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Myocardial Dysfunction in Patients with Acute Ischemic Stroke Assessed by Echocardiogram

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1. Abstract

Stroke has considerable impacts on sensorimotor and autonomic nervous system that eventually influences on cardiovascular function and myocardial function is utmost important during rehabilitation of stroke patients. The purpose of this study was to evaluate myocardial dysfunction in acute ischemic stroke patients by comparing echocardiographic data with those of control subjects. Out of total 248 subjects enrolled in this study, 124 patients who suffered from first-ever ischemic strokes and assessed by echocardiography within 7 days after onset were allocated to the stroke group. Age and gender matched 124 individuals were selected for the control group from the regular hospital check-up data. The echocardiographic data of the left ventricular systolic and diastolic function were obtained in detail for both groups. There was no significant difference in the left ventricular ejection fraction, left ventricular internal diameter at end diastole, or left ventricular internal diameter at end systole between the stroke and control groups. However, stroke patients showed statistically significant increases in early diastolic transmitral velocity/peak early diastolic mitral annular velocity ratio (E/e' ratio) and left atrial volume compared to control subjects. Increases in cardiac stiffness during the relaxation phase were significant in acute phase of ischemic stroke patients. Assertive evaluation of myocardial dysfunction should be performed during rehabilitation of stroke patients as well as provision of proper cardiac rehabilitation.

2. Introduction

Stroke causes abnormalities in overall physiological function of the body, thus, it results not only in sensorimotor abnormalities, but also in various autonomic nervous system dysfunction including neurogenic bladder and bowel, and cardiac dysfunction such as ventricular tachycardia [1]. Not only the motor symptoms after stroke characterized as upper motor neuron syndrome that leads to a loss of motor function and increase in reflex and muacle tone [2], autonomic nervous system dysfunction after stroke also could influence the myocardial system. According to a study by Baronn et al, total cardiac autonomic innervation decreased after stroke of either hemisphere due to significant reduction of parasympathetic innervation [3]. The autonomic nervous system abnormality quickly followed by a stroke, which includes orthostatic hypotension, ischemic heart disease, deep vein thrombosis, pulmonary embolism, and autonomic dysreflexia [4-7]. It was evident that the hazard ratio of all cardiovascular events increased in patients with Left Ventricular (LV) diastolic dysfunction and elevated LV filling pressure [8], therefore, it should be important to diagnose LV dysfunction as early as possible after stroke to prevent further cardiac event.

In this study, we retrospectively analyzed echocardiographic findings obtained from stroke patients for delineating early myocardial dysfunctions after ischemic stroke. Specifically, diastolic dysfunctions such as LV stiffness and LV filling pressures were precisely

assessed by using echocardiographic measures [9].

3. Methods

3.1. Subjects

The medical records of 124 patients with acute cerebral infarction, corresponded to code I63 based on the International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD-10), who received inpatient treatment between February 2013 and January 2014 and underwent echocardiograms within 7 days after stroke onset were reviewed retrospectively. Mean duration after stroke onset to echocardiogram was 3.22 days (standard deviation ± 4.4 days). The exclusion criteria were accompanying underlying myocardial disease such as Myocardial Infarction (MI), valvular disease, and heart failure that may independently affect examinations. However, patients with hypertension or Atrial Fibrillation (AF) without known heart failure and angina without MI were included. In order to obtain the most efficiency, we designed a randomly matched case-control study. The matching pool for the control group included 124 adults without histories of stroke who visited the health inspection center for regular check-ups. Each subject in the control group was matched with stroke subjects in terms of age, sex, and underlying disease. The echocardiographic data of the control group were obtained during the same period at the same hospital. The control group also had similar proportions of underlying diseases such as hypertension, Diabetes Mellitus (DM), and AF. Echocardiographic data for 248 subjects were finally analyzed in this study.

Our institutional review board approved the study protocol and its implementation. The Institutional Review Board also approved the exemption of consensus on the medical record information collection of each patient. Security of personal information and research results were maintained by substituting the name and ID of patients with a subject code in a different format.

3.2. Echocardiographic Measurement

Two-dimensional trans-thoracic echocardiography and Doppler measurements were performed by certified cardiologists in all participants for both stroke and control groups using a Philips-iE33 Ultrasound system and transducer (Yorba Linda, CA, USA). Subjects were positioned in the left decubitus position if possible and two Dimensional (2D) image, color M-mode, and tissue Doppler were performed in apical four-chamber view.

The left heart indices including the Left Atrium (LA) volume, the diameter of the LV at the systolic phase (LVIDs), and the diameter of LV at the diastolic phase (LVIDd) were measured. In order to assess the systolic function of the LV, the LV ejection fraction was measured on color M-mode of the echocardiogram. To assess LV diastolic function, the early diastolic trans-mitral velocity (E wave), late diastolic trans-mitral velocity (A wave), and peak early diastolic mitral annular velocity (e') were measured using tissue Doppler of the echocardiogram, and then the E/A ratio and the E/e' ratio data were calculated (Figure 1).

3.3. Statistical Analysis

The eight parameters measured in this study were analyzed by McNemar's test for proportions or independent t-tests for mean values as appropriate to compare the stroke group with the control group. Statistical significance was set at a p value less than 0.05. The statistical package SPSS for Windows version 14.0 was used for all analyses.

4. Results

4.1. Subject Characteristics

Demographic and clinical characteristics of 124 stroke patients and 124 healthy subjects are shown in (Table 1). The average age was 66.02 ± 15.22 years in the stroke group and 68.0 ± 14.71 years in the control group, and there was no significant difference between the two groups. The percentage of males in the two groups was the same at 43.55% (54 males). There were no significant differences in proportion of underlying medical diseases such as hypertension, DM, AF, and angina.

4.2. Differences in Echocardiogram

Although no significant differences were observed between the two groups in the LV ejection fraction, LVIDs, or LVIDd through color M-mode, there was a significant difference in LA volume between groups. In the stroke group, LA volume was 28.83 ± 15.32ml/m, whereas it was 23.82 ± 12.86ml/m ($p<0.05$) in the control group. Furthermore, the E/A ratio and the E/e' ratio were significantly different between the stroke and control groups. The average values were 0.93 ± 0.38m/s and 0.76 ± 0.22m/s for the E wave ($p<0.05$), 1.25 ± 0.66 and 0.92± 0.44 for the E/A ratio ($p<0.05$), 14.35 ± 7.99 and 11.93 ± 4.72 for the E/e' ratio ($p<0.05$) in the stroke and control groups, respectively (Table 2).

5. Discussion

In this study, we demonstrated significant end-diastolic dysfunction of LV in early stage of ischemic stroke by echocardiographic evaluation, which might give insight for importance of monitoring myocardial dysfunction during rehabilitation phase of these patients. Stroke can also influence the cardiovascular system due to autonomic dysfunction and decreased vagal activity, which eventually cause cardiac rhythm dysfunctions [10-12]. Echocardiograms are the most effective tool available to reveal the causes of stroke in patients without occlusive cerebrovascular disease [9], and also used for precise measurement of the specific myocardial dysfunctions. In Doppler echocardiogram, the ratio of E to e' was related to end-diastolic pressure of the LV [13, 14]. These specific parameters of echocardiogram have high sensitivity for detecting relaxation impairment and showing stiffness in cardiac muscle [15-17]. In this study, the stroke group showed inadequate cardiac relaxation and increased cardiac muscle stiffness during the relaxation phase of the LV, as revealed by increased LA volume

and increased E/e' ratio. Increased LA maximum volume provides important diagnostic and prognostic information about the cardiac muscle stiffness of the LV [17,18]. The E/e' ratio is an important age-independent variable that is useful for determining LV relaxation function [17]. An E/e' ratio greater than 14 reflects high specificity for increased LV filling pressure and supports the relaxation of abnormalities or cardiac stiffness [17].

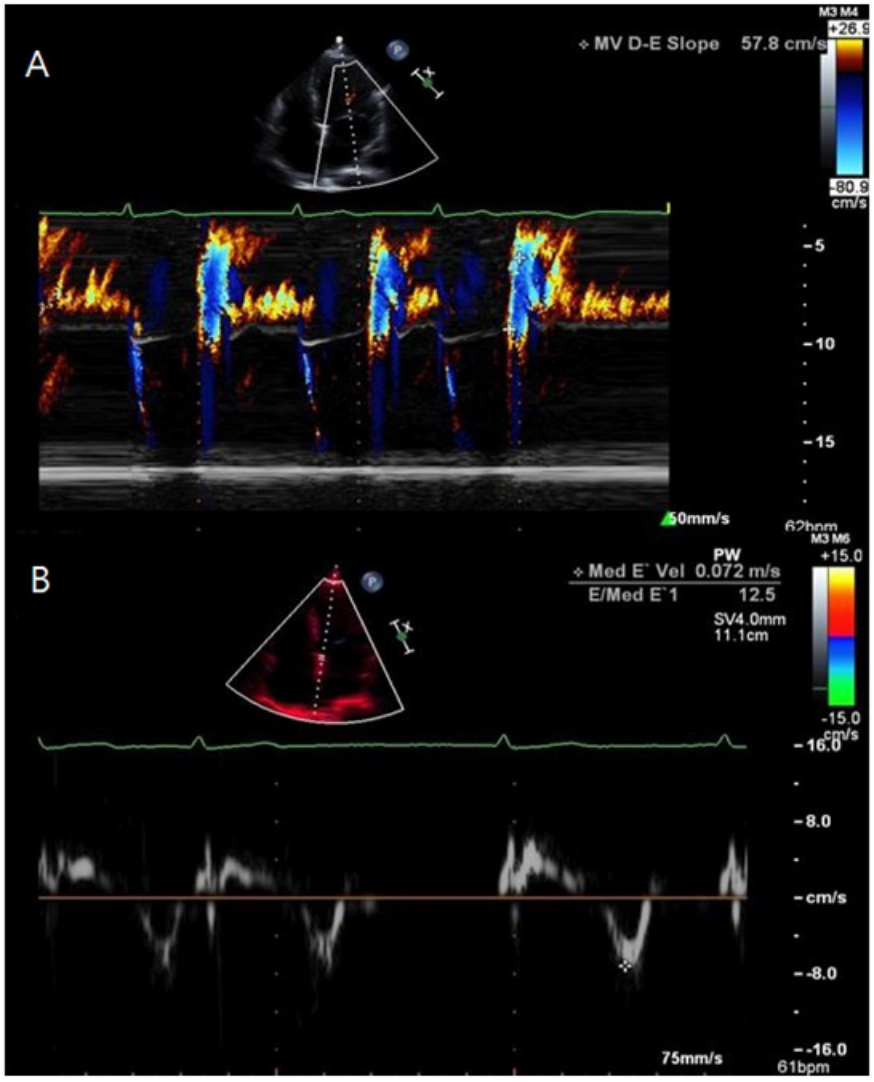

Figure 1: M-mode and tissue Doppler echocardiographic recording examples. (A) Regional wall motion abnormalities were assessed by a visual technique. The left atrium (LA) with left ventricular (LV) volume and LV ejection fraction (EF) were recorded by color M-mode echocardiogram. (B) E/e' ratio and E/A ratio were measured by two-dimensional color-coded tissue Doppler imaging.

Table 1: Demographic and Clinical Characteristics of Participants

	All (n=248)	Stroke group (n=124)	Control group (n=124)	*p*-value
General Characteristics				
Age, yrs.	67.00 ± 15.36	68.0 ± 14.71	66.02 ± 15.22	0.623
Range	20 - 96	20 – 96	22 – 92	
Male (%)	108 (43.55)	54 (43.55)	54 (43.55)	1
Alcohol drinking	39	22	17	0.316
Height (cm)	162.26 ± 9.26	162.66 ± 8.62	162.37 ± 9.47	0.789
Weight (kg)	63.88 ± 11.14	63.14 ± 10.76	63.88 ± 10.88	0.572
BMI	24.16 ± 3.85	23.91 ± 3.40	24.11 ± 4.03	0.652
Onset to exam period (days)	-	3.22 ± 4.4	-	
Underlying disease				
Hypertension (%)	142 (57.25)	69 (55.64)	73 (58.87)	0.56
Diabetes mellitus (%)	72 (29.03)	37 (29.83)	35 (28.22)	0.812
Atrial fibrillation (%)	36 (14.51)	17 (13.70)	19 (15.32)	0.701
Angina (%)	28 (11.29)	16 (12.90)	12 (9.67)	0.438

Data are expressed as mean ± standard deviation (SD) or n (%).

Table 2: Comparison of Echocardiographic Parameters Between the Stroke and Control Groups

Echocardiographic modes	Stroke group (n=124)	Control group (n=124)	*p*-value
Doppler mode			
E (mean ± SD), m/s	0.93 ± 0.38	0.76 ± 0.22	0.000*
A (mean ± SD), m/s	0.76 ± 0.33	0.81 ± 0.21	0.256
E/A ratio (mean ± SD)	1.25 ± 0.66	0.92 ± 0.44	0.000*
E/e' ratio (mean ± SD)	14.35 ± 7.99	11.93 ± 4.72	0.002*
M-mode / 2D			
LVEF (mean ± SD), %	66.39 ± 9.15	65.28 ± 9.15	0.711
LA volume (mean ± SD), ml/m	28.83 ± 15.32	23.82 ± 12.86	0.003*
LVIDd (mean ± SD), mm	46.63 ± 5.56	46.92 ± 6.97	0.683
LVIDs (mean ± SD), mm	29.57 ± 5.60	30.00 ± 6.63	0.537

Values are shown as mean ± standard deviation (SD).

E: Early diastolic transmitral velocity, A: Late diastolic transmitral velocity, e': Peak early diastolic mitral annular velocity. LVEF: Left ventricular ejection fraction, LA: Left atrium, LVIDd: Left ventricular internal diameter at end diastole, LVIDs: Left ventricular internal diameter at end systole.

*$p < 0.05$, according to independent t-test

In addition, the E/A ratio that shows a strong inverse relationship with age [19] was higher in the stroke group than the control group. An E/A ratio < 1.0 is usually interpreted as a relaxation pattern of diastolic dysfunction while an E/A ratio>1.5 is interpreted as a restrictive pattern [15,16]. Since there was no age difference between groups, increased E/A ratio in the stroke group might be interpreted as increased cardiac muscle stiffness progressing towards a restrictive pattern [15,16]. The cause of increased stiffness of cardiac muscle during relaxation phase in stroke patients were uncertain, nonetheless, multiple factors such as autonomic dysfunction or excitability change of cardiac musculature due to upper motor neuron dysfunction could be considered. In any case, careful follow up of myocardial dysfunction with provision of proper cardiac fitness training might be important during the rehabilitation phase.

Early exercise on stroke patients is still in controversy. However, depending on exercise type, intensity, and initiation time, exercise could give benefit by generating neuroprotection [20]. A study reported that supervised endurance and resistance exercise in patients with diastolic heart failure showed significantly decreased E/e' ratio and LA volume, which means exercise improved myocardial dysfunction [21]. In this view, proper cardiac rehabilitation for ischemic stroke patient should be considered in early phase along with neurologic rehabilitation, especially in patients who showed diastolic dysfunction in acute stage of stroke.

The main limitation of this study is that our sample size was not large enough to compare each echocardiographic measure between subgroups of stroke according to the initial severity or location of the stroke lesion. Another limitation is that no direct measurements of myocardial stiffness were performed since such measurements would have been too invasive. Instead, we used only a non-invasive method. Finally, each patient's echocardiogram was performed once during the first week after stroke without follow-up examination. The follow-up echocardiograms will give us more information about the subsequence of myocardial dysfunction during the subacute or chronic phase of stroke patients after rehabilitation.

6. Conclusions

We observed increased cardiac stiffness in relaxation phase of acute ischemic stroke patients Such increased cardiac stiffness can exert a negative influence on cardiopulmonary fitness during rehabilitation. Therefore, assertive evaluations and careful follow up of myocardial function should be performed in stroke patients to prevent further cardiac dysfunction such as heart failure.

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