	.000	.000	1.056
LASRe(s-1)	-12.693	6.503	3.810	1	.051	.000	.000	1.053
CHADS2vasc	2.378	1.405	2.864	1	.091	10.786	.687	169.432

LVGLS: left ventricular global strain, DD: diastolic dysfunction, LAVI: Left atrium volume

index, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate(during Left ventricular systole), LASRe: Left atrium strain rate in early diastole, LASRa: Left atrium strain rate in late diastole

By using Multivariate binary logistic regression for prediction of adverse outcomes (recurrent stroke) in patients with atrial fibrillation and acute ischaemic stroke through the 180 days follow up period the Echo parameters (LAVI, Reservoir Strain , Reservoir Strain rate, Conduit Strain rate)were statistically best fitted for such prediction with P value < 0.005 but CHADSVASC was non significant for prediction of recurrent stroke, P value 0.091 (**Table 6**).

Table (7): Validity CHADS2VASC alone as a predictor for recurrent stroke

Area	Std. Errora	Asymptotic Sig.b	Asymptotic 95% Confiden Interval		
		0	Lower Bound	Upper Bound	
.833	.048	.000	.739	.928	

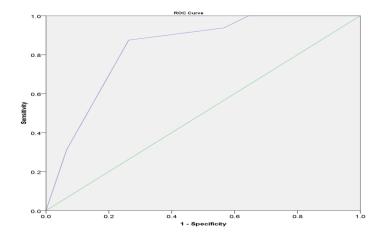


Figure (1): ROC curve for CHADSVASC as apredictor of recurrent stroke.

By Receiver operating characteristic (ROC) curve the cut off value for CHADS2VASC for prediction of adverse outcomes in patients with atrial fibrillation was 5.5 point, area under the curve 0.833 with sensitivity 87.5% and specificity 73.7%, (P value <0.05). (**Table 7& fig 1**).

Table (8): Validity left atrium parameters as predictors for recurrent stroke :

Test Result	Area	Std.	Asymptotic	_	totic 95% nce Interval
Variable(s)	22200	Errora	Sig.b	Lower Bound	Upper Bound
LAVI ml/m ²	.926	.029	.000	.869	.984
LASRe (%)	.670	.064	.033	.545	.794
LASr (s-1)	.858	.057	.000	.746	.971
LASRs (s- ¹)	.867	.058	.000	.753	.981

LAVI: Left atrium volume index, SRe: Left atrium strain rate in early diastole, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate(during Left ventericular systole).

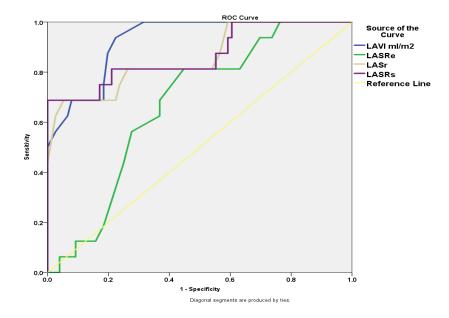


Figure (2): ROC curve for left atrium parameters as predictors of recurrent stroke in group A.

By Receiver operating characteristic (Roc) curve the cut off value for **LAVI** for prediction of adverse outcomes in patients with atrial fibrillation was 36.5 ml/m^2 , area under the curve 0.926 with sensitivity 93.8% and specificity 77.6%, **for Conduit Strain rate** was -1.55 s^{-1} with area under the curve 0.670 with sensitivity 81.3%, specificity 55.3% (P value <0.05), the cut off value

Left Atrial Dysfunction and Deformation as Predictors of Recurrent Stroke in Patients with Atrial Fibrillation and First Acute Ischemic Stroke

for **Reservoir Strain** was 13.5% with area under the curve 0.858with sensitivity 68.8%, specificity 94.7% **and Reservoir Strain rate** was 0.885 s⁻¹ with area under the curve 0.867 with sensitivity 68.8%, specificity 100% (P value <0.05). (**Table 8 & fig 2**).

Table (9): Add-on value of different Left atrium Echo parameters to CHADS₂vasc as predictor for recurrent stroke:

Time-Dependent ROC Analysis	AUC	Sensitivity %	Specificity %	DeLong's Test P Value
1-CHA ₂ DS ₂ -VASc score	0.833	68.8	94.7	
2-CHA ₂ DS ₂ -VASc score+LA strain	0.893	93.8	73.7	0.000
3-CHA ₂ DS ₂ -VASc score+LAVi	0.941	93.8	84.2	
4-CHA ₂ DS ₂ -VASc score+LAVi+LA strain	0.974	93.8	88.2	0.000
5-CHA ₂ DS ₂ -VASc score+LASRs	0.888	75	90.8	
6-CHA ₂ DS ₂ -VASc score+LASRs+LA strain+LAVI	0.978	93.8	92.1	0.000
7-CHA ₂ DS ₂ -VASc score+LASRe	0.849	93.8	68.4	
8-CHA ₂ DS ₂ -VASc score+LAVi+LASRe+LA strain+LASRs	0.987	93.8	93.4	0.000
9-CHA ₂ DS ₂ -VASc score+ LA strain+ LASRe+ LASRs	0.905	93.8	75	0.000

LAVI: Left atrium volume index, LASRe: Left atrium strain rate in early diastole, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate(during Left ventericular systole),

It was noticed that area under the curve (AUC) for CHADSVASc score alone was 0.833 but when any of left atrium echo parameters added to CHADSVASC score area under the curve increased as summarized in the table below and the maximum AUC reached by adding left atrium parameters (LAVI, SRe, LA strain, SRs) and it was 0.987 with sensitivity 93.8%, specificity 93.4% (P value <0.05). (**Table 9& fig.3**)

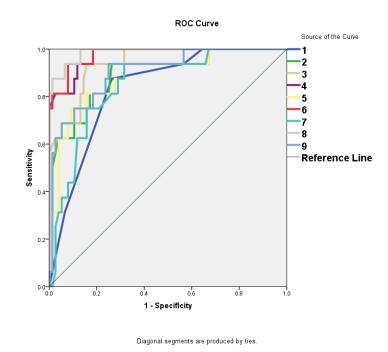


Figure 3: Add-on value of different Left atrium Echo parameters to CHADS₂vasc as predictor for recurrent stroke. LAVI: Left atrium volume index, LASRe: Left atrium strain rate in early diastole, LASr: left atrium reservoir Strain, LASRs:left atrium reservoir Strain rate(during Left ventericular systole).

Table (10): Probability of recurrent stroke patients regarding Left atrial parameters by Echocardiography:

LAVIml/m ²	Estimated Mean of no	T-4-1 N	Event	C	Censored	P –value
LA VIMI/M	readmission time	Total N	N	N	%	Log Rank
≥ 36.5	151.844	32	15	17	53.1%	
< 36.5	179.917	60	1	59	98.3%	0.0001
Overall	170.152	92	16	76	82.6%	
LASRe(S ⁻¹)		'				
≥-1 .55	161.170	47	13	34	72.3%	
<-1.55	179.533	45	3	42	93.3%	0.006
Overall	170.152	92	16	76	82.6%	

Tob Regul Sci. ™ 2023; 9(1): 5830 - 5849

LASr (%)						
≤13.5	123.267	15	11	4	26.7%	
>13.5	179.286	77	5	72	93.5%	0.0001
Overall	170.152	92	16	76	82.6%	
LASRs(S ⁻¹)						
≤0.885	102.636	11	10	1	9.09%	
>0.885	179.321	81	5	76	93.8%	0.0001
Overall	170.152	92	16	76	82.6%	

LAVI: Left atrium volume index, SRe: Left atrium strain rate in early diastole, LASr: left atrium reservoir Strain, LASRs: left atrium reservoir Strain rate(during Left ventericular systole).

According to Kaplan Meier curve the mean free time of adverse outcomes was longer in patients with better left atrium parameters rather than those with left atrium deformation or dysfunction, ,there is significant statistical difference, Log Rank test p-value <0.05 (**Table 10**)

Discussion

Left atrium volume index was larger in our studied patients parallel to Chew et al., 2020 that showed patients with AF had left atrial volume index $(53.2\pm20.0 \text{ vs } 31.0\pm9.2 \text{ mL/m2}; p=0.004)$.

In the current study, there is significantly positive correlation between left atrium strain ,strain rate during LV systole(reservoir phase) and left atrium strain and strain rate during early diastole (conduit phase) between each other and between LV GLS,LV EF, CHADS2VASC score in our studied patients. But negative correlation between LA dysfunction parameters strain, strain rate and LAVI and diastolic dysfunction and these findings parallel to **Liao et al.**, **2020** who discovered Among AF patients, a significantly graded reduction in overall LA strain was noted. Diastolic characteristics and the LA volume index (LAVi) were linked to LA strain, according to restricted cubic spline analysis. Compared to individuals with a high LAVi, those with a small LAVi had a LA strain level that was approximately 1.5 times higher.

However, Chen et al., 2023 discovered that the longitudinal strain rate in Los Angeles

changed earlier than the strain in Los Angeles, indicating that it was a sign of damage to the deformability of Los Angeles early on. Multivariate logistic regression analysis revealed that in his study, LA SRE was an independent risk factor (P < .05) for stroke in patients with paroxysmal AF; that is, the greater the risk of stroke/TIA, the smaller the absolute value of SRE.

Comparing young patients with cryptogenic stroke to age- and risk-matched controls, mechanistic studies have found reductions in LA strain (Bhat et al., 2019; Pirinen et al., 2020). These findings suggest early subclinical changes to the left atrium in this population without primary causative risk factors. The value of LA strain in the distinction of stroke subtypes has been assessed by several research, such as the I-LASER study conducted by Johansen et al. in 2021 and the work conducted by Sade et al. in 2022. Researchers led by Sade discovered a connection between lower LASr and unidentified cryptogenic and embolic strokes, which persisted despite variations in LA size measurements and stroke risk algorithms like the CHA2DS2VASc score. In our investigation, we also discovered declines in LASr and LASct.

In the present study, patients who developed recurrent stroke were elder, hypertensive, diabetic parallel to results of **Kim et al., 2021.**

On the other hand patients who developed recurrent stroke were with higher CHADSVASC score not going with **Kim et al.,2021** that concluded Patients with non-valvular AF who survive the initial phase of an ischemic stroke do not yet have a validated risk prediction tool for recurrent stroke. Rather, the standard risk scores are applied even to patients who have already received a score of at least two on the CHADS2 and CHA2DS2-VASc risk schemas, meaning that anticoagulation is automatically recommended for them.

We concluded in our study that LAVI was statistically different between both subgroups (recurrent and non recurrent stroke) among those suffering from atrial fibrillation These results are similar to those of **Ogata et al. (2017)**, who found that adding indexed-left atrial diameter to the baseline model made up of the factors in the CHADS2 score or those in the CHA2DS2-VASc score significantly improved risk prediction for recurrent stroke. They suggest that left atrial enlargement is associated with an increased risk of recurrent stroke in non-valvular atrial fibrillation patients with ischemic stroke.

According to this investigation, in individuals with atrial fibrillation, strain rate and LA strain as measured by speckle-tracking were both significantly and independently linked to recurrent stroke. Additionally, both showed an incremental predictive value over clinical and standard TTE parameters. These results were consistent with those of **Kawakami et al.** (2020),

who discovered that in acute ischemic stroke patients at significant risk for AF, both LA and LV strain are significantly and independently associated with AF and can show an incremental predictive value over clinical and standard echocardiographic parameters.

Moreover, these results are consistent with those of **Azemi et al. (2012)**, who discovered that decreased LA strain is a potentially sensitive marker for increased risk for stroke or TIA in individuals with low-risk CHADS2 scores, atrial fibrillation, and stroke or TIA. These findings imply that LA strain might be useful in assisting in this patient group's decision for oral anticoagulation.

It was noticed that area under the curve (AUC) for CHADSVASc score alone was 0.833 but when any of left atrium echo parameters added to CHADSVASC score area under the curve increased as summarized in and the maximum AUC reached by adding left atrium parameters (LAVI, SRe, LA strain, SRs) and it was 0.987 with sensitivity 93.8%, specificity 93.4% followed by CHADSVASc with LAVI and LA strain with AUC 0.974 with sensitivity 93.8%, specificity 88.2% parallel to **Liao et al.,2020** who found AUC was 0.81 for CHADSVASc with LAVI and LA strain higher than CHADSVASc with LAVI alone in which AUC was 0.79.

This study found that BMI was higher in recurrent stroke group with mean 32.41±5.78 and that was in line with **Skolarus et al.,2014** who found which When the BMI was less than 31 kg/m2, there was a protective relationship between a 1-unit higher BMI and death, even after taking into consideration demographics, stroke severity, and stroke and mortality risk factors. In the fully adjusted model, higher BMI values >38 kg/m2 were linked to higher mortality, but in reverse to **Andersen et al. (2013),** who concluded that the obesity paradox in stroke can also extend to stroke recurrence. Higher BMI values >31 kg/m2 did not render significant protective associations. Compared to stroke patients of normal weight, those who were obese or overweight had had fewer prior strokes.

Research has revealed a connection between patients' acute ischemic stroke and atrial fibrillation **Providência et al., 2013** and impaired LA strain and LA appendage stasis and thrombus development. The **Kim group (2016)**. Studies conducted by **Yaghi et al. (2015)** and **Ogata et al. (2017)** in the general ischemic stroke population have also discovered a correlation between LAVI and stroke recurrence; however, these studies have not yet evaluated this endpoint in individuals with cardioembolic stroke and non-atrial fibrillation. In addition, LAVI is a late indicator of LA remodelling and is consequently unreliable in patients with early LA dysfunction and atrial cardiopathy. It's interesting to note that in patients suffering from acute

ischemic stroke, LA strain was also a predictor of stroke recurrence.

Left atrium deformation and dysfunction in AF patients are predictors of recurrent stroke.

Our study's results demonstrate the usefulness of echocardiography in identifying atrial dysfunction in the context of stroke. We used both conventional and 2D-STE methods to evaluate LA size and function simultaneously. Additionally, echocardiographic cut-off points were computed for the characteristics that were independently linked to patients who had recurrent stroke or atrial fibrillation.

According to Jordan et al. (2019), LA expansion indicates unfavourable LA structural remodelling, which is linked to electrical instability and thrombus development. However, AF was also seen in individuals with normal LA size, which was explained by functional remodelling of the LA (Ble et al., 2021). According to Morris et al. (2014), there is a reduction in cardiac distortion as evidenced by increased sensitivity in identifying subclinical atrial dysfunction. According to Thomas et al. (2017), atrial remodelling denotes morphologic alterations in the atrial tissue along with the emergence of interstitial fibrosis. According to **De** Sensi et al. (2021) there exists an inverse correlation between the strain measured by echocardiography and the degree of atrial fibrosis, which can be graded by cardiac imaging techniques. According to retrospective research done on individuals who had cryptogenic strokes, STE increased the accuracy of AF identification (Rasmussen et al., 2019).

Our findings confirm the value of routinely assessing atrial function in stroke patients whose cause is unknown. Reduced contractility in the atrium indicates an irregular blood stasis that carries a risk of cerebral embolisation and thrombus development. According to **Padfield et al.** (2017), there is evidence to support the theory that atrial cardiomyopathy is the cause of stroke in cases of paroxysmal to chronic atrial fibrillation.

Conclusion:

In conclusion, Patients with larger LA dimensions and impaired LA function assessed by strain and strain rate are more liable for recurrent stroke than those with normal dimensions and function. LA strain and strain rate outperformed the CHA2DS2-VASc score in predicting ischemic stroke in a broader and greater clinical risk cohort, independent of important AF baseline demographics and conventional echocardiography measures. LA strains could be used as possible risk stratification markers.

References:

- **Andersen, K. K., & Olsen, T. S.** (2013). Body mass index and stroke: overweight and obesity less often associated with stroke recurrence. Journal of Stroke and Cerebrovascular Diseases, 22(8), e576-e581.
- Azemi, T., Rabdiya, V. M., Ayirala, S. R., McCullough, L. D., & Silverman, D. I. (2012). Left atrial strain is reduced in patients with atrial fibrillation, stroke or TIA, and low risk CHADS2 scores. Journal of the American Society of Echocardiography, 25(12), 1327-1332.
- **Bhat A, Khanna S, Chen HH, Lee L, Gan CH, Negishi K, et al.** Impairment of left atrial function and cryptogenic stroke: Potential insights in the pathophysiology of stroke in the young. Int J Cardiol Heart Vasc. 2019;26:100454.
- **Biteker M, Kayataş K, Başaran Ö, et al.,** The Role of Left Atrial Volume Index in Patients with a First-ever Acute Ischemic Stroke. J Stroke Cerebrovasc Dis. 2017;26(2):321-326. doi:10.1016/j.jstrokecerebrovasdis.2016.09.023.
- **Ble M, Benito B, Cuadrado-Godia E, et al.** Left atrium assessment by speckle tracking echocardiography in cryptogenic stroke: seeking silent atrial fibrillation. J Clin Med. 2021;10(16):3501–3511
- Cameli M, Mandoli GE, Loiacono F, et al., Left atrial strain: a useful index in atrial fibrillation. Int J Cardiol. 2016;220:208–213. doi: 10.1016/j.ijcard.2016.06.197.
- **Chao TF, Liu CJ, Tuan TC et al.,** Lifetime risks, projected numbers, and adverse outcomes in Asian patients with atrial fibrillation: are port from the Taiwan nationwide AF cohort study. Chest. 2018;153:453–466. doi: 10.1016/j.chest.2017.10.001.
- Chen, J., Zhao, Y., Ma, C., Du, X., He, Y., & Li, H. (2023). Left atrial deformation and risk of transient ischemic attack and stroke in patients with paroxysmal atrial fibrillation. Medicine, 102(4), e32745-e32745.
- Chew, N. W., Ngiam, J. N., Tan, B. Y. Q., Sia, C. H., Sim, H. W., Kong, W. K., ... & Poh, K. K. (2020). Differences in clinical and echocardiographic profiles and outcomes of patients with atrial fibrillation versus sinus rhythm in medically managed severe aortic stenosis and preserved left ventricular ejection fraction. Heart, Lung and Circulation, 29(12), 1773-1781.

- **De Sensi F, Penela D, Soto-Iglesias D, et al.** Imaging techniques for the study of fibrosis in atrial fibrillation ablation: from molecular mechanisms to therapeutical perspectives. J Clin Med. 2021;10:2277
- Gallo, A., Galliazzo, S., Grazioli, S., Guasti, L., Ageno, W., & Squizzato, A. (2019). Epidemiology and secondary prevention of ischemic stroke in patients on antiplatelet drug: a retrospective cohort study. Journal of Thrombosis and Thrombolysis, 48, 336-344.
- Johansen MC, Doria de Vasconcellos H, Nazarian S, Lima JAC, Gottesman RF. The Investigation of Left Atrial Structure and Stroke Etiology: The I-LASER Study. J Am Heart Assoc. 2021; 10:e018766
- **Jordan K, Yaghi S, Poppas A, et al.** Left atrial volume index is associated with cardioembolic stroke and atrial fibrillation detection after embolic stroke of undetermined source. Stroke. 2019;50:1997–2001
- Kawakami, H., Ramkumar, S., Pathan, F., Wright, L., & Marwick, T. H. (2020). Use of echocardiography to stratify the risk of atrial fibrillation: comparison of left atrial and ventricular strain. European Heart Journal-Cardiovascular Imaging, 21(4), 399-407.
- **Kim D, Shim CY, Hong GR, Kim MH, Seo J, Cho IJ, et al.** Clinical Implications and Determinants of Left Atrial Mechanical Dysfunction in Patients With Stroke. Stroke. 2016;47:1444-51.
- Kim, B. J., Lee, K. J., Park, E. L., Tanaka, K., Koga, M., Yoshimura, S., ... & CRCS-K Investigators. (2021). Prediction of recurrent stroke among ischemic stroke patients with atrial fibrillation: Development and validation of a risk score model. Plos one, 16(10), e0258377.
- **Liao Jo-Nan, Tze-fan Chao, Jen-Yaun Kuo et al.** "Global Left Atrial Longitudinal Strain Using 3-Beat Method Improves Risk Prediction of Stroke Over Conventional Echocardiography in Atrial Fibrillation." Circulation: Cardiovascular Imaging, vol. 13, no. 8, 2020, doi:10.1161/circimaging.119.010287.
- Liao, J. N., Chao, T. F., Kuo, J. Y., Sung, K. T., Tsai, J. P., Lo, C. I., ... & Yeh, H. I. (2020). Global left atrial longitudinal strain using 3-beat method improves risk prediction of stroke over conventional echocardiography in atrial fibrillation. Circulation: Cardiovascular Imaging, 13(8), e010287.

- Marwick TH, Thomas L, Popescu BA, et al., Left atrial structure and function, and left ventricular diastolic dysfunction: JACC state-of-the-art review. J Am Coll Cardiol. 2019;73:1961–1977.
- **Morris DA, Takeuchi M, Krisper M, et al.** Normal values and clinical relevance of left atrial myocardial function analysed by speckle-tracking echocardiography: multicentre study. Eur Heart J Cardiovasc Imaging. 2014;16:364–372.
- Ogata T, Matsuo R, Kiyuna F, Hata J, Ago T, Tsuboi Y, et al. Left Atrial Size and LongTerm Risk of Recurrent Stroke After Acute Ischemic Stroke in Patients With Nonvalvular Atrial Fibrillation. J Am Heart Assoc. 2017;6:e006402.
- **Padfield GJ, Steinberg C, Swampillai J, et al.** Progression of paroxysmal to persistent atrial fibrillation: 10-year follow-up in the Canadian Registry of Atrial Fibrillation. Heart Rhythm. 2017;14:801–807
- **Peñafiel, S. Baloian, N. Sanson H.et al.,** "Predicting Stroke Risk With an Interpretable Classifier," in IEEE Access, vol. 9, pp. 1154-1166, 2021, doi: 10.1109/ACCESS.2020.3047195.
- Pirinen J, Järvinen V, Martinez-Majander N, Sinisalo J, Pöyhönen P, Putaala J. Left Atrial Dynamics Is Altered in Young Adults With Cryptogenic Ischemic Stroke: A CaseControl Study Utilizing Advanced Echocardiography. J Am Heart Assoc. 2020;9:e014578
- Providência R, Faustino A, Ferreira MJ, Gonçalves L, Trigo J, Botelho A, et al. Evaluation of left atrial deformation to predict left atrial stasis in patients with nonvalvular atrial fibrillation a pilot-study. Cardiovasc Ultrasound. 2013;11:44.
- Rasmussen SMA, Olsen FJ, Jørgensen PG, et al. Utility of left atrial strain for predicting atrial fibrillation following ischemic stroke. Int J Cardiovasc Imaging. 2019;35:1605–1613.
- **Roberto M. Lang, Luigi P. Badano, Victor Mor-Avi, et al;** Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, European Heart Journal Cardiovascular Imaging, Volume 16, Issue 3, 1 March 2015, Pages 233–27.

- Sade LE, Keskin S, Can U, Çolak A, Yüce D, Çiftçi O, et al. Left atrial mechanics for secondary prevention from embolic stroke of undetermined source. Eur Heart J Cardiovasc Imaging. 2022;23:381-391
- Skolarus, L. E., Sanchez, B. N., Levine, D. A., Baek, J., Kerber, K. A., Morgenstern, L. B., ... & Lisabeth, L. D. (2014). Association of body mass index and mortality after acute ischemic stroke. Circulation: Cardiovascular Quality and Outcomes, 7(1), 64-69.
- **Steinberg JS, O'Connell H, Li S et al.** Thirty-second gold standard definition of atrial fibrillation and its relationship with subsequent arrhythmia patterns: analysis of a large prospective device database. Circ Arrhythm Electrophysiol 2018;11:e006274
- **Thomas L, Abhayaratna W.** Left atrial reverse remodeling. JACC Cardiovasc Imaging. 2017; 10:65–77
- Yaghi S, Moon YP, Mora-McLaughlin C, Willey JZ, Cheung K, Di Tullio MR, et al. Left atrial enlargement and stroke recurrence: the Northern Manhattan Stroke Study. Stroke. 2015;46:1488-93.
- **Zhang Q, Yip GW, Yu CM et al.,** Approaching regional left atrial function by tissue Doppler velocity and strain imaging. Europace. 2008;10(suppl 3):iii62–iii69.