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☐ Original Article ☐

MRI Features of Infarcts with Potential Cardiac Source of Embolism in the Yonsei Stroke Registry (YSR), Korea

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Abstract

The determination of the embolic source is crucial to understanding the pathogenesis of ischemic stroke, the initiation of appropriate therapy, and the prevention of recurrent infarctions. In this study we undertook to identify the characteristic features on magnetic resonance images of patients who had suffered from stroke due to cardiac embolism (CE), as classified by TOAST (possible and probable). We retrospectively studied magnetic resonance imaging (MRI) findings of patients with ischemic stroke from the Yonsei Stroke Registry (YSR). On the basis of the TOAST classification, 92 patients were identified to have a potential cardiac source of embolism (PCSE), in which 69 patients were found to have high-risk PCSE and 23 patients medium-risk PCSE. To compare their imaging characteristics, another group of 49 patients who were found to have had a stroke due to large artery-to-artery (ATA) embolism-common or internal carotid artery (CCA, ICA)-were identified. Involvement of the simultaneous superficial and deep territories (58.7%; 6.1%, $p<0.001$), and combined new anterior and old posterior circulation (15.2%; 2.0%, $p=0.016$) were more frequent in PCSE than ATA embolism. Bilateral anterior hemispheric involvement was also more frequent in the PCSE group, but it did not reach statistical significance (13.0%; 4.1%, $p=0.090$). ATA embolism tended to involve only superficial territories compared to PCSE (71.4%; 28.3%, $p<0.001$). There were no topographic differences between the high-risk and medium-risk groups. With respect to the etiology of PCSE in our population, atrial fibrillation was the most common. Characteristic MRI features of patients with PCSE, which were not documented previously by computed tomography (CT) included: old and new, involvement of multiple different vascular territories, bilateral anterior hemisphere, as well as anterior and posterior circulation. These MRI features, together with simultaneous superficial and deep territorial involvement, help to differentiate the underlying embolic sources, whether they are cardiac or ATA in origin.

Key Words: Cerebral infarction, potential cardiac source of embolism, MRI

INTRODUCTION

Cardioembolic stroke represents the second most common cause of cerebral infarctions next to artery-to-artery (ATA) embolism due to extracranial large-artery atherosclerosis.[1] Since the prevention of stroke and the treatment of acute cerebral infarction depends upon the etiology, proper subtype classification of cerebral infarction based on the identifiable causes becomes an issue of key importance. The correct etiological subtype diagnosis of ischemic stroke often requires a thorough laboratory evaluation, which includes cerebral angiography and transesophageal echocardiography, which are not readily available during the acute stage of stroke. Therefore, the identification of the characteristic features of either cardiac or ATA embolism by MRI conducted at the time of evaluation is important for the appropriate management of ischemic stroke.[2]

Although many authors have reported some characteristic radiological features of CE patients on CT scan,[3-5] we wanted to clarify these issues on MRI. A few reports have attempted to differentiate between PCSE and ATA embolism or determine that PCSE is absent on the basis of CT findings alone.[5-8] However, for more precise topographic analysis, we analyzed MRI findings in both PCSE and ATA embolism groups. In addition, we tried to determine if there were any differences between high-risk and lower-risk groups in PCSE, as performed in a previous report.[6]

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MATERIALS AND METHODS

The Yonsei Stroke Registry (YSR), a prospective hospital-based stroke registry and data bank, contained 879 patients who were admitted with acute cerebral infarct ($\leq$1 week from onset) for the period Oct. 1994 to June 1998. The standard protocol of YSR has includes history, physical examination, neurological examination, standard blood tests, and brain CT. MRI screening, including diffusion-weighted imaging (DWI), magnetic resonance angiography (MRA), digital subtraction angiography (DSA), transcranial doppler ultrasonography (TCD), transthoracic echocardiography (TTE) or transesophageal echocardiography (TEE) were performed according to the various clinical conditions of patients. A subtype classification of acute cerebral infarction was adopted according with the TOAST classification.

Among 879 patients enrolled at the YSR, 92 patients with PCSE were found to have had MRI and to have new lesions in the territory of anterior circulation. Another 49 patients were identified by MRI to have acute lesions in the anterior circulation due to ATA embolisms, as evidenced by a lack of PCSE and stenosis of more that 50% of the thickness of arterial lumen or deep ulceration of more than 2 mm in the relevant extracranial large artery (CCA, ICA) in DSA/MRA. We excluded posterior circulation infarct because the vertebrobasilar artery was difficult to accurately grade for degree of stenosis, and also excluded patients with total obstruction of CCA and ICA because of the possibilities of hemodynamic extra-territorial infarct[9] or cardioembolic obstruction.[10] The grading of stenosis was based on the NASCET protocol.[11] Nine patients were excluded due to coexisting large artery atherosclerosis and PCSE.

Using a previously reported protocol,[12] PCSEs were divided into high-risk and medium-risk groups. Patients with two or more cardiac risks, including high-risk sources, were assigned to the high-risk group. According to a previous report,[13] lone atrial fibrillation was defined when; patients were younger than 60 years of age, and there was no evidence of other heart disease, hypertension, or prior thromboembolism.

The topography of infarcts was based on high signal intensity in T2-weighted images. To minimize the potential for bias in the MRI description, two members of the neurology staff and two members of the neuroradiology staff reviewed the MRI and MRA/DSA images. Symptomatic lesions were selected from old and multiple lesions according to the clinical manifestations and high signal intensity on DWI, which was performed in 48 of 92 patients (51.2%). Infarcts in the middle cerebral artery (MCA) were divided into the following categories: deep, superficial, simultaneously superficial and deep, as well as the superior, inferior and combined superior and inferior divisions of MCA. Other topographical characteristics of the old and new cerebral infarctions associated with the involvement of vascular territories were investigated.

The SPSS software package (SPSS for Windows, Release 7.0, 1995, Chicago, IL, USA) was used for statistical analysis. To compare the radiological features of ATA embolism and the embolisms related with PCSE, and of those of embolisms associated with high and medium-risk PCSE, Pearson's chi-square test was used to indicate trends.

RESULTS

All patients with PCSE had either a history of cardiac disease, abnormal EKGs, or abnormal TEE, with or without TTE. TEE was performed in 61 patients. Patients with PCSE were categorized into high-risk (N=69) and medium-risk (N=23) groups, according to the guidelines issued by TOAST (Table 1).[12] Atrial fibrillation with/without mitral stenosis was the most common etiology in the high-risk group and a lone atrial fibrillation was the most common etiology in the medium-risk group. MRA was performed in 3 patients and DSA in 34 patients, but no patients showed significant atherosclerotic changes of the extra and intra-cranial large vessels. These patients belonged to the 'probable' CE group, while the remaining 55 patients were classified as 'possible' CE.

In the case of the ATA embolism group, diagnosis in all patients was supported by either MRA (N=10) or DSA (N=45). These patients did not have any PCSE, and TEE and TTE performed in 20 patients were normal. These patients were classified as having large artery atherosclerosis (LA-A) by the TOAST classification.

Table 2 shows the radiological features of patients with ATA embolism and PCSE. Combined new anterior and old posterior circulation involvement

(15.2% vs 2.0%, $p=0.016$) was significantly more frequent in the PCSE group than in the ATA embolism group. Bilateral anterior hemispheric involvement was more frequent in the PCSE group than the ATA embolism group, but the difference was not statistically significant (13.0% vs 4.1%, $p=0.090$). The MRI lesions of the PCSE group also showed more frequent involvement of simultaneous superficial and deep MCA territories than the ATA embolism group, which was highly significant (58.7 vs 6.1%, $p<0.001$). On the other hand, the ATA embolism group more frequently involved only superficial territories than the PCSE group, with a high level of statistical significance (71.4% vs 28.3%, $p<0.001$). No significant differences in any topographical characteristics were found between the high and medium-risk PCSE groups. However, recurrences in the high-risk PCSE group were higher than in the medium-risk PCSE group, 34.8% and 13.0% respectively ($p=0.047$).

Table 1. Cardiac Risk Sources in Patients Assigned to High- and Medium-risk Groups

	High (N=69)	Medium (N=23)
High-risk sources		
Mechanical prosthetic valve	0	
Mitral stenosis with atrial fibrillation	15	
Non-rheumatic arial fibrillation	44	
Left atrial, atrial appendage thrombus	6	
Sick sinus syndrome	2	
Recent myocardial infarction (<4 weeks)	4	
Left ventricular thrombus	3	
Dilated cardiomyopathy	3	
Akinetic left ventricular segment	4	
Medium-risk sources		
Mitral valve prolapse	0	2
Mitral annulus calcification	4	2
Mitral stenosis without atrial fibrillation	1	3
Left atrial turbulence	3	2
Atrial septal aneurysm	0	1
Patent foramen ovale	0	3
Atrial flutter	1	0
Lone atrial fibrillation	0	10
Congestive heart failure	12	8
Hypokinetic left ventricular segment	2	4
Myocardial infarction (>4 weeks, <6 month)	2	3

DISCUSSION

Our aim was to determine any specific radiological features in embolic stroke, which are capable of discriminating the lesions associated with PCSE from ATA embolism by detailed MRI analysis.

Our study showed a statistically significant difference between combined new anterior and old posterior circulation involvement and a weak tendency of difference in bilateral anterior circulation

Table 2. Topographic Patterns in Patients with Artery-to-Artery (ATA) Embolism and Potential Cardiac Source of Embolism (PCSE)

	ATA embolism (n=49)	PCSE			
		High (n=69)	Medium (n=23)	Total (n=92)	
Bilateral anterior circulation	2 (4.1%)	8 (11.6%)	4 (17.4%)	12 (13.0%)	p=0.090
Anterior and posterior circulation	1 (2.0%)	11 (15.9%)	3 (13.0%)	14 (15.2%)	* p=0.016
ACA	3 (6.1%)	6 (8.7%)	1 (4.3%)	7 (7.6%)	
MCA and ACA	2 (4.1%)	0 (0.0%)	6 (8.7%)	6 (6.5%)	
MCA					
Superficial	35 (71.4%)	21 (30.4%)	5 (21.7%)	26 (28.3%)	* p<0.001
Superficial and deep	3 (6.1%)	42 (60.9%)	12 (52.2%)	54 (58.7%)	* p<0.001
Deep	10 (20.4%)	6 (8.7%)	5 (21.7%)	11 (12.0%)	
Upper branch	12 (24.5%)	17 (24.6%)	5 (21.7%)	22 (23.9%)	
Lower branch	9 (18.4%)	16 (23.2%)	6 (26.1%)	22 (23.9%)	
Upper and lower branch	18 (36.7%)	28 (40.6%)	6 (26.1%)	34 (37.0%)	
Prior stroke history		24 (30.4%)	3 (13.0%)		† p=0.047

ACA, anterior cerebral artery; MCA, middle cerebral artery.

* The statistical significance was seen not only between ATA embolism and PCSE, also between ATA embolism and each high-risk or medium-risk group. † Prior stroke history was much more prevalent in the high-risk group than the medium-risk group. There was no statistically significant topographic difference between the high-risk and medium-risk groups.

involvement ($p=0.090$) between PCSE group compared to the ATA embolism group. These findings are consistent with previous reports involving CT scans or autopsy study,[2,10] in which PCSE was found to have a positive association with multiple, bilateral vascular infarcts. A previous NINDS study[6] failed to confirm these issues, probably because of the use of different methodologies. With respect to the NINDS study, we used MRI instead of CT scan and the ATA embolism group as the control instead of the medium-risk group. In addition, our data showed a higher percentage of bilateral anterior and combined new anterior and old posterior circulation involvement than did the previous reports.[5,6] This result might be related to a more precise analysis, by MRI and a higher detection rate of lesions, especially in the posterior circulation.

Deep subcortical infarcts were found in 12.0% of patients in our study, which was similar to that reported in a previous study.[5] The role of hypertension in lacunar infarction has been questioned for two decades.[14] Many reports, including autopsy studies, could not exclude embolism as the possible cause of small deep infarcts in normotensive patients with PCSE.[14,15] Occasionally, a single small infarct may be caused by cardiogenic embolism, especially from valvular sources.[16]

An autopsy study by Jorgensen et al.[10] showed that cerebral infarct due to cardiogenic embolism occurs most frequently in MCA group. Other pathologic data supports this topography.[17,18] The location of infarcts in MCA differed strikingly between the two groups, which was similar to that found by Timsit et al.,[7] using CT. Superficial infarcts were only more frequent in ATA embolism, whereas combined superficial and deep territory infarcts were more frequent in embolism with PCSE. The size of the embolus and its tendency to break up and disperse into distal vessels to cause infarcts appeared to depend in part on its composition.[2] Although the nature of the embolic substances for ATA embolism and PCSE is quite heterogeneous, more recently it has been proposed that embolism from large vessels is primarily caused by white thrombus (platelet aggregates), and that embolism from the heart is mainly caused by red thrombus (platelet and fibrin aggregates).[19] In addition, the status of the collateral circulation and timing of recanalization may explain the infarct size and location, while the timing of recanalization itself mainly depends on the size and composition of the embolus.[20] These variables were not specifically investigated in our study, but more frequent involvement of combined cortical and subcortical territories in the PCSE group suggested larger emboli lodged in a more proximal arterial segment than the atherosclerotic emboli.

A previous NINDS study[6] reported that a high-risk PCSE has a tendency to have a larger infarct, and combined superficial and deep territorial involvement, than does a medium-risk PCSE, which raises a question concerning the different characteristics of emboli in the two groups. However, we could not find any differences in the topographical patterns of the two groups, which might suggest that the size or composition of the emboli were more or less identical. However, the lower recurrence rate of stroke in medium-risk PCSE than in high-risk PCSE suggests that the rate of emboli formation might be different in various cardiac diseases. The discrepancy between our results and NINDS's certainly requires further investigation.

In conclusion, our data, based on MRI study, shows that certain characteristic infarctions combine cortical and subcortical MCA infarctions and the involvement of different vascular territories simultaneously or from previous stroke, and therefore, provides important discriminatory information concerning the relationship between PCSE and ATA. We propose that future studies should also include patients with posterior circulatory involvement for a more comprehensive analysis of the MRI features of embolic infarctions related with PCSE.

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