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Assessment of left atrial function by strain in patients with acute ıschemic stroke left atrial function and acute stroke

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SUMMARY

OBJECTIVE: Myocardial speckle-tracking echocardiography can detect subtle abnormalities in the left atrial function. In this study, we aimed to investigate the relationship between left atrial myocardium and tissue function n assessed by two-dimensional speckle-tracking echocardiography and the National Institutes of Health Stroke Scale score in patients with acute ischemic stroke.

METHOD: The study was composed of 80 patients (45 men, 35 women, mean age: 67±15 years) with acute ischemic stroke. The patients were divided into two groups based on the calculated National Institutes of Health Stroke Scale score (group 1, National Institutes of Health Stroke Scale score < 16; group 2, National Institutes of Health Stroke Scale score ≥ 16). Demographic, clinical, and laboratory data for all patients were collected. Cardiac functions were evaluated using two-dimensional speckle-tracking echocardiography within 48 hours from admission to the neurology care unit.

RESULTS: There were no significant differences between the patients' clinical parameters. Left ventricular ejection fraction was significantly higher in group 1 than in group 2 (59.2±5.6 to 51.4±6.3, p=0.024). Left atrial longitudinal strain was significantly higher in group 1 than in group 2 (34.48±9.73 to 26.27±7.41, p=0.019). There were no significant differences between other echocardiographic parameters.

CONCLUSION: Our results suggest that left atrial longitudinal strain is associated with stroke severity during admission in patients with acute ischemic stroke. Left atrial longitudinal strain is an indicator of left atrial myocardial function.

KEYWORDS: Atrial function. Heart atria. Echocardiography. Stroke.

INTRODUCTION

Acute stroke is an important cause of morbidity and mortality[1,2]. Cardiovascular complications are common after an acute stroke[3]. Increasing sympathetic activation leads to myocardial injury. Neurogenic stress cardiomyopathy (NSC) is a condition of acute left ventricular systolic dysfunction caused by acute neurological diseases, such as acute ischemic or hemorrhagic stroke, cranial trauma, intracranial hemorrhage, and epilepsy[4]. However, there is no significant obstruction of the coronary arteries in patients with NSC. Acute systolic heart failure caused by NSC is an important cause of lethal ventricular dysrhythmia and mortality[4].

Echocardiography is most commonly used for the assessment of cardiovascular functions in acute ischemic stroke (AIS) patients. Few authors have demonstrated that left atrial enlargement (LAE) is independently associated with new neurological events in patients with first-ever AIS. Assessment of left atrial (LA) function is important in acute stroke patients[5,6].

Two-dimensional (2D) speckle-tracking echocardiography (STE) allows for the assessment of global and local myocardial tissue function[7]. It calculates the regional ratio of myocardial tissue deformation. This novel echocardiographic technique evaluates the left ventricular (LV) myocardium and tissue.

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However, this technique has seldom evaluated the tissue function and the atrial myocardium[8].

In our study, we aimed to investigate the association between the tissue function and the atrial myocardium assessed by 2D-STE and National Institutes of Health Stroke Scale (NIHSS) score in AIS patients.

METHODS

Study participants and design

Patient selection

We prospectively studied 97 consecutive patients (males, 42; females, 55; mean age, 65±16 years; range 41–80 years) within ≤24 hours from the onset of AIS symptoms admitted to the neurology care unit, between October 2016 and December 2017. Seventeen patients were excluded. The patients' demographic and baseline clinical characteristics, including the severity assessment of neurological deficit with NIHSS upon admission to the neurology care unit, were recorded. Patients with a well-defined time of symptom onset of acute ischemic stroke were included in this study. Baseline stroke severity was evaluated using the NIHSS score[9].

All patients underwent immediate computed tomography after being admitted to the emergency care unit. Troponin values were calculated, and an electrocardiogram (ECG) was recorded after admission to the neurology intensive care unit. Echocardiography was performed within the first 48 hours after admission. The study was certified by our hospital's Ethics Committee. Informed consent was obtained from all patients.

Echocardiographic examination

All patients underwent detailed 2D transthoracic echocardiographic study at rest according to the echocardiographic recommendation[9], using a Philips EPIQ 7C ultrasound system (Philips Healthcare, Andover, MA, USA) coupled with a multifrequency transducer (3–8 MHz) and tissue harmonic imaging ability. A single-lead ECG was placed permanently during the study, and 2D echocardiographic images of the LA and LV were acquired in the apical four-chamber and two-chamber view at end-inspiration. The frame rate was adjusted between 60 and 80 frames per second. At least three successive cardiac cycles of 2D echocardiographic images in the apical four-chamber and two-chamber view were stored in order to choose the images with the best quality for off-line speckle-tracking analysis[8].

Two-dimensional speckle-tracking analysis

Strain analysis was carried out by a skilled investigator who was blinded to the clinical parameters, using the latest commercially available 2D wall motion tracking software (Philips Healthcare Systems). For speckle-tracking analysis, apical four- and two-chamber view images were obtained using conventional 2D grayscale echocardiography, at end-inspiration with a stable ECG logger. Particular attention was paid to obtain an adequate grayscale image, allowing a reliable delineation of the myocardial tissue and the extracardiac structures. The average recording of three consecutive heart cycles was taken. The frame rate was set between 60 and 80 frames per second. These settings are recommended to combine temporal resolution with adequate spatial definition and to enhance the feasibility of the frame-to-frame tracking technique[7].

To evaluate LA myocardial tissue function, LA endocardium was manually traced when the left atrium was at its maximum volume, just before mitral valve opening, as recognized in the apical four-chamber and two-chamber views. The LA basal septal, basal lateral and apical myocardial borders were manually traced, followed by automatic tracing of the LA endocardial and epicardial borders. This described an area of interest composed of six segments. Longitudinal strain curves were generated by the software for each atrial segment after analysis of segmental tracking quality and manual adjustment of the area of interest. LA longitudinal speckle tracking was calculated in six segments of the atrium (Figure 1)[8]. Pathan et al.[10] found a normal reference range of 39% for left atrial longitudinal strain (LALS) (38–41%).

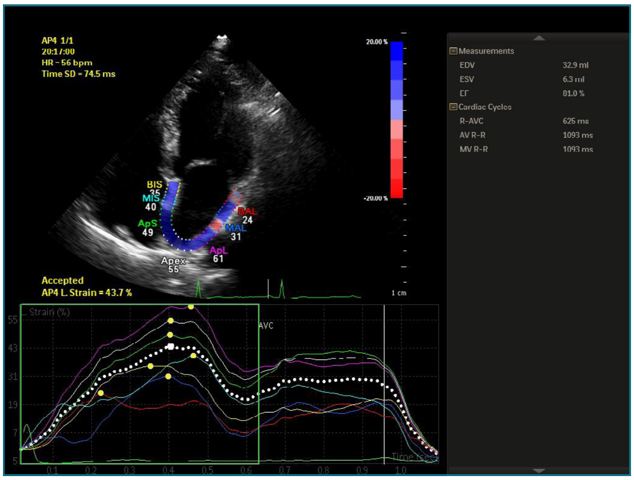
Definition of Stroke and Assessment of Stroke Severity

The updated definition of stroke in the American Heart Association/American Stroke Association guidelines states that ischemic stroke is diagnosed based on the combination of symptoms and/or signs of typical neurological dysfunction and imaging that is proof of cerebral infarction[11].

The NIHSS is a simple, valid, and reliable systematic assessment tool that measures acute stroke–related neurological deficit[12]. The higher the NIHSS score, the higher the impairment of a stroke patient. There are five stroke severity groups: NIHSS=0 (no stroke), NIHSS=1–4 (minor stroke), NIHSS=5–15 (moderate stroke), NIHSS=16–20 (moderate to severe stroke), and NIHSS=21–42 (severe stroke). A baseline NIHSS score >16 indicates a strong probability of patient disability and death[12]. Patients were categorized into two groups according to severity: group 1, composed of patients with non-severe stroke (NIHSS<16; n=58); group 2, composed of patients with severe stroke (NIHSS≥16; n=22).

Cerebral Infarction Volume Measurements

A neurolog computed the "cerebral infarction volume" in each patient by using Analyze 12.0, a software package for biomedical imaging analysis (Biomedical Imaging Resource, New York, NY, USA). The regions of interest were segmented using the Region Grow in the Volume Edit module, with manual removal of artifacts when necessary. The total volume was reported in milliliters.



AVC: aortic valve closure.

Figure 1. Example of echo-derived left atrial strain using speckle tracking. Regional strains are denoted by the colored lines, longitudinal strain by the white dotted line.

Statistical analysis

Statistical analysis was conducted with the SPSS statistical package (version 12.0; SPSS Inc., Chicago, IL, USA). All baseline parameters were analyzed. Continuous variables were expressed as mean ± SD; and categorical variables were expressed as percentage rates. Intraobserver variability was calculated as the absolute difference between the two measurements as a percentage of their mean. The Mann-Whitney U test and the Chi-square test were used appropriately for comparing data. P-values of < 0.05 were considered as statistically significant. Pearson's correlation was used to determine the association between LA 2D-STE and other echocardiographic parameters. The Pearson's or Spearman's correlation was used for assessing correlations between variables.

RESULTS

Baseline characteristics

The patients' baseline characteristics are summarized in Table 1. Clinical characteristics of groups were similar with

Table 1. Patients' clinical characteristics.

	Group 1 (NIHSS score <16) n=58	Group 2 (NIHSS score ≥l6) n=22	p-value
Age (years)	65.4±12.7	69.8±17.7	0.619
Gender (F/M), n	32/26	13/9	0.718
Hypertension, (n%)	28 (48)	13 (59)	0.062
SBP (mmHg)	143.5±15.2	159.8±18.5	0.043
DBP (mmHg)	76.4±8.6	84.3±12.7	0.048
Heart Rate (bpm)	92.3±14.7	115±16.5	0.027
Diabetes Mellitus, (n%)	14 (24)	6 (29)	0.091
Smoking, (n%)	7 (12)	4 (16)	0.076
Dyslipidemia, (n%)	9 (15)	8 (36)	0.043
Infarct volume (mL)	16 mL±2.3	44 mL±4.1	0.034
Troponin (ng/L)	6.143	14.705	0.037
HbA1c (%)	6.24±1.43	9.56±1.53	0.009
Glucose (mg/dL)	143.5±37.4	192.7±48.5	0.026
Creatinine (mg/dL)	1.3±0.4	1.8±0.6	0.023
LDL cholesterol (mg/dL)	103.3±27.1	128.4±39.5	0.008
HDL cholesterol (mg/dL)	42.1±12.3	39.4±10	0.384

NIHSS: National Institutes of Health Stroke Scale. F: Female. M: Male. SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure. LDL: Low Density Lipoprotein. HDL: High Density Lipoprotein.

respect to age, gender, hypertension, diabetes, and smoking ($p > 0.05$). Systolic blood pressure (BP), diastolic BP, heart rate, dyslipidemia, infarction volume, glucose, creatinine, and troponin levels in group 2 were significantly higher than group 1 ($p < 0.05$). Serum hemoglobin HbA1c and low-density lipoprotein (LDL) cholesterol levels were significantly higher in group 2 than group 1 ($p < 0.05$).

Echocardiographic findings

Echocardiographic findings are summarized in Table 2. LV wall thickness and E/e' values were significantly higher in group 2 than in group 1 ($p < 0.05$). The absolute value of LALS and LVEF were significantly higher in group 1, with lower NIHSS scores, than in group 2, with higher NIHSS scores. Around 10 patients (12%) were randomly assigned to assess intraobserver variability and it was calculated as 3.8%.

Correlation analysis was performed to investigate the relationship between the NIHSS score and echocardiographic parameters. A negative correlation was found between the NIHSS score and LVEF and the absolute value of the LALS. There was a positive correlation between the absolute value of the NIHSS score and age, heart rate, and E/e' (Table 3). Logistic regression analysis was performed to identify the potential predictors for stroke severity. Results of the multivariate analysis revealed age, LVEF, and LALS as powerful predictors of severe ischemic stroke (Table 4).

DISCUSSION

Ischemic stroke and heart failure are important causes of morbidity and mortality. Heart failure is associated with an increased risk of ischemic stroke[13]. LV dysfunction occurs frequently after cerebrovascular events[14]. LVEF is a beneficial marker of systolic function; however, it was not detected in early LV systolic dysfunction. Global longitudinal strain (GLS) is an indicator of myocardial deformation, which is different from LVEF. GLS can detect early myocardial dysfunction despite the preserved LVEF[15].

LV longitudinal strain is an important parameter of LA myocardial function. LV function has an effect on the systolic

Table 3. Correlation between the National Institutes of Health Stroke Scale score and clinical parameters in acute ischemic stroke patients.

Parameters	Pearson's correlation coefficient (r value)	p-value
LALS	-0.573	0.026
LVEF	-0.314	0.038
E/e'	0.217	0.026
Age	0.320	0.042
Heart rate	0.419	0.023

LALS: Left atrial longitudinal strain. LVEF: Left ventricular ejection fraction.

Table 2. Patients' echocardiographic parameters.

	Group 1 (NIHSS score<16) n=58	Group 2 (NIHSS score≥l6) n=22	p-value
LV septal thickness, mm	11.2±1.8	12.7±1.7	0.027
LVDd (mm)	51.2±6.3	54.6±6.8	0.348
LV posterior Wall thickness, mm	10.8±1.5	11.9±1.6	0.034
LVSs (mm)	40.5±4.2	43.2±5.8	0.241
LVEDV (mL)	86.0±17.7	95.4±24.3	0.192
LVESV (mL)	41.1±12.4	44.7±14.2	0.246
LAD (mm)	39.5±4.3	42.4±4.6	0.624
RAD (mm)	32.6±3.4	34.7±3.7	0.590
RVDd (mm)	28.1±2.5	30.7±2.8	0.369
LVEF (%)	59.2±5.6	51.4±6.3	0.024
LALS (%)	34.48±9.73	26.27±7.41	0.019
LV GLS (%)	-1.4±2.2	-15.9±2.7	0.003
E/e'	8.7±2.9	10.4±3.6	0.017

NIHSS: National Institutes of Health Stroke Scale. LV: Left Ventricle. LVDd: Left ventricular diastolic diameter. LVSs: Left ventricular systolic diameter. LVEDV: Left ventricular end-diastolic volume. LVESV: Left ventricular end-systolic volume. LAD: Left atrial diameter. RAD: Right atrial diameter. RVDd: Right ventricular diastolic diameter. LVEF: Left ventricular ejection fraction. LALS: Left atrial longitudinal strain. LV GLS: Left ventricular global longitudinal strain.

Table 4. Multivariate logistic regression analysis between the National Institutes of Health Stroke scale score and clinical parameters in acute ischemic stroke patients.

Parameters	OR	95%CI	p-value
LALS	0.571	0.289–0.752	0.042
LVEF	0.835	0.770–0.920	0.025
Age	1.218	1.090–1.465	0.030
Heart rate	1.130	0.972–1.223	0.453

OR: Odds ratio. LALS: Left atrial longitudinal strain. LVEF: Left ventricular ejection fraction.

descent of the mitral plane[16]. As a result, an impaired LV longitudinal strain causes a low LA longitudinal strain. The evaluation of LV longitudinal strain is an indirect calculation of LA myocardial function and compliance[17].

Both atrial fibrillation (AF) and cardiovascular risk factors have been related with abnormalities of LA myocardial mechanical function[18]. The occurrence of strain imaging allows a sensitive evaluation of myocardial deformation, involving the analysis of LA myocardial function[19]. Impaired LA myocardial speckle tracking has been defined in patients with arterial hypertension and/or diabetes mellitus, but with normal LA diameter[20]. The Atherosclerosis Risk in Communities (ARIC) study demonstrated that LA size is an important predictor of cardiovascular death, morbidity, and mortality[21].

LA myocardial STE is a beneficial marker for assessment of LA myocardial function. Very little is known about the association between AIS severity and LA myocardial function. Our study is the first-ever to assess LA function using 2D-STE in the early period of AIS. The novel and most important finding is that even mildly impaired LA function was detected with 2D-STE after AIS. We found that the absolute value of LALS was significantly higher in patients with lower NIHSS scores.

Lower LALS is reportedly associated with hypertension, LV hypertrophy, and diabetes mellitus[22]. We found that BP at admission is significantly higher in severe ischemic stroke patients. However, Bonardo et al.[23] found that young patients with AIS and large infarction volume did not show high blood pressure at admission. We found that LDL cholesterol and HbA1c were significantly increased in patients with higher NIHSS scores. Hendrix et al[24]. found that history of diabetes mellitus was an important predictor of stroke severity.

Regardless of the previous cardiovascular situation, an early period of stroke prominently affects systemic BP, heart rate, LV function, and biochemical parameters (glucose, troponin, and creatinine)[14]. Our study showed that troponin values were significantly higher in severe ischemic stroke patients. Chang et al.[25] observed that cardiac biomarkers, especially serum troponin levels, were related with acute large-vessel occlusion in ischemic stroke patients. Lindsberg et al. observed elevated blood glucose was frequent in the early period of the stroke[26]. Blood glucose levels were significantly higher in severe stroke patients during admission in our study. Also, E/é' value was significantly higher in severe stroke patients. Ryu et al.[27] suggested that E/e' ratios were related with acute arterial occlusion in AF-associated stroke and may play an important role in recognizing patients at high risk of severe stroke. Our study showed that creatinine levels were significantly higher in severe stroke patients. Mostofsky et al.[28] demonstrated that underlying risk factors for cardiovascular diseases, including age, diabetes mellitus, hypertension, and left ventricular hypertrophy, may represent an important vascular pathogenesis resulting from impaired renal clearance. Renal function is a very important predictor of survival in AIS patients.

CONCLUSIONS

The results of our study suggest that LALS is associated with stroke severity in AIS patients upon admission. LALS can evaluate LA myocardial function and stress in patients with acute neurological diseases. LALS can detect early atrial myocardial dysfunction. Therefore, this study suggests that LALS can detect early LA myocardial dysfunction in AIS patients.

AUTHORS' CONTRIBUTIONS

UO: Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **OO:** Conceptualization, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing.

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