Original Article

Assessment of Left Atrial Global Longitudinal Strain in Patients With Cerebrovascular Ischemic Accidents and No Evidence of Atrial Fibrillation

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ABSTRACT

Background: Cardioembolic strokes cause more severe disabilities than other subtypes of ischemic strokes. Considering that thrombus formation predominantly occurs in the left atrium (LA), the structure and function of the LA may cause a risk for embolic strokes even in the absence of atrial fibrillation (AF). We hypothesized that functional and structural LA alterations could be associated with acute ischemic strokes regardless of AF occurrence and history.

Methods: This comparative cross-sectional study assessed 40 patients with cerebrovascular accidents (CVA) and 40 healthy controls. We included patients aged above 18 years with ischemic CVA within the preceding 6 months and without AF rhythm. Global longitudinal strain (GLS) was calculated using 2D speckle-tracking echocardiography.

Results: Significant differences existed between the 2 groups regarding the mean values of LAA4C GLS (P=0.01), LAA3C GLS (P=0.002), LAA2C GLS (P=0.002), LA TOTAL GLS (P=0.001), LVA4C GLS (P=0.01), and LV TOTAL GLS (P=0.04). Nevertheless, no significant differences existed in the LA area, LA diameter, EF, LVEDV, LVESV, LVA3C GLS, and LVA2C GLS between the groups.

Conclusions: Our findings suggested the possible involvement of LA morphofunctional dysfunction in CVA events in patients with sinus rhythm. ***(Iranian Heart Journal 2023; 24(2): 77-83)***

KEYWORDS: Left atrium, Emboli, Atrial fibrillation, CVA, GLS score

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Globally, strokes were the second leading cause of death (11.6%) and a major cause of death and disability combined (5.7%) in 2019. [1] Ischemic strokes account for about two-thirds of strokes. Cardiac embolism causes a significant proportion of ischemic strokes. [2] Cardioembolic strokes create more severe disabilities than other subtypes of ischemic strokes, [3] making the cardiac disease a particularly significant target for stroke preventive approaches. Multiple cardiac conditions have been identified as risk factors for stroke, including atrial fibrillation (AF), ischemic heart disease, heart valve disease, and congestive heart failure. [4] Recent evidence indicates that our comprehension of the structure and function of the heart and ischemic strokes is still inadequate. [5] Furthermore, almost one-third of ischemic strokes have no identified etiology. [6] A deeper comprehension of the association between heart disease and ischemic strokes may potentially shed light on previously unknown causes of strokes, leading to enhanced stroke preventive strategies. Considering that thrombus formation predominantly occurs in the left atrium (LA), the structure and function of this chamber may cause a risk for embolic strokes even in the absence of AF, implying that AF occurrence may not necessarily be required for LA thromboembolism formation. [7] Previously, several studies [8-10] have employed LA volumetric assessments to investigate the etiology of adverse cerebrovascular events. Nonetheless, only a few researchers have shown that LA enlargement is independently associated with an increased risk of acute ischemic strokes.

Accordingly, we hypothesized that functional and structural LA alterations could be associated with acute ischemic strokes regardless of AF occurrence and history. We investigated whether LA global longitudinal strain (GLS) and changes in the LA volume index detected by 2D speckle-tracking strain analysis were associated with cerebrovascular accidents (CVA) in patients with sinus rhythm.

METHODS

Patient Population

The present comparative cross-sectional study aimed to compare GLS parameters between 2 groups: patients with and without CVA.

The required sample size was determined based on the formula for comparing the proportions of the 2 groups. With the assumption of a type I error of 0.05, a power of 80%, a 95% confidence level, an estimated 70% proportion of LA dysfunction in patients with CVA,[11] and 40% proportion of LA dysfunction in patients without CVA,[12] a sample size of 40 for each group was required.

$$n = (Z_{\alpha/2}+Z_{\beta})^2 * (P_1(1-P_1) + P_2(1-P_2)) / (P_1-P_2)^2$$

Accordingly, 80 individuals, comprising 40 patients with CVA and 40 healthy individuals, were included. The study was performed at Shariati Hospital, Tehran University of Medical Sciences, Iran, between January 2020 and December 2021.

One group consisted of patients older than 18 years, with ischemic CVA within the preceding 6 months and without AF rhythm. The diagnosis of ischemic CVA was confirmed by expert neurologists. The other group consisted of concurrent patients with sinus rhythm and no history of CVA referred for echocardiography.

Patients who refused to grant consent for study participation and those with severe comorbidities, hemorrhagic CVA, confirmed history of AF, moderate or severe heart valvular diseases, and recent myocardial infarction were excluded. For the identification of participants with AF or paroxysmal AF, all the participants underwent 24 hours of ECG Holter monitoring. The patients' characteristics, including age, sex, and smoking status, as well as previous history of diabetes mellitus, hypertension, and CVA, were recorded.

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1399.1292). Informed consent was obtained from the participants.

Echocardiography

Standard Doppler echocardiographic studies were performed using a 3.5-MHz multiphase-array probe, with the patients lying in the left lateral decubitus position. Traditional left ventricular (LV) parameters were assessed based on the guidelines of the American Society of Echocardiography (ASE). LV volume and ejection fraction (EF) were measured using the biplane 2D method, and LV mass was measured using the 2D area-length method.

M-Mode Echocardiography

Pulsed-wave Doppler echocardiography was used to attain transmittal flow patterns from the apical 4-chamber view. The peak of the late diastolic flow velocity (A) and the peak of the early diastolic flow velocity (E) were measured.

Tissue velocities were calculated using the pulsed-wave tissue Doppler imaging from the apical 2 and 4-chamber views. The following velocities were recorded: the mitral annulus early diastolic velocity (E'), the mitral annulus late diastolic velocity (A′), and the mitral annulus systolic velocity (S′). All the parameters were measured at the end of expiration at a frame rate of 50 to 90 per second and were averaged from 3 substantial sinus beats.

LA Strain Measurement

The point-and-click approach was utilized to manually determine the endocardial border. The system automatically traces the epicardium, although the wall thickness can be modified manually to cover the full thickness of the myocardium.

The smallest region of interest was 8 mm wide. A cine-loop preview was employed prior to the processing to visually confirm whether the internal line of the region of interest followed the movement of the LA endocardium during the cardiac cycle. The program generated time-strain and time-strain rate charts automatically. Peak positive strain and strain rate were measured during ventricular systole to define the LA reserve index. The peak negative conduit strain rate (LASn) was measured throughout early LV filling from strain rate curves.

Statistical Analysis

The statistical analyses were conducted using the SPSS software, version 22. Continuous variables were expressed as the mean ± the standard deviation (SD). Categorical variables were represented as absolute and relative frequencies. Continuous variables were compared between the 2 groups using the Student *t* test. A *P* value of less than 0.05 was regarded as statistically significant.

RESULTS

We included 40 patients with ischemic CVA and 40 control patients. The mean (±SD) age of the study and control groups was 60.6±13.77 years and 51.81±11.35 years, respectively. The demographic and clinical characteristics of the participants are presented in Table 1.

Various GLS parameters in the study and control groups are depicted in Table 2. As shown in Table 2, there was a significant difference between the 2 groups regarding the mean values of LAA4C GLS (*P*=0.01), LAA3C GLS (*P*=0.002), LAA2C GLS (*P*=0.002), LA TOTAL GLS (*P*=0.001), LVA4C GLS (*P*=0.01), and LV TOTAL GLS (*P*=0.04). Nevertheless, no significant differences were detected in the LA area, LA diameter, EF, LVEDV, LVESV, LVA3C GLS, and LVA2C GLS parameters between the case and control groups.

Table 1: Patients' demographic and clinical characteristics

Variable	Ischemic CVA Group	Control Group	*P* value
Age (mean ± SD)	60.6 ± 13.77	51.81 ± 11.35	0.003
Sex (%) male female	 52% 48%	 62.5% 37.5%	0.36
Diabetes mellitus (%)	35%	32.5%	0.81
Hypertension (%)	67.5%	47.5%	0.002
CVA history (%)	27.5%	NA	NA
Smoking (%)	40%	10%	0.002

CVA, Cerebrovascular accident

Table 2: Patients' echocardiographic parameters (mean ± SD)

Parameter	Ischemic CVA Group	Control Group	*P* value
LAA4C GLS (%)	24.97 ± 7.52	31.93 ± 8.94	0.01*
LAA3C GLS (%)	24.68 ± 6.92	31.07 ± 5.	0.002*
LAA2C GLS (%)	24.82 ± 8	32.11 ± 6.80	0.002*
LA TOTAL GLS (%)	25.79 ± 7.98	32.76 ± 4.95	0.001*
LA area (cm^2/m^2)	16.16 ± 3.95	16.05 ± 4.12	0.92
LA diameter (mm)	33.04 ± 3.87	32.00 ± 2.95	0.32
EF (%)	55.54 ± 3.1	56.76 ± 2.38	0.14
LVEDV (mL)	79.88 ± 22.45	71.95 ± 9.64	0.15
LVESV (mL)	33 ± 11.46	31.35 ± 4.68	0.55
LVA4C GLS (%)	-16.6 ± 7.78	-21.25 ± 2.6	0.01*
LVA3C GLS (%)	-17.59 ± 3.20	-19.12 ± 3.81	0.14
LVA2C GLS (%)	-18.24 ± 4.51	-20.45 ± 4.11	0.09
LV TOTAL GLS (%)	-18.35 ± 3.94	-20.52 ± 3.01	0.04*

GLS, Global longitudinal strain; LAA, Left atrial appendage; EF, Ejection fraction; LV, Left ventricle; LVEDV, Left ventricular end-diastolic volume; LVESV, Left ventricular end-systolic volume

DISCUSSION

In the current study, we demonstrated the relationship between CVA occurrence and the LA strain index and LAA GLS in patients with sinus rhythms.

In a wide range of diseases and conditions, a strong linear relationship between LA volume and longitudinal deformation echocardiographic indices has been observed. [13, 14] Participants in a cohort study with normal EF, sinus rhythm, and no history of AF were evaluated to determine the relationship between subclinical cerebral infarction and LA reservoir function and stiffness. LA reservoir function and stiffness, addressed by E/e' divided by LA GLS and LA GLS, were related to higher odds of subclinical cerebral infarction and stroke. These indices exhibited a significant interaction between age groups for subclinical cerebral infarction. [13]

Sonaglioni et al [15] conducted a prospective study on patients with acute ischemic strokes and without documented AF to assess the predictive relevance of global LA peak strain. Their results demonstrated that the index was significantly impaired in patients with acute ischemic strokes. The pathophysiological process is described by the fibrosis, dilatation, and stiffening of the chamber, resulting in an impaired global LA peak strain value. LA fibrosis limits the compliance of the chamber during its reservoir phase, resulting in blood flow stasis in the LAA and LA and significantly increasing the risk of hospital admission for cardiovascular diseases as well as mortality at the 1-year follow-up.

Although found no association between CVA occurrence and LA diameter and volume, previous research has discovered that LA size and volume are also significant predictors of strokes. Increased LA size and volume are linked to a greater risk of ischemic strokes. [8, 9]

Multiple hypotheses have been proposed to clarify the mechanism whereby LA size and subsequent morbidity are linked. One plausible cause is that as the size of the LA expands, blood stasis and thrombus development become more common.[16]

Moreover, increased intra-atrial pressure causes LA enlargement and a reduction in LA flow velocity, promoting thrombus development and potential embolic strokes. LA enlargement is a major risk factor for the development of AF, which is a known risk factor for embolic strokes and death. [16, 17]

Further, LA enlargement is a sign of structural heart disease, hypertension, or LV hypertrophy and is, therefore, related to an increased risk of strokes and death.[8] LA enlargement is a result of atrial remodeling caused by volume and/or pressure overload.[18]

Another study demonstrated that LA deformation parameters determined via the 2D speckle-tracking approach predicted reduced LAA function and the development of LAA thrombi in patients with ischemic strokes who were in sinus rhythm, with suspected cardioembolism [19] and those with LA strain who developed cryptogenic strokes independent of other cardiovascular risk factors. [20]

In a retrospective study by Park et al, [21] the predictive value of LA GLS was evaluated in patients with acute heart failure and sinus rhythm. During a follow-up period of about 30 months, 100 patients experienced strokes. Patients with strokes had higher LA diameters and lower LA GLS values than those without strokes. The univariate analysis showed that age, diabetes, the LA volume index, the LA diameter, and LA GLS were significant risk factors for strokes. The multivariate analysis revealed that every 1% reduction in LA GLS was associated with a 3.8% raised risk of stroke. Park and colleagues also showed that in patients with sinus rhythm and acute heart failure, a decrease in LA GLS to less than 14.5% was associated with about twice the risk of strokes with an annual incidence of 2.38%.

The LA is a sensitive heart chamber, which might detect the early impact of pressure overload, diastolic dysfunction, and increased LV volume. [22] LA strain and volume reveal supplementary details of structural alterations in the LA. [15]

Speckle-tracking image methods can be utilized to evaluate atrial phasic dysfunction and stiffness in addition to the characterization of LV diastolic dysfunction. Peak atrial longitudinal strain (LA strain) or strain rate calculated by 2D speckle-tracking echocardiography is emerging as a helpful method for analyzing atrial mechanical features and prognosis. [23]

Limitations

Our study has some limitations worth mentioning. Firstly, it was carried out at a single cardiology center with a limited number of patients from the same ethnic group. Accordingly, it is necessary to validate the findings with larger-scale studies. Secondly, a possible noncardiac source of emboli in stroke patients was not proven. Additionally, despite ECG monitoring, it is possible that some included participants experienced silent paroxysmal AF.

Future studies may indicate the potential of atrial GLS as a noninvasive approach to identify LAA thrombi and predict CVA in susceptible patients with sinus rhythm.

CONCLUSIONS

Our findings suggested that LA morphofunctional dysfunction might be involved in the occurrence of CVA events in patients with sinus rhythm. These findings could have clinical relevance in that a lower global LA peak strain value in a patient with stroke and without previous AF history could strengthen the indication for anticoagulation therapy and/or loop recorder implantation to find probable atrial arrhythmias due to atrial cardiomyopathy.

Acknowledgments

None

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical Approval

All the procedures performed in the current study were in accordance with the guidelines laid down in the Declaration of Helsinki and approved by the Ethics Committee of Tran University of Medical Sciences (TUMS) (No. IR.TUMS.THC.REC.1399.047). All the participants or their legal guardians were asked to provide written informed consent before data collection.

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