Silent Cerebral Lesions on Magnetic Resonance Imaging in Subjects with Coronary Artery Disease

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Summary

MRI of subjects with silent intracranial damages may provide more evidence than CT. Our objectives were to determine the prevalence of silent MRI lesions in patients with coronary artery disease. The study included 72 consecutive patients with angiographically proven coronary artery disease and 26 age and sex matched controls with normal coronary angiography. All subjects were evaluated for coronary atherosclerosis (Gensini and coronary angiography scores), the number of silent cerebral lesions detected by MRI, carotid stenosis and the risk factors for stroke. Thirty one of 72 (43.0%) patients had silent brain lesions on MRI while 8 of 26 (30.7%) control subjects showed silent brain infarction. The main finding on T_2-weighted MRI was white matter hyperintensities (WMH) which were seen in all patients with silent brain lesions. The mean age of the patients with coronary artery disease and with silent cerebral lesions was significantly higher than that of patients without silent brain lesions. The Gensini score, coronary angiography score and prevalence of carotid stenosis are significantly higher in patients with silent cerebral lesions than that of patients without silent cerebral lesions. There was no significant difference between silent cerebral lesions and the other risk factors for stroke.

Silent brain lesions are a common complication in patients with coronary artery disease. In patients with coronary artery disease, carotid artery stenosis and age were important risk factors for the development of silent brain infarction. (Jpn Heart J 1998; 39: 611–618)

Key words: Silent cerebral lesion, Coronary artery disease, Magnetic resonance imaging

NEW diagnostic techniques, such as brain magnetic resonance imaging (MRI) and computed tomography (CT), have provided evidence of silent (asymptomatic) intracranial morphologic damage in subjects without any focal

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Received for publication June 15, 1998.

Accepted July 15, 1998.

neurologic abnormalities. However, MRI is more superior for the detection of asymptomatic brain lesions than CT.[1,2] Correlation between white matter lesions on T_2-weighted MRI images and age and certain risk factors for stroke has been shown in several studies.[3-6] Patients with a history of atherosclerotic disease and having risk factors for stroke are believed to be at high risk for silent brain lesions because of their vascular etiology.[7-9] So far, there has been only one prospective study showing a relation between silent cerebral lesions in subjects without any focal neurologic findings and ischemic heart disease.[9]

The aim of our study was to investigate the frequency of silent MRI lesions in patients with angiographically proven coronary artery disease.

Materials and Methods

Subjects: We prospectively studied 72 consecutive patients, 47 men and 25 women, aged between 34–71 (mean: 53.8 ± 8.3 years), admitted to the Department of Cardiology for coronary angiography because of chest pain. Furthermore, 26 age and sex matched normal control subjects (19 men and 7 women; age range 36–70 years, mean: 53.3 ± 9.1) were also prospectively investigated clinically and angiographically in the same department. The risk factors for stroke such as hypertension, diabetes mellitus, smoking, high cholesterol level, high LDL level, high triglyceride level and carotid stenosis were compared in both groups and no significant differences were found ($p = 0.64$, $p = 0.57$, $p = 0.11$, $p = 0.57$, $p = 0.08$, $p = 0.80$ and $p = 0.41$, respectively). Throughout the study the principles of the 1964 Declaration of Helsinki for clinical research were considered and informed consent was obtained from all patients before they were included in the study.

Clinical examination: Cardiological and neurological examinations were completed in all subjects. No abnormal neurological finding was encountered. Patients with previous neurologic illness were excluded. The diagnosis of hypertension was made with consistent values above 140 for systolic and 90 mm Hg for diastolic pressures[10] or a history of arterial hypertension under antihypertensive medication.

Coronary angiography: Selective coronary angiography was performed in all patients by the Judkins technique. MRI of the brain and ultrasonography of the carotid arteries were also performed in all cases within 1 week after coronary angiography.

The Gensini[11] and coronary angiography scores[12] were used to estimate the degree of coronary atherosclerosis. Gensini score was calculated from the results of selective coronary angiography as reported.[11] The coronary angiography score was defined as the number of coronary arteries (right and left anterior descending

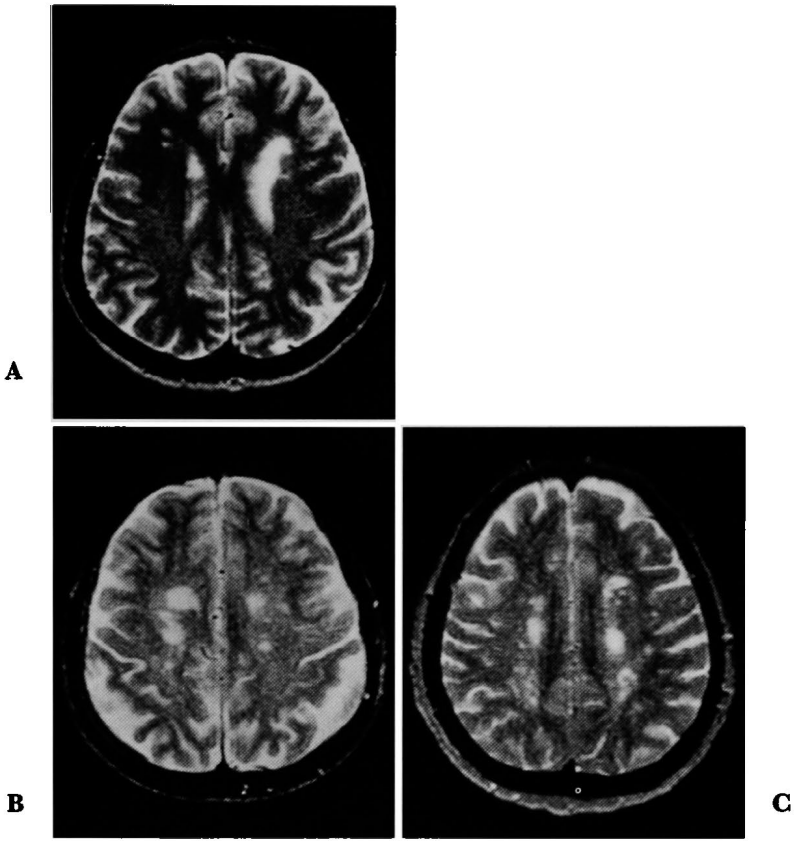


Figure. Deep and periventricular white matter hyperintensities on T_2-weighted images: a punctate lesion (grade 1; **A**); early confluent (grade 2; **B**); and confluent signal hyperintensities (grade 3; **C**).

and left circumflex) with 75% or more stenosis. The scores ranged from 0 to 3.[12]

MRI of the brain: All patients had a brain MRI scan that used a superconducting magnet at a field strength of 0.5 T on proton density, T_1 and T_2-weighted images in sagittal, coronal, and axial planes, respectively. Slice thickness was uniformly 5 mm. All scans were interpreted independently by two investigators (A.Ö. and Y.S.) without knowledge of the patients' risk factors. In cases of disagreement, a joint interpretation was obtained.

Deep and periventricular white matter hyperintensities (WMH) on T_2-weighted images were graded as punctate (grade 1), early confluent (grade 2), and confluent (grade 3)[13] (Figure). Hyperintensities in the subcortical structures (basal ganglia and thalamus), and signs of infarctions in the cerebral cortex, cerebellum and brain stem were evaluated separately.

Twelve-lead ECG recordings: A 12-lead electrocardiogram was obtained in

all cases and evaluated according to the Minnesota Code.

Ultrasonography of the carotid arteries: Ultrasonography of the carotid arteries was performed with B-mode, colour Doppler and duplex Doppler technique (Sonochrome, General Electric) with a 5-Mhz probe. The severity of the carotid artery stenosis (diameter stenosis %) was classified as mild (35–50%), moderate (50–75%), or severe (> 75%).[8]

Other risk factors of stroke: Diabetes mellitus was considered if patients had a fasting blood glucose level exceeding 110 mg/d*l* or if they were being treated with oral antidiabetic agents or insulin. Patients were considered hypercholesterolemic if the serum total cholesterol level exceeded 240 mg/d*l*, and hypertriglyceridemic if the serum triglyceride level exceeded 170 mg/d*l*. A high low-density lipoprotein (LDL) level was diagnosed if the serum LDL level exceeded 150 mg/d*l*. Smoking was evaluated by a questionnaire.

Statistical analysis: Unpaired t and χ^2 tests were used to determine the relations between risk factors and coronary and carotid atherosclerosis scores in patients with and without silent brain lesions.

Results

Thirty-one of 72 (43.0%) patients had silent brain lesions on MRI while in 8 of 26 (30.7%) age and sex-matched normal controls SBI were seen ($p = 0.35$). The locations of these lesions are shown in Table I. The main finding on T_2-weighted MRI was WMH which was seen in all patients with silent brain lesions. In addition to WMH, lacunar (< 6 mm) gray matter hyperintensities were also seen in some of the patients.

The mean age, gender and frequency of risk factors of stroke in patients with and without silent brain lesions are shown in Table II.

The mean age of the 31 patients with silent cerebral lesions was 56.6 ± 7.6 years, which was significantly higher than that of patients without silent brain

Table I. Silent Brain Lesions on Brain Magnetic Resonance Imaging in Normal Control and Patient Groups

Silent brain lesions	Normal controls ($n = 8$)	Patients ($n = 31$)
Silent white matter hyperintensities		
Grade 1	8	15
Grade 2	1	10
Grade 3	—	6
Other locations (gray matter hyperintensities)		
Thalamus	1	4
Basal ganglia	2	4
Cerebellum	—	1
Cerebral cortex	—	1

Table II. The Demographic Characteristics and Risk Factors of Patients with and without Silent Brain Lesions

	Silent brain lesion		*p*
	Negative	Positive	
Number of patients	41	31	
Age (mean ± SD)	51.8 ± 8.4	56.6 ± 7.6	.0077
Gender (Male/female)	27/14	20/11	NS
Risk factors of stroke			
% of patients			
Hypertension	53.6	54.8	NS
Diabetes mellitus	21.9	22.5	NS
Smoking	58.5	54.8	NS
High cholesterol level	19.5	25.8	NS
High LDL level	34.1	35.4	NS
High triglyceride level	29.2	32.2	NS

NS = non significant.

Table III. The Gensini and Coronary Angiography Scores and Frequency of Carotid Artery Stenosis in Patients with and without Silent Cerebral Lesions

	Silent brain lesion		*p*
	Negative ($n = 41$)	Positive ($n = 31$)	
Gensini score (mean ± SD)	18.1 ± 24.9	41.8 ± 35.0	.0013
Coronary angiography score (mean ± SD)	0.87 ± 1.0	1.77 ± 0.9	.0003
Carotid artery stenosis (*n*)			.0393
Mild (35–50%)	5	2 (1)*	
Moderate (50–75%)	1	7 (5)*	
Severe (> 75%)	0	3 (3)*	
Total (%)	6 (14.6%)	12 (38.7)	

*The numbers in parentheses indicate the number of patients with stenosed carotid artery ipsilateral to the silent brain lesion(s).

lesions (51.8 ± 8.4 years) ($p < 0.01$). There was no significant difference between sexes, nor in the prevalance of risk factors for stroke (hypertension, diabetes mellitus, smoking, high serum cholesterol, triglyceride and LDL cholesterol levels) between the groups with and without SBI.

As shown in Table III, the Gensini score, coronary angiography score and incidence of carotid stenosis are significantly higher in patients with silent cerebral lesions than that in patients without silent lesions ($p < 0.01$, $p < 0.001$ and $p < 0.05$, respectively).

Discussion

Our data suggests that atherosclerosis (ischemic heart disease and carotid

artery stenosis) is the main cause of the silent brain lesions. The prevalence of silent cerebral lesions in our study is 43.0%. This rate is higher than that of previous CT studies.[14 16] In our study, the most common abnormality in MRI was WMHs. These lesions have many causes, such as dilated perivascular spaces (Virchow-Robin spaces), gliosis, arteriosclerosis, vascular ectasia, small infarctions and demyelinated areas.[17 20] However, a sharply demarcated lesion from the surrounding tissues suggests the presence of an infarction and there is a positive correlation between these hyperintense areas on T_2-weighted MR images and enlarged Virchow Robin spaces and lacunar infarctions.[18] In evaluating gray and white matter hyperintensities, we have used proton density-weighted MR images, in which cystic infarctions and enlarged Virchow-Robin spaces have a lower signal than the surrounding brain, whereas non-cystic lacunar infarctions are hyperintense compared with brain parenchyma.[6] Our interpretation is that the hyperintensities seen in the MR images are mostly due to lacunar silent infarctions. Furthermore, we found deep gray matter hyperintensities in 8 cases, cerebellar hyperintensity in 1 and cerebral cortical hyperintensity in 1 case. Similar causes may be responsible in both WMHs and gray matter hyperintensities.[6]

Silent brain lesions have been clearly associated with risk factors for stroke such as hypertension, diabetes mellitus, hypercholesterolemia and smoking.[2,4,9] Similarly, aging has also been shown to be a risk factor for silent brain lesions.[4,6,9,21] The correlation between these lesions and atrial fibrillation and coronary artery disease has been extensively studied,[9,22,23] but these two factors solely did not account for the occurrence of silent brain lesions. As in our study, Tanaka *et al.*[9] pointed out that coronary atherosclerosis and aging were the risk factors for development of silent brain lesions. We found that Gensini and coronary angiography scores in patients with silent cerebral lesions were significantly higher than those of patients without these lesions and there is an association between severe coronary atherosclerosis and silent brain lesions. We also observed that silent brain lesions were associated with carotid artery stenosis. Carotid stenosis was found in 38.7% of patients with silent brain lesions. This rate was higher than that of patients without silent brain lesion (14.6%). In 9 of 12 patients with carotid stenosis and silent brain lesion, silent lesions were ipsilateral to carotid stenosis. Grigg *et al.*[24] suggested that small microemboli from the surface of carotid plaques do not cause any symptoms, because of their small size. However, there was no significant difference between silent cerebral lesions and the other risk factors for stroke (hypertension, diabetes mellitus, smoking, high serum cholesterol, triglyceride and LDL cholesterol levels) in our study.

In conclusion, in patients with ischemic heart disease, silent brain lesions are a common complication. Carotid artery stenosis and age were also important risk factors for the development of silent brain lesions in cases with coronary

artery disease, but not in subjects with normal coronary circulation.

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