Relationship Between Carotid Intima-Media Thickness and Silent Cerebral Infarction in Japanese Subjects With Type 2 Diabetes

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OBJECTIVE — We examined the relationship between intima-media thickness of common carotid artery (CCA-IMT) and silent cerebral infarction (SCI) with the magnetic resonance imaging (MRI) study in Japanese subjects with type 2 diabetes.

RESEARCH DESIGN AND METHODS — The brain MRI study and the carotid ultrasonography were performed in a total of 217 consecutive Japanese subjects with type 2 diabetes. Various risk factors for SCI were examined using multiple logistic analyses.

RESULTS — The SCI was found in 60.4% of the diabetic subjects. In the diabetic subjects, age, systolic blood pressure (SBP), pulse wave velocity, and CCA-IMT were significantly higher in the subjects with SCI than in those without it. Multiple logistic analyses indicated that age, SBP, and CCA-IMT were significant and independent risk factors of SCI in the diabetic subjects.

CONCLUSIONS — CCA-IMT, but not pulse wave velocity, was independently associated with SCI in Japanese subjects with type 2 diabetes.

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People with type 2 diabetes are at high risk for silent cerebral infarction (SCI) compared with people without diabetes (1,2). Because SCI is the preclinical stage for symptomatic stroke and associated with cognitive decline, it is clinically important to identify SCI in patients with diabetes.

The measurement of intima-media thickness of the common carotid artery (CCA-IMT) by ultrasonography has been recognized as a powerful method to identify subclinical atherosclerosis. Increased CCA-IMT is reported to be associated with stroke in subjects including those with diabetes (3–5). However, few studies have investigated the relationship between CCA-IMT and SCI detected by magnetic resonance imaging (MRI) in subjects with type 2 diabetes. In the present study, we examined the relationship between CCA-IMT and SCI in subjects with type 2 diabetes.

RESEARCH DESIGN AND METHODS — The subjects included 226 consecutive patients with type 2 diabetes who visited our hospital during 2003–2006. All of them underwent carotid ultrasonography and brain MRI. Patients with history of stroke or other neurological disease or who had cardioembolic risk factors including atrial fibrillation, valvular heart disease, and myocardial infarction were excluded. A total of 217 Japanese subjects with type 2 diabetes were analyzed. No patients refused to participate in this study. The study was approved by our institutional ethics committee.

Brain MRI

Brain MRI was performed using a 1.5-T NovaDual (Philips, Best, the Netherlands) to obtain T1- and T2-weighted and fluid-attenuated inversion recovery (FLAIR) images. SCI was defined as an area of focal hyperintensity on T2-weighted images with corresponding low signal intensity on T1-weighted images, which was ≥3 mm in diameter. The diagnosis was made when a lesion was surrounded by a hyperintense gliotic rim on fluid-attenuated inversion recovery images to exclude dilated perivascular space (6).

Carotid ultrasonography and brachial-ankle pulse wave velocity measurement

The CCA-IMT was measured with high-resolution B-mode ultrasonography (SSA-770A; Toshiba, Tokyo, Japan) with a 7.5-MHz linear transducer, as previously reported (4). Any focal thickening of the intima-media (≥2.0 mm) was excluded. Brachial-ankle pulse wave velocity was measured using an automated device (Omron-Colin, Tokyo, Japan) (7,8). Ankle brachial pressure index was the ratio of ankle systolic blood pressure (SBP) to brachial SBP.

Data analyses

Differences in variables were examined for statistical significance using the *t* test. Results are expressed as the mean ± SD. The relationship between SCI and various factors were examined by univariate and multiple logistic analyses. Statistical analysis was performed using SPSS11.0J (SPSS, Chicago, IL). Statistical significance was determined as $P < 0.05$.

RESULTS — The SCI was found in 60.4% of the diabetic subjects. By univariate analysis, age, pulse wave velocity, SBP, and CCA-IMT were significantly

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Table 1 —*The clinical characteristics of the subjects and association between SCI and various risk factors on multiple logistic regression analysis*

	Clinical characteristics of the diabetic subjects				Multiple logistic regression analysis		
	Total	SCI^{-}	SCI^{+}	*P*	Odds ratio	*P*	95% CI
	n = 217	*n* = 86 (39.6%)	*n* = 131 (60.4%)				
Male/female	116/101	45/41	71/60	0.895	1.48	0.287	0.72–3.07
Age (years)	67.1 ± 8.6	63.7 ± 9.6	69.3 ± 6.9	<0.01*	1.09	<0.001†	1.04–1.15
SBP (mmHg)	136.2 ± 18.1	129.4 ± 15.8	140.6 ± 18.1	<0.01*	1.06	0.003*	1.02–1.10
Diastolic blood pressure (mmHg)	77.5 ± 9.6	75.9 ± 9.5	78.5 ± 9.5	0.057	0.97	0.364	0.91–1.03
Ankle brachial pressure index	1.15 ± 0.10	1.16 ± 0.10	1.14 ± 0.12	0.318	0.10	0.152	0.00–2.36
Pulse wave velocity (cm/s)	1,831.9 ± 415.8	1,718.0 ± 431.2	1,906.7 ± 398.1	<0.01*	1.00	0.617	1.00–1.00
CCA-IMT (mm)	1.20 ± 0.33	1.10 ± 0.29	1.27 ± 0.33	<0.01*	4.16	0.012‡	1.37–12.62
Triglycerides (mmol/l)	1.69 ± 0.91	1.67 ± 0.92	1.71 ± 0.90	0.738	1.00	0.678	1.00–1.01
LDL cholesterol (mmol/l)	3.02 ± 0.75	3.00 ± 0.77	3.04 ± 0.73	0.820	1.01	0.600	0.99–1.01
HDL cholesterol (mmol/l)	1.46 ± 0.41	1.47 ± 0.42	1.45 ± 0.40	0.735	1.01	0.620	0.98–1.03
A1C (%)	7.61 ± 1.45	7.67 ± 1.34	7.58 ± 1.52	0.434	1.07	0.538	0.86–1.34

Data are means ± SD unless otherwise indicated. *$P < 0.01$, †$P < 0.001$, ‡$P < 0.05$. The odds ratios and 95% CIs for SCI were calculated by multiple logistic regression analysis.

higher in the subjects with SCI than in those without it (69.3 vs. 63.7 years, 1,906.7 vs. 1,718.0 cm/s, 140.6 vs. 129.4 mmHg, 1.27 vs. 1.10 mm, respectively, $P < 0.01$). Furthermore, multiple logistic regression analyses indicated that age (odds ratio 1.09, 95% CI 1.04–1.15), SBP (1.06, 1.02–1.08), and CCA-IMT (4.16, 1.37–12.62) were independent risk factors of SCI (Table 1).

CONCLUSIONS— The present study found SCI in 60.4% of the diabetic subjects. It seems likely that SCI exists more frequently in subjects with type 2 diabetes than in subjects without it, since a frequency of SCI was reported to be 42% in general Japanese patients (9) and 47.5% in nondiabetic subjects (our unpublished data). Several risk factors have been identified for the occurrence of SCI, including age, hypertension, diabetes, and carotid atherosclerosis (10). It was reported that type 2 diabetes showed a tendency to be associated with SCI (11). Another study reported that CCA-IMT was associated with symptomatic ischemic stroke in Japanese patients with type 2 diabetes (12). In the present study, we found that CCA-IMT was thicker in the subjects with SCI than in those without it and that increased CCA-IMT correlated significantly with SCI in the diabetic subjects after the various risk factors were adjusted. This is in line with our previous report that CCA-IMT is a better tool than pulse wave velocity to detect early atherosclerotic changes (8).

In previous reports, Eguchi et al. (2) reported that the prevalence of SCI increased threefold in Japanese hypertensive patients with diabetes, whereas Johnsen et al. (13) concluded that CCA-IMT was associated with hypertensive vascular disease rather than atherosclerosis, especially at an early stage. These studies suggest a possibility that CCA-IMT may be related to SCI through hypertension. However, our results with multiple logistic regression analysis clearly showed that CCA-IMT was a risk factor for SCI independently of hypertension in Japanese diabetic subjects.

This study was limited by several factors. First, the current study is a cross-sectional one, making it impossible to draw any definite conclusion about the causal relationships. Second, it is often difficult to differentiate the perivascular space from infarcts in the basal ganglia (14). Finally, we could not get any information on smoking, which is an important risk factor.

Despite these limitations, the present study suggests that SCI is associated with age, SBP, and CCA-IMT in Japanese subjects with type 2 diabetes.

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