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Relationship between left atrial spontaneous echo contrast and the features of middle cerebral artery territory in nonvalvular atrial fibrillation

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Summary. We investigated the relationship between left atrial spontaneous echo contrast (SEC) and cerebrovascular features in nonvalvular atrial fibrillation (NVAF). Few reports have been published to compare cardiac and cerebrovascular imaging in patients with NVAF. Forty-four patients with NVAF were studied using transesophageal echocardiography and noninvasive imaging including magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and transcranial color Doppler imaging (TCD) in the middle cerebral artery (MCA) territory. The symptomatic severity was divided into asymptomatic, transient ischemic attack (TIA), and stroke. The severity of the MRI findings was divided into normal, small, and large infarcts. The severity of the MRA findings was divided into normal, attenuation, and occlusion. MCA was bilaterally scanned and a side-to-side asymmetry ratio of pulsatility index (PI) was measured. The severity of SEC was divided into normal, SEC, and thrombi. Five patients with other thromboembolic risk or poor results of TCD were excluded. SEC and thrombi were detected in 12 (30%) and in 3 patients (5%), respectively. TIA and stroke were detected in 8 (21%) and in 17 patients (44%), respectively. Small and large infarcts were detected in 9 (23%) and in 18 patients (46%), respectively, on MRI. Attenuation and occlusion were detected in 14 (36%) and in 8 patients (21%), respectively, on MRA. PI ratio was 1.21 ± 0.25. SEC severity was highly associated with PI ratio and MRA severity in monovariate analysis ($P < 0.005$), $P < 0.01$, respectively). SEC severity was highly associated with PI ratio and MRA severity in stepwise multiple regression analysis ($P = 0.0001$, $r = 0.630$, $n = 39$). In patients with NVAF, left atrial SEC was highly related to attenuation or occlusion on MRA and imbalance of cerebral blood flow on TCD in the MCA territory.

Key words: Spontaneous echo contrast – Cerebrovascular imaging – Nonvalvular atrial fibrillation

Introduction

Detection of left atrial spontaneous echo contrast (SEC) using transesophageal echocardiography (TEE) and evaluation of the cerebrovascular disease is helpful for the management of nonvalvular atrial fibrillation (NVAF). In many previous studies of SEC in NVAF, natural history and anticoagulation were the main topics discussed [1–6]. However, the relationship between left atrial SEC and the details of neurological imagings in NVAF were not described. We compared the severity of SEC and of cerebrovascular features in the middle cerebral artery (MCA) territory evaluated by magnetic resonance image (MRI), magnetic resonance angiography (MRA), and transcranial color Doppler imaging (TCD) in patients with NVAF. The aim of this study was to clarify the relationship between SEC and cerebrovascular characteristics evaluated by several noninvasive methods.

Subjects and methods

Forty-four consecutive patients with NVAF confirmed by the results of Holter monitoring of electrocardiography were examined by transthoracic echocardiography, TEE, sonography of the carotid artery, TCD, MRI, and MRA. All the examinations were completed within 4h in each patient. This study was approved by

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the local institutional review board and informed consent was obtained from each patient.

Sonography and Doppler measurements

Transthoracic echocardiography, TEE, sonography of carotid artery, and TCD were performed using an echocardiographic system (Sonolayer SSA-260A, Toshiba, Tokyo, Japan). Left atrial dimension and ejection fraction was measured using a 3.75-MHz probe (PSH-37LT, Toshiba) [7]. Bilateral carotid arteries were examined to evaluate the carotid arterial disease with a 7.5-MHz linear probe (PLF-703NT, Toshiba). The horizontal part of MCA (M1) was bilaterally scanned through the temporal windows using a 2.5-MHz probe (PSH-25GT, Toshiba). Pulsatility index (PI) was measured as (maximum velocity-end-diastolic velocity)/mean velocity. The side-to-side asymmetry ratio was calculated and the maximum asymmetry of PI was expressed as the PI ratio. The left atrium was observed using a biplane TEE technique (5 MHz, PEF-507SB, Toshiba) under local nasopharyngeal anesthesia. The presence of SEC was confirmed by decreasing the gain settings to exclude background noise. Left atrial characteristics were divided into normal, SEC, and thrombi (SEC severity) [8–10]. Left ventricular ejection fraction and Doppler measurements were expressed as the average value obtained at 5 beats of the signals. All data were collected and analyzed by a single investigator (K.K.).

MRI and MRA

Brain MRI and cerebrovascular MRA were performed immediately after the sonographic investigations (MR Vectra 0.5 T, Yokogawa, Japan. T1 weight: spin echo technique; T2 weight: fast spin echo technique; 2-D MRA: time-of-flight method). The findings of MCA territory were divided into normal, small infarcts (less than 1 cm in diameter), and large infarcts (more than 1 cm in diameter) (MRI severity). The findings of MRA were divided into normal, attenuation, and occlusion (MRA severity). All the findings were evaluated by a single neurologist (K.M.) and were blinded until later statistical analysis.

Patient characteristics

Neurological events were reviewed from previous medical records. Neurological symptoms were divided into asymptom confirmed by the Mini-Mental State Examination, previous history of transitional ischemic attack (TIA) without the presence of neurological deficit, and previous history of stroke with the presence of focal neurological deficit (neurological severity) [11, 12]. The effects of anticoagulants were categorized into no medication, mild (antiplatelets only or INR $\leqq 3$), and excellent (INR > 3) [13]. The medical records of all patients were reviewed to determine the following clinical features: age, associated disease (diabetes, hyperlipidemia, and hypertension), and duration of atrial fibrillation. Excluded criteria were the presence of congestive heart failure, previous myocardial infarction, patients with ejection fraction less than 30%, mitral valve disease, left ventricular aneurysm, atrial septal defect, protruding aortic atheromas, and carotid artery disease. Thus, one patient with moderate mitral regurgitation due to anterior mitral leaflet prolapse, one patient with both protruding atheromatous change in aortic arch and with 50% stenosis in the right common carotid artery, one patient with previous myocardial infarction, and two patients whose TCD signals were apparently unclear were excluded.

Statistical analysis

We analyzed the data obtained from 39 patients, comprising 27 men (69%) and 12 women (31%). Continuous variables were expressed as mean value ± SD with its range. Monovariate analysis was performed using the chi-squared and Kruskal-Wallis tests. A commercially available, computerized statistical package was used for the mutivariate analysis (Stat View-4.5J, Abacus Concepts, CA, USA). Stepwise multiple regression analyses with were used to determine the effect of independent variables on a continuous dependent variable. We considered results significant when P was less than 0.05.

Results

All the data are summarized in Tables 1 and 2. Ages ranged from 48 to 85 years (70 ± 9 years). SEC and thrombi were detected in 12 (30%) and 3 patients (5%), respectively. TIA and stroke were detected in 8 (21%) and 17 patients (44%), respectively. Small infarcts were detected in 9 patients (23%) and large infarcts in 18 patients (46%) on MRI. Attenuation was detected in 14 patients (36%) and occlusion in 8 patients (21%) on MRA. The maximum PI ratio was 1.21 ± 0.25. In the monovariate analysis, MRA severity and the PI ratio were highly associated with SEC severity ($P < 0.005$ and $P < 0.01$, respectively) (Figs. 1 and 2). Stepwise multiple regression analyses were used to determine the effect of independent variables including age, sex, associated disease (diabetes, hyperlipidemia, and hypertension), the effect of anticoagulation, V_{max} ratio, PI ratio, and neurological-, MRI- and MRA-severity scores on a continuous dependent variable (SEC severity). SEC severity was significantly associated with the PI ratio and MRA severity ($P = 0.0001$, $r = 0.630$, $n = 39$).

Discussion

Because MCA is a main cerebral artery, which covers 80% of the white matter, and is the most reliable and accurate object for the TCD measurements, findings of the MCA territory have been analyzed [14, 15]. We defined the scores of the neurological symptoms, anticoagulation, and cerebrovascular imagings, all of which were divided into three categories. Stepwise multiple regression was chosen for the statistical analysis among the scores.

A simple measure of the severity of cerebral infarction is needed to perform a statistical analysis among several imaging studies. Previous reports demonstrated the usefulness of volume measurement for symptomatic large infarction on brain MRI [16]. However, it is difficult to express the severity of multiple lacunar-type

Table 1. Patient characteristics and echocardiographic measurements ($n = 39$)

Patient characteristics	
Age	70.4 ± 9.0 years (48–85 years)
Duration of atrial fibrillation	44.9 ± 38.7 months (0–142 months)
Chronic atrial fibrillation	26 patients (67%)
Diabetes	8 patients (20.5%)
Hyperlipidemia	7 patients (5%)
Hypertension	25 patients (64%)
Echocardiography	
Left atrial dimension	41 ± 5.4 mm (31–50 mm)
Ejection fraction	61.6% ± 8.7% (41%–67%)

Data presented are mean ± SD and its range or number (%) of patients

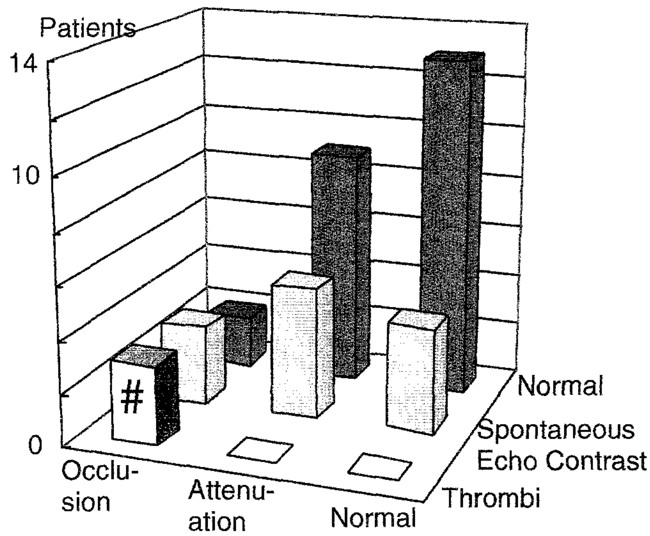

Fig. 1. In chi-squared analysis, magnetic resonance angiography severity was highly associated with spontaneous echo contrast (SEC) severity ($^{\#}P < 0.005$)

Table 2. Left atrial spontaneous echo contrast and findings of middle cerebral artery territory in 39 patients

Left atrial spontaneous echo contrast	Normal (n = 24)	SEC (n = 12)	Thrombi (n = 3)
Effect of anticoagulation			
None	10	4	2
Mildly effective	11	8	0
Excellent effectiveness	3	0	1
Transcranial Doppler			
PI ratio	1.0–1.4	1.0–2.2	1.3–1.5
Neurological severity			
Asymptom	11	3	0
TIA	6	2	0
Stroke	7	7	3
Magnetic resonance imaging			
Normal	10	2	0
Small infarcts	8	3	0
Large infarcts	6	7	3
Magnetic resonance angiography			
Normal	13	4	0
Attenuation	9	5	0
Occlusion	2	3	3

Data presented are number of patients or range of PI ratio. PI ratio = side-to-side asymmetry ratio of pulsatility index of middle cerebral artery. TIA, transient ischemic attack

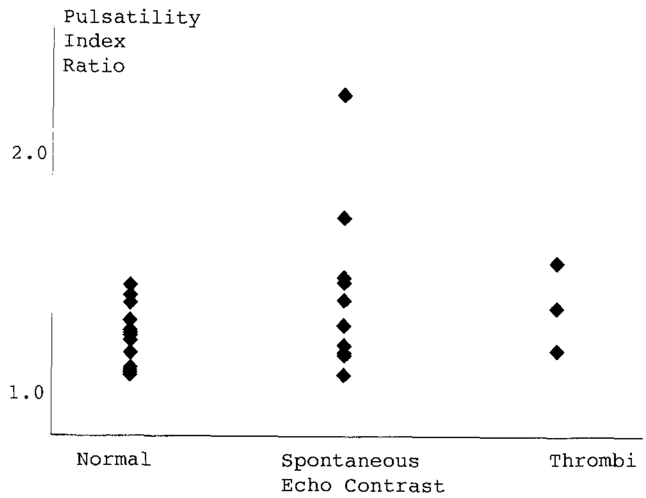

Fig. 2. In Kruskal-Wallis analysis, the pulsatility index ratio was highly associated with SEC severity ($P < 0.01$)

infarction. Because a focal lesion of more than 1 cm in diameter can be easily distinguished from the lacunar-type infarction, MRI severity was classified into three categories as described above. The manifestations of thromboembolism in NVAF are as follows: large infarction with severe neurological deficit, thromboembolism in a large cerebral artery, and high possibility of recanalization [1–5]. Thus, not only evaluation of the focal lesion by MRI but that of the vascular features is needed to assess the severity of cerebrovascular disease associated with NVAF.

MRA and TCD are considered to be complementary techniques in cerebrovascular imaging. MRA is a standard noninvasive technique and an alternative method to cerebrovascular angiography. However, it is difficult to determine the accurate location or severity of stenosis. Thus, we simply classified the arterial features as described previously [17]. Color flow imaging (CFI) of the intracranial vessels is a new method and an alternative approach to the conventional TCD technique which has been the standard for cerebral blood flow monitoring for years [15, 18, 19]. More accurate and reproductive Doppler signals are confirmed by using the B-mode function of CFI. Among the TCD-derived measurements, the PI value is a reliable tool for estimating the vascular resistance and blood flow without the interference of changing blood pressure [15, 20]. The side-to-side asymmetry ratio of PI can predispose the side-to-side imbalance of cerebral blood flow [21].

Neurological severity and MRI severity were not significantly associated with SEC severity. Recanalization in the acute stage of thromboembolism in NVAF would explain this discrepancy between the MRA and MRI findings in NVAF patients. However, in the 22 patients with attenuation or occlusion of M1 on MRA, 2 patients had no history of thromboembolic events and no infarcts on MRI. Thus, we could not conclude that these arterial lesions were due to the presence of intracranial arteriosclerotic lesions or were caused by the microscopic emboli which were detected as circulating embolic signals by TCD monitoring.

In our statistical analysis, cerebral arterial attenuation or occlusion on MRA and imbalance of cerebral arterial blood flow on TCD were frequently observed in the patients with left atrial SEC. In the management of NVAF, our results suggest that cerebrovascular features should be investigated in patients with SEC. More clinical trials, including anticoagulation, arteriosclerotic lesions, circulating embolic signals, natural history, and neurological findings versus brain and cerebrovascular imagings are needed to clarify cerebrovascular lesions in patients with NVAF.

References

1. Stroke Prevention in Atrial Fibrillation Investigators (1991) Stroke prevention in atrial fibrillation study. Circulation 84:527–539
2. European Atrial Fibrillation Trial Study Group (1993) Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. Lancet 342:1225–1263
3. Jorgensen HS, Nakayama H, Reith J, Raaschou HO, Olsen TS (1996) Acute stroke with atrial fibrillation. The Copenhagen stroke study. Stroke 27:1765–1769
4. Wolf PA, Abbott RD, Kannel WB (1991) Atrial fibrillation as an independent risk factor for stroke: the Framingham study. Stroke 22:983–988
5. Stroke Prevention in Atrial Fibrillation Investigators (1992) Predictors of thromboembolism in atrial fibrillation: I. Clinical features of patients at risk. Ann Intern Med 116:1–5
6. Tsai LM, Chen JH, Lin LJ, Teng JU (1997) Natural history of left atrial spontaneous echo contrast in nonrheumatic atrial fibrillation. Am J Cardiol 80:897–900
7. Stroke Prevention in Atrial Fibrillation Investigators (1992) Predictors of thromboembolism in atrial fibrillation: II. Echocardiographic features of patients at risk. Ann Intern Med 116:6–12
8. Chimowitz MI, DeGeorgia MA, Poole RM, Hepner A, Armstrong WA (1993) Left atrial spontaneous echo contrast is highly associated with previous stroke in patients with atrial fibrillation or mitral stenosis. Stroke 24:1015–1019
9. Black IW, Fatkin D, Sagar KB, Khandheria BK, Leung DY, Galloway JM, Feneley MP, Walsh WF, Grimm RA, Stollberger C (1994) Exclusion of atrial thrombus by transesophageal echocardiography does not preclude embolism after cardioversion of atrial fibrillation. Circulation 89:2509–2513
10. Pohjasvaara T, Erkinjuntti T, Vataja R, Kaste M (1997) Comparison of stroke features and disability in daily life in patients with ischemic stroke aged 55 to 70 and 71 to 85 years. Stroke 28:729–735

11. Black IW, Hopkins A, Lee LC, Walsh WF (1991) Left atrial spontneous echo contrast: a clinical and echocardiographic analysis. J Am Coll Cardiol 18:398–404
12. Fillenbaum GG, George LK, Blazer DG (1988) Scoring nonresponse on the Mini-Mental State Examination. Psychol Med 18:1021–1025
13. Fuster V, Verstraete M (1997) Hemostasis, thrombosis, fibrinolysis and cardiovascular disease. In: Braunwald (ed) Heart disease, 5th edn. Saunders, Philadelphia, pp 1830–1832
14. Heinsius T, Bogousslavsky, Van Melle G (1998) Large infarcts in the middle cerebral artery territory. Etiology and outcome patterns. Neurology 50:341–350
15. Otis SM, Ringelstein EB (1996) The transcranial Doppler examination: principles and applications of transcranial Doppler sonology. In: Tegeler CH, Babikian VL, Gomez CR (eds) Neurosonology. Mosby, St. Louis, pp 113–128
16. Saunders DE, Clifton AG, Brown MM (1995) Measurement of infarct size using MRI predicts prognosis in middle cerebral artery infarction. Stroke 26:2272–2276
17. Kenton AR, Martin PJ, Abbott RJ, Moody AR (1997) Comparison of transcranial color-coded sonography and magnetic resonance angiography in acute stroke. Stroke 28:1601–1606
18. Baumgartner RW, Arnold M, Gonner F, Staikow I, Herrmann C, Rivoir A, Muri RM (1997) Contrast-enhanced transcranial color-coded duplex sonography in ischemic cerebrovascular disease. Stroke 28:2473–2478
19. Knappertz VA, Tegeler CH (1996) Color flow imaging. In: Tegeler CH, Babikian VL, Gomez CR (eds) Neurosonology. Mosby, St. Louis, pp 113–128
20. Zbornikova V (1997) Different flow patterns in infarction of the middle cerebral artery. J Neuroimag 7:69–77
21. Mayer SA, Thomas CE, Diamond BE (1996) Asymmetry of intracranial hemodynamics as an indicator of mass effect in acute intracerebral hemorrhage. A transcranial Doppler study. Stroke 27:1788–1792