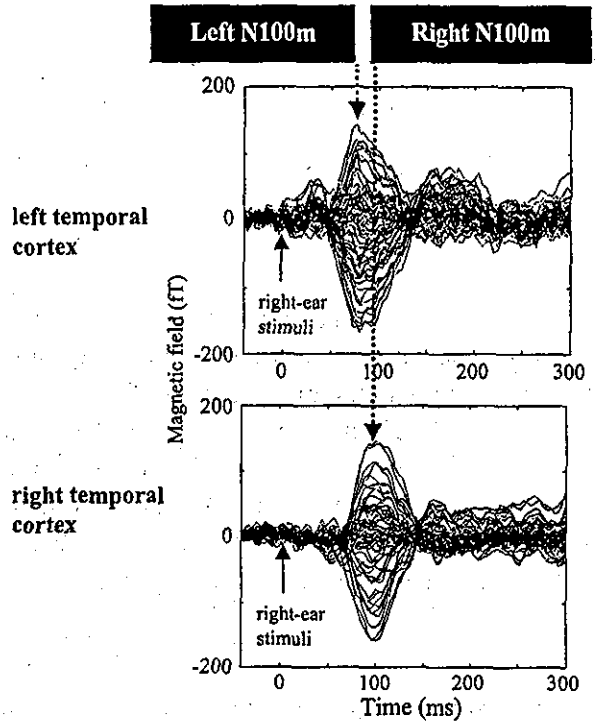

Fig. 1. Left N100m and right N100m peak latencies in a patient (right-ear stimuli). Interhemispheric neural conduction time (INCT) (ms) = right N100m peak latency – left N100m peak latency.

right and left N100m peak latencies. The INCT was compared between the two groups.

3. Results

MMSE scores were normal in 23 patients (Group A: MMSE score 24–30; 71 ± 12 years of age) and reduced in 10 patients (Group B: MMSE score 19–23; 73 ± 6 years of age). The ages in the two groups were the same. With the right ear stimuli, the N100m peak latency at the left temporal cortex was almost the same in Group A (92.8 ± 15.3 ms) and Group B (93.9 ± 13.9 ms), whereas the N100m peak latency at the right temporal

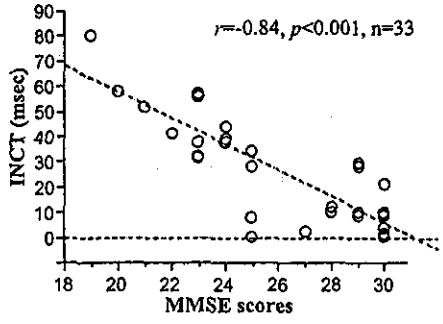

Fig. 2. The relationship between MMSE scores and interhemispheric neural conduction time (INCT) in 33 patients (right ear stimuli).

cortex was significantly longer in Group B (143.3 ± 13.7 ms) than in Group A (109.3 ± 16.7 ms, $p < 0.01$). The INCT was significantly longer in Group B (50.5 ± 14.7 ms) than in Group A (15.6 ± 13.9 ms, $p < 0.05$). When analyzed in the entire patient group, there was a significantly negative correlation between MMSE scores and INCT ($r = -0.84$, $p < 0.001$) (Fig. 2).

4. Discussion

Cognitive function takes place under rapid interactions of multiple cerebral regions interconnected with neurons. The results of the present study suggest that cognitive function may deteriorate correlating with the prolongation of INCT in elderly patients with unstable gait and dizziness. The INCT may represent the time required for the inter-regional neural process to perform cognitive function. Dizziness is related with gait unstableness that is known to be a predictor of non-Alzheimer's dementia. The measurement of INCT with AEFs may be useful for early detection of cognitive impairment in elderly patients with unstable gait and dizziness who may later develop dementia.

Acknowledgements

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Quantitative magnetic detection of finger movements in patients with Parkinson's disease

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Abstract

To develop a new measurement tool for quantitatively detecting the finger movement of a patient with Parkinson's disease (PD), we designed a magnetic sensing system consisting of a magnetic induction coil, a sensing coil, and a circuit unit. The sensing coil detects the inducted magnetic field that varies with the distance between the two coils, and the detected signals are demodulated in the circuit unit in order to obtain the variation voltage from the oscillation frequency. To obtain a coefficient for converting voltage to distance, we measured the output voltages for seven fixed finger positions of 12 normal volunteers. The voltage differences corresponding to the finger movement in 20 PD patients, six age-matched controls, and 12 normal volunteers were then recorded for 30 s. To investigate the velocity and acceleration of the finger movement, we calculated their waveforms from the measured displacement waveform. We also detected the main frequency of the tapping rhythm by using a fast Fourier transform (FFT). The averaged amplitude of each waveform decreased with the disorder in the Hoehn–Yahr (HY) stage, while the averaged tapping frequency of PD patients did not have any correlation with this stage. It can be concluded that this magnetic sensing system can assess finger movement quantitatively.
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Keywords: Parkinson's disease; Finger tapping; Magnetic detection

1. Introduction

The most prominent clinical feature of Parkinson' disease is movement disability including rigidity, tremor, bradykinesia, akinesia, and disturbances of rhythm formation. Since the assessment of these symptoms depends on the skill of individual neurologists, a common objective assessment is needed.

It has been suggested that the basal ganglia facilitate sequential movement, engaging subsequent movements in a movement sequence (Marsden, 1990), and the bradykinesia and disturbances of rhythm formation that occur in Parkinson's disease (PD) are usually assessed by using a finger-tapping test. The finger movement in finger-tapping tests has been analyzed by electrical-switch tapping (Shimoyama et al., 1990), metal-loop tapping (Freeman et al., 1993), keyboard tapping (Giovannoni et al., 1999; Homann et al., 2000; Bronte-Stewart et al., 2000), and three-dimensional optoelectronic camera tracking (Konczak et al., 1997; Agostino et al., 2003). The methods other than the one using an optoelectronic camera system, however, can analyze only the bradykinesia and incoordination of the index finger because they can monitor only the movement of 'on' and 'off'. Furthermore, the data processing of the optoelectronic camera system is very complex because of the use of a two-dimensional image. There has been no study on sequential-motion analysis of finger-to-thumb opposition using a simple apparatus.

We therefore developed a new apparatus for quantitatively studying the dynamics of finger movement by using data

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obtained from a magnetic sensor. This apparatus is small enough for use in a consultation room or by the bedside. The main purpose of the work reported here was to determine whether this apparatus could be used to objectively assess the symptoms of patients with Parkinson' disease. A major advantage of our magnetic sensor is that it enables the degree of finger opening and the incoordination of finger-to-thumb oppositions to be analyzed without being affected by involuntary movement including tremors. This sensor can also sensitively detect the subtle finger movement of hastened taps.

2. Materials and methods

2.1. Subjects

The subjects in this study were 12 healthy volunteers (six male and six female) between 26 and 43 years old, 20 Parkinson's patients (10 male and 10 female) between 46 and 82 years old, and six age-matched controls (three male and three female) between 62 and 89 years old. We classified the PD patients into five stages based on the Hoehn–Yahr (HY) stage system (Hoehn and Yahr, 1967). HY-I patients had effects on one side of the body, HY-II patients had effects on both sides of the body, HY-III patients showed impairments in balance and walking, HY-IV showed marked impairments in balance and walking, and HY-V patients were completely immobile. Informed consent was obtained from all subjects. The 12 volunteers also participated in calibration experiments determining the relation between movement distance and output voltage of the new measurement tool (see Section 2.3).

2.2. Configuration of magnetic detection system

The magnetic detection system (Fig. 1) consists of oscillation and detection coils (each 14 mm in diameter and comprising 30 loops of copper wire), a circuit unit (170 mm × 120 mm × 50 mm), and a personal computer. The oscillator and one amplifier in the circuit unit produce a 100-mA ac current (20 kHz) that flows through the oscillation coil, producing a magnetic field oscillating at the same frequency. The magnetic field inducts a voltage with the same frequency in the detection coil. This voltage is amplified by a pre-amplifier and fed to a phase-shift detector to be demodulated by using a 20-kHz reference signal whose phase was adjusted because the inducted signal has a phase delay. The output of the phase-shift detector is run through a low-pass filter (corner frequency = 30 Hz) and amplified. The final output is digitized at 100 Hz by an analog-digital (AD) board in the computer.

The oscillation and detection coils are attached to the thumb and index finger with two-sided tape as shown in Fig. 1b and connected by a twisted lead wire 1 m long to the circuit unit, whose output is recorded by the notebook personal computer with the AD board. The data size for a 30-s recording is only 7 kB.

2.3. Measurement of the relationship between output voltage and movement distance

The thumb and index finger are not always parallel during finger-tapping, and the strength of detected magnetic field is not linearly related to the distance over which the fingers move because its magnitude is inversely proportional to the square of the distance between the oscillation and detection coils. Calibration data are therefore needed to determine the movement distance.

Using the six male and six female healthy volunteers, we measured the output signals for movement distances of 0, 20, 40, 60, 80, 100, and 120 mm. After investigating the difference between male and female subjects and the difference between left and right fingers in the calibration data (see Section 3), we used this data to convert the output signals obtained with all subjects to movement distances.

2.4. Finger-tapping measurement

We measured the output signals due to the finger movement of each hand of all subjects (12 healthy volunteers, six age-matched controls, and 20 PD patients) for 30 s. These subjects were instructed to tap as rapidly as possible while moving their fingers as far as they could. All subjects practiced tapping before the measurement so they could make the finger movements correctly.

2.5. Data analysis

The measured tapping waveforms included almost no artifacts due to movements such as tremor of the fingers. We therefore think that finger precise velocity and acceleration can be estimated accurately from the measured waveforms.

Thirty seconds of data digitized at 100 Hz were stored in the PC. The stored voltage was converted to movement distance D by using the calibration data given in Section 2.4, and the velocity and acceleration of the finger movements were calculated from the derivatives of (dD/dt and d^2D/dt^2). The waveforms for movement distance, velocity, and acceleration were used to determine the differences between the finger movements of healthy volunteers and PD patients. The differences were evaluated by calculating a displacement value (i.e., |maximum value| − |minimum value|) in each waveform during the 30-s period.

We analyzed the tapping rhythm by using the fast Fourier transform (FFT). Before the FFT algorithm was used, the mean value of the 30-s data (3000 points) was subtracted from a raw waveform in order to determine the tapping frequency. And the main cyclic timing was determined by finding the frequency with the highest peak in the obtained power spectrum.

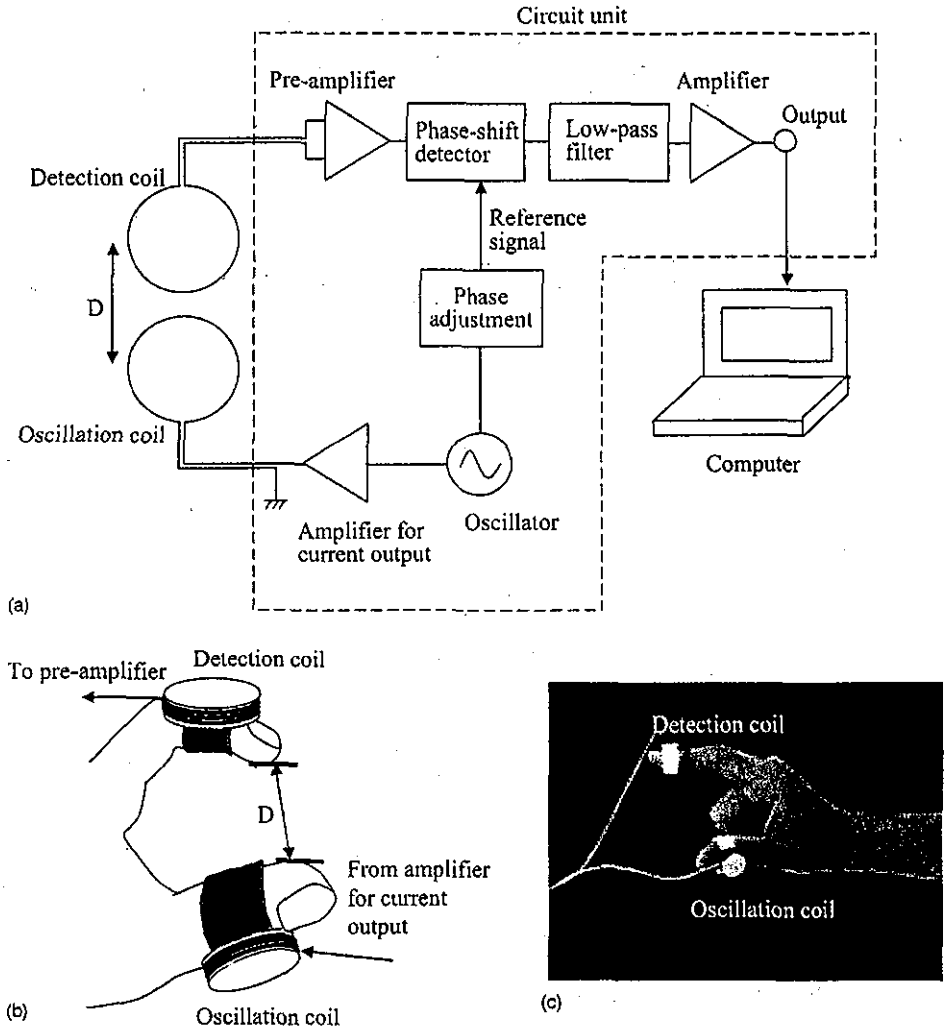

Fig. 1. (a) Block diagram of the magnetic detection system; (b) configuration of detection and oscillation coils. D is the movement distance between the index finger and thumb; and (c) photograph of detection and oscillation coils attached to the fingers by two-sided tape.

3. Results

The output voltages measured to obtain the calibration data are summarized in Table 1, where the difference between male and female subjects is seen to be not significant for either hand. Furthermore, the values for the right and left hand are also very similar at each distance. The calibration data was therefore simplified by averaging all 12 volunteers' data for each position. The averaged data are plotted in Fig. 2, which shows that the output voltage decreases with increasing distance D. The voltage waveform was changed to the movement-distance waveform by using the interpolated line shown in Fig. 2.

Table 1
Output voltages measured for seven movement distances D in 12 young volunteers

Right hand				Left hand		
D (mm)	Male ($n = 6$)	Female ($n = 6$)	P-value	Male ($n = 6$)	Female ($n = 6$)	P-value
0	−2.2 ± 0.2	−3.0 ± 0.4	NS	−2.2 ± 0.3	−2.8 ± 0.4	NS
20	−1.1 ± 0.2	−1.3 ± 0.1	NS	−1.1 ± 0.2	−1.4 ± 0.3	NS
40	−0.55 ± 0.2	−0.54 ± 0.1	NS	−0.51 ± 0.09	−0.57 ± 0.08	NS
60	−0.28 ± 0.08	−0.27 ± 0.06	NS	−0.27 ± 0.05	−0.29 ± 0.02	NS
80	−0.16 ± 0.04	−0.16 ± 0.04	NS	−0.16 ± 0.02	−0.15 ± 0.02	NS
100	−0.098 ± 0.02	−0.094 ± 0.02	NS	−0.093 ± 0.008	−0.090 ± 0.01	NS
120	−0.062 ± 0.01	−0.056 ± 0.01	NS	−0.057 ± 0.004	−0.061 ± 0.01	NS

The difference between female and male is not significant for any distance, and the left- and right-hand data are very similar. P-value: Pearson t-test.

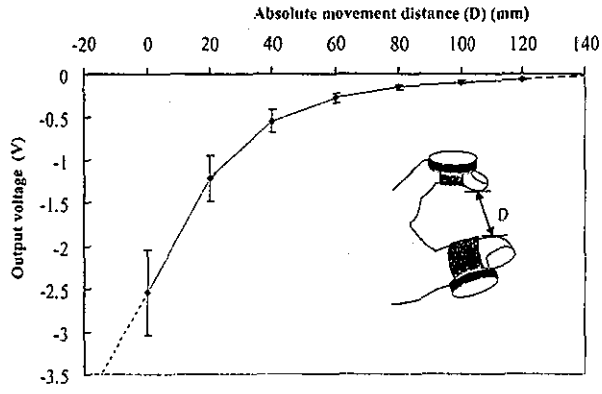

Fig. 2. Relation between movement distance D and the output voltage of the magnetic detection system. The relation is plotted by averaging all 12 volunteers data (including both left- and right-hand data). The averaged relation is in inverse proportion.

To compare the calibrated waveform with the raw waveform, see the two waveforms for a normal case that are drawn in Fig. 3. The voltage waveform near a 0 V does not include detailed movement, but the calibrated waveform (Fig. 3b) gives more detailed information.

Distance, velocity, and acceleration waveforms for a healthy volunteer are shown in Fig. 4. Although the amplitude of the distance waveform is constant, the amplitudes of the velocity and acceleration waveforms decrease. This pattern was evident in the waveforms for all the healthy volunteers. The distance, velocity, and acceleration amplitudes (|maximum value| − |minimum value|) and main tapping frequencies (determined as shown in Fig. 5) for the healthy volunteers are listed in Table 2. All parameters (D, dD/dt, d^2D/dt^2, and F) have no significant value in males and females, although female's d^2D/t^2 is slight smaller than those of males.

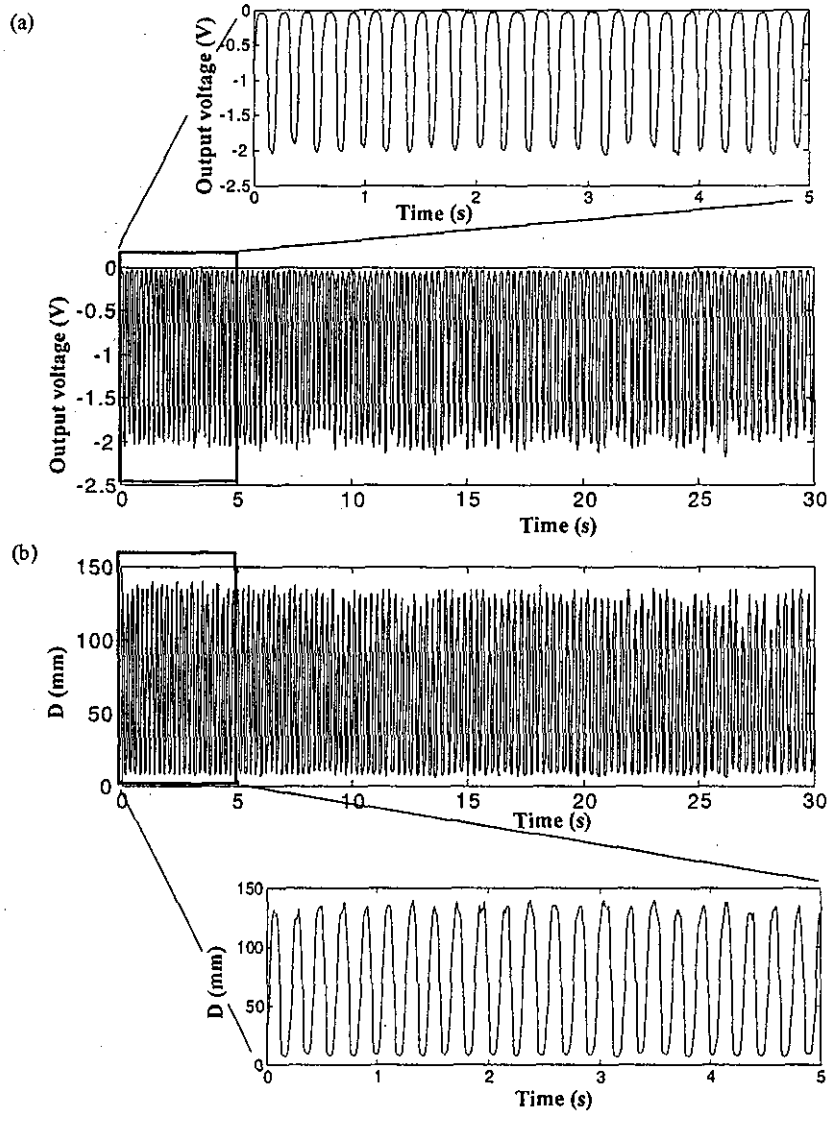

Fig. 3. (a) Output voltage waveform of magnetic detection system in the case of a young healthy volunteer. The wave near 0 V does not reflect a detailed motion and (b) movement-distance waveform changed from (a). The wave reflects a real finger motion.

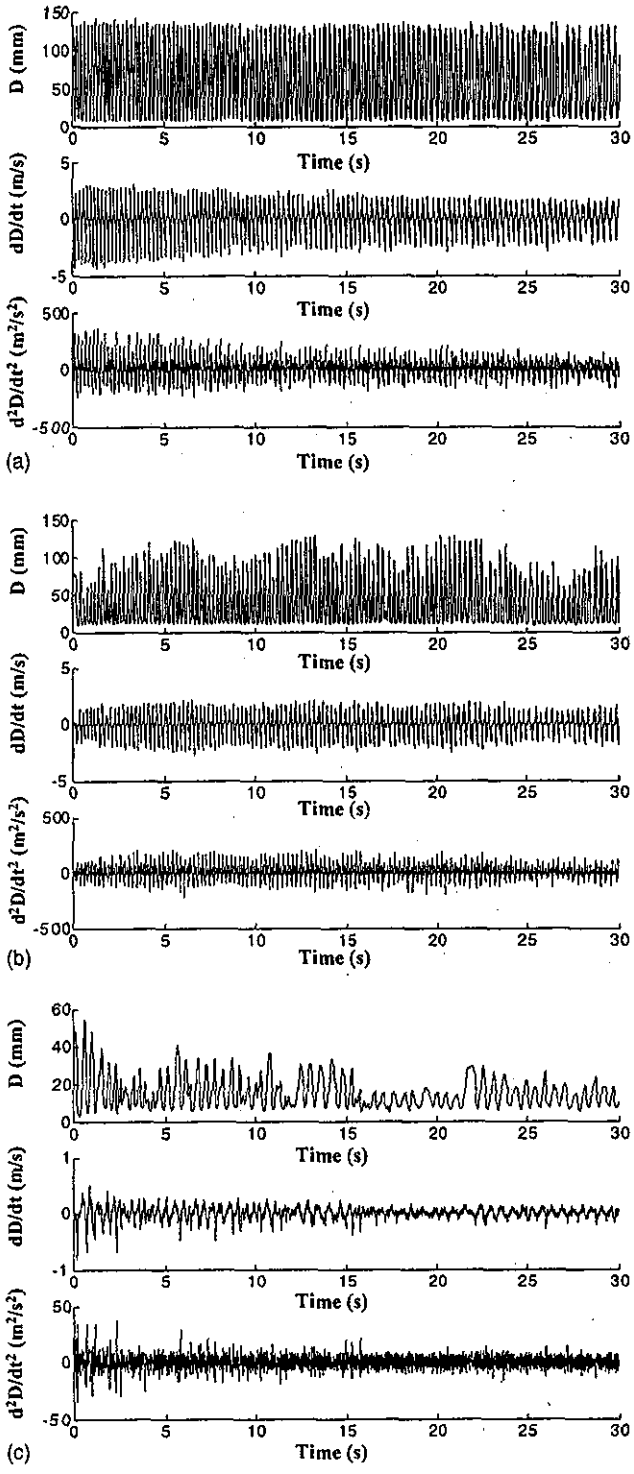

Fig. 4. (a) Movement-distance waveform of a young healthy volunteer. (The waveform is the same as that in Fig. 3b.) Velocity waveform calculated from the distance waveform. Acceleration waveform calculated from the waveform the velocity waveform; (b) movement-distance waveform of age-matched elderly control. Velocity waveform calculated from the distance waveform. Acceleration waveform calculated from the velocity waveform; (c) movement-distance waveform of PD patient (HY-III). Velocity waveform calculated from the distance waveform. Acceleration waveform calculated from the velocity waveform.

The amplitudes of the velocity and acceleration waveforms for the age-matched normal control were roughly constant (as shown in Fig. 4b), but the amplitude of the distance waveform for the age-matched normal control varied more than that of the younger normal volunteers did.

Typical distance, velocity, and acceleration waveforms of a Parkinson-disease patient are shown in Fig. 4c. The amplitude of each varies arrhythmically.

Power spectra calculated from the movement-distance waveforms of a control and a PD patient are shown in Fig. 5. The highest peak in each is the main frequency F; it is 4.3 Hz for the control and 1.8 Hz for the PD patient. The power spectrum for the PD patient is also shown on an expanded scale, since its magnitude is much less than that of the power spectrum for the control.

For all subjects in this study, the average displacement value (|maximum value| − |minimum value|) in each waveform (D, dD/dt, and d^2D/dt^2) during the 30 s is plotted in Fig. 6 along with the average main frequency F. All values are shown with their standard deviations. The amplitudes of the average displacements plotted in Fig. 6a–c decrease as the HY stage becomes more severe. Furthermore, the amplitude of each displacement value differs significantly between the young and old volunteers. The averaged main frequency, on the other hand, is weakly correlated with the HY stage. Furthermore, the deviation of the main frequency is very large.

4. Discussion

In this study, we have demonstrated the possibility of quantitatively detecting finger-movement disorders in PD patients by using a magnetic sensor system. This apparatus can easily measure the degree of finger opening and the incoordination of finger-to-thumb oppositions. In this report, we cannot show the effect of involuntary movements (e.g., tremors) because none of our subjects was afflicted with tremors. Note, however, that the sensor would hardly detect tremors because the finger-to-thumb distance does not vary greatly during tremor. Therefore, we can directly observe finger opening and incoordination of finger-to-thumb oppositions.

Using the magnetic detection system, we found that the mean values of three parameters (D, dD/dt, and d^2D/dt^2) decrease as the severity of Parkinson symptoms (as indicated by the patient's HY stage) increases. The main frequency, on the other hand, is more weakly correlated with the severity of a patient's symptoms. The decrease in these three parameters reflects an increasing degree of dyskinesia, such as muscle stiffness and loss of strength. A kinesia score decrease in accordance with the HY stage has been reported by investigators using the total number of computer keystrokes (Homann et al., 2000). The keystroke number is identified from the main frequency in Fig. 6d. Their results (with a large distribution in kinesia score)

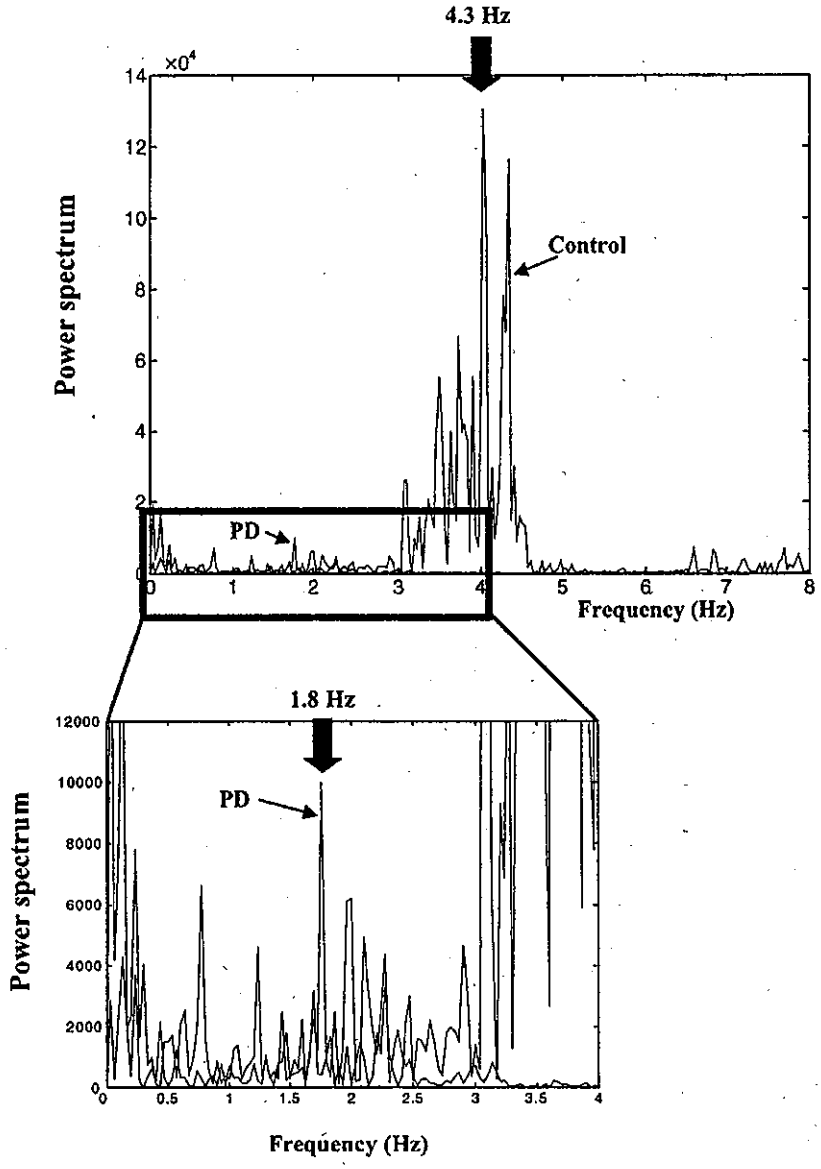

Fig. 5. Power spectra calculated from the movement-distance waveforms of a typical control (red line) and a HY-III PD patient (blue line). The main frequency is 4.3 Hz in the control's power spectrum and 1.8 Hz in the PD patient's power spectrum. Furthermore, the magnitude of the PD's spectrum is much weaker than that of the control's power spectrum.

are very similar to our findings. It can thus be considered that the magnetic-sensor system can determine a kinesia score.

Furthermore, it must be noted that the parameters D, dD/dt, and d^2D/dt^2 for our young volunteers (averaging 32.5 years old) are much larger than those of our elderly controls (averaging 71.3 years old). This significant difference is caused by a deterioration of the brain motor function with age. The deterioration has been reported by investigators using tapping frequency (Shimoyama et al., 1990). In their results and ours (Fig. 6d), the tapping frequencies of young people cannot be distinguished from those of elderly people. The parameters D, dD/dt, and d^2D/dt^2 of young people, however, can be distinguished from those of elderly people. This clear discrimination might indicate that our magnetic detection system can accurately detect the deterioration of motor function.

None of the output voltages obtained from the 12 healthy volunteers differed between sexes or the right and left hands at any of the movement distances (Table 1). This shows the size of the hand and the fingers has little effect on this magnetic detection system. We need, however, to consider the maximum possible distance between the thumb and the index finger because a size-dependence of this distance might affect the parameters used to evaluate the degree of motor disorder in Parkinson patients.

In summary, the simple magnetic detection system we developed for the finger-tapping test can be used to assess the severity of PD patient symptoms quantitatively.

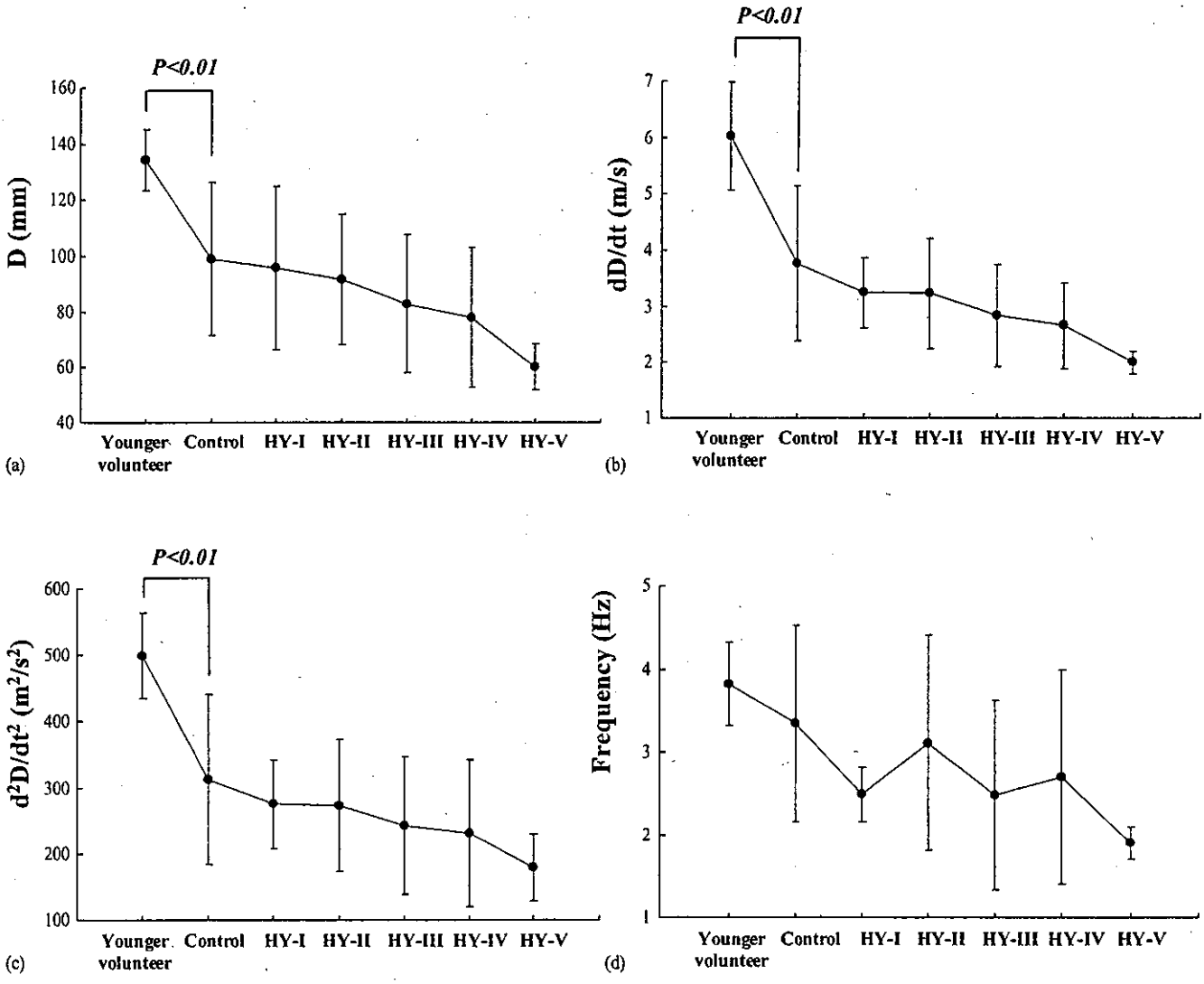

Fig. 6. (a) Maximum displacement of the movement-distance D. (b) Maximum replacement of the velocity (dD/dt). (c) Maximum displacement of the acceleration (d^2D/dt^2). (d) Main frequency F. In (a), (b), and (c), the mean values decrease with the degree of disorder. In (d), the main frequency has a similar tendency.

Furthermore, it may also offer a new strategy for treatment of these patients.

4.1. Limitations of this study

There are several limitations of this study. First, a comparison with many age-matched patients and controls is needed. Second, to obtain more detailed information, a new identification parameter for detecting disorders such as an arrhythmic repetitive movement may be needed. Third, the effect of the maximum possible distance between thumb and the index finger should be taken into account when the simple magnetic-detection method we developed is used. Despite these limitations,

Table 2
List of three parameters (D, dD/dt, and d^2D/dt^2) in 12 young volunteers

	Left hand			Right hand		
	Male ($n = 6$)	Female ($n = 6$)	P-value	Male ($n = 6$)	Female ($n = 6$)	P-value
D (mm)	137 ± 4	134 ± 18	NS	133 ± 6	134 ± 15	NS
dD/dt (m/s)	6.6 ± 0.8	5.5 ± 1.2	NS	6.5 ± 0.8	5.5 ± 1.0	NS
d^2D/dt^2 (m^2/s^2)	554 ± 53	460 ± 75	NS	546 ± 58	437 ± 72	NS
F (Hz)	3.7 ± 0.3	3.8 ± 0.5	NS	4.0 ± 0.7	3.8 ± 0.5	NS

The difference between female and male is not significant for any parameter. Furthermore, left- and right-hand data are very similar.

however, the method is very useful for measuring finger movement.

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AJNR Am J Neuroradiol 25:1796–1801, November/December 2004

Predictors of Clinical Outcome in Patients Receiving Local Intra-Arterial Thrombolysis without Subsequent Symptomatic Intracranial Hemorrhage against Acute Middle Cerebral Artery Occlusion

Tatsuro Takada, Masahiro Yasaka, Kazuo Minematsu,
Hiroaki Naritomi, and Takenori Yamaguchi

BACKGROUND AND PURPOSE: **The factors that predict favorable outcome after local intra-arterial thrombolysis (LIT) remain unknown. We aimed to clarify these factors in patients with middle cerebral artery occlusion treated by LIT.**

METHODS: **We performed LIT in 26 consecutive patients who had middle cerebral artery occlusion with a modified Rankin scale (mRS) score ≤2 before stroke onset. We assessed background characteristics, angiographic findings, and mRS score at discharge. We compared these factors between patients with good outcome (mRS score, ≤2) and those with poor outcome (mRS score, ≥3).**

RESULTS: **The duration from symptom onset to hospital admission was 0.96 ± 0.87 (mean ± SD) hour and from onset of stroke to LIT was 3.78 ± 1.17 hours. No patients developed symptomatic intracerebral hemorrhage or died. Thirteen patients achieved good outcomes. No significant differences existed between the two groups in baseline National Institutes of Health Stroke Scale (NIHSS) scores, time from stroke onset to LIT, blood pressure, early CT signs, or subsequent hemorrhagic transformation shown by CT. However, univariate analysis showed that patients with good outcomes were younger, more often had absence of hypertension history, had better collaterals shown by angiography, and had better recanalization rates than those with poor outcomes. NIHSS scores after LIT were lower in patients with good outcomes than in patients with poor outcomes. Logistic regression analysis indicated improvement of the NIHSS scores by ≥2 immediately after LIT was independently associated with good outcome.**

CONCLUSION: **Improvement of the NIHSS score by ≥2 immediately after LIT is a useful predictor of patient outcome at discharge.**

In 1995, the National Institute of Neurologic Disorders and Stroke rt-PA Stroke Study Group reported that IV thrombolytic therapy using recombinant tissue plasminogen activator (rt-PA) within 3 hours of ischemic stroke onset improved patient outcomes (1). However, a randomized trial that used rt-PA within 6 hours of onset failed to show the therapeutic efficacy (2). No benefits were shown in the Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke study (known as the ATLANTIS Trial), a randomized controlled trial with patients receiving rt-PA from 3 to 5 hours after onset (3). Therefore, the American Heart Association guidelines for acute ischemic stroke recommend that the IV administration of rt-PA has to begin within 3 hours of onset (4). On the other hand, local intra-arterial thrombolysis (LIT) was reported to be efficacious in patients with middle cerebral artery (MCA) occlusion if performed within 6 hours of onset. In the Prolyse in Acute Cerebral Thromboembolism II study, LIT improved the prognosis of stroke within 6 hours of onset (5).

In 6% to 20% of patients who undergo thrombolysis, a serious side effect of symptomatic intracerebral hemorrhage (SICH) develops (1–6). SICH in patients

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receiving rt-PA was found to be related to tissue plasminogen activator dose, National Institute of Health Stroke Scale (NIHSS) score, and diastolic blood pressure (7, 8).

Early ischemic changes revealed by CT, such as cortical effacement (9), were also involved in the occurrence of SICH. The American Heart Association guidelines warn about the administration of rt-PA in patients with high blood pressure and early signs revealed by CT (4). We performed LIT in patients with acute MCA occlusion during the past 4 years in a prospective study design. We strictly adhered to predefined inclusion and exclusion criteria, and no patient developed SICH. Our purpose was to determine which clinical factors are predictors of favorable outcome.

Methods

Inclusion and Exclusion Criteria

The clinical inclusion criteria for LIT were acute embolic stroke within 6 hours of symptom onset, patient age from 20 to 85 years, and NIHSS score from 5 to 29. The exclusion criteria included the following: 1) neurologic symptoms caused by subarachnoid hemorrhage, neoplasm, septic embolism, moyamoya disease, or vasculitis; 2) seizure at onset; 3) rapidly improving neurologic signs at any point before LIT; 4) history of stroke within the previous 4 weeks (except transient ischemic attacks); 5) surgery, biopsy, or trauma with internal injuries within 2 weeks; 6) active or recent hemorrhage within 2 weeks; 7) baseline international normalized ratio of prothrombin time >1.7 or baseline platelet count $<10 \times 10^4$/L; 8) uncontrolled hypertension defined by systolic blood pressure >185 mmHg or diastolic blood pressure >100 mmHg; 9) pregnancy or puerperal period. CT of the brain exclusion criteria included intracranial tumor, hemorrhage, and an early sign revealed by CT (acute hypoattenuated parenchymal lesion) in more than one-third of the MCA territory.

In patients who satisfied all the clinical and CT inclusion criteria, diagnostic cerebral angiography was performed. The angiographic exclusion criteria were occlusion of the internal carotid artery or long segment basilar artery occlusion and aneurysms or arterial dissections.

From April 1997 to December 2001, we screened 364 patients by using cerebral angiography. We found internal carotid artery occlusion in 51 patients, MCA occlusion in 135, basilar artery occlusion in 13, cerebral artery dissections in eight, cerebral aneurysms in eight, and other arterial occlusion or no occlusion in the other 149. Forty-seven patients (mean age, 66.4 ± 11.6 years; men, 35; women, 12) who were diagnosed as having MCA occlusion based on cerebral angiography findings within 6 hours of symptom onset were admitted to our Stroke Care Unit. Excluded were 18 patients: one with a malignant tumor, one with rapid improvement of symptoms before cerebral angiography, three who were older than 85 years, two with high blood pressure, and 11 with early CT signs involving more than one-third of the MCA territory. The remaining 29 patients underwent LIT. None of the 29 patients developed SICH or died during the hospital stay. Three of the 29 patients were not independent (modified Rankin scale score, ≥3) before the index stroke. We analyzed the remaining 26 patients who had modified Rankin scale (mRS) scores <2 before stroke onset.

Thrombolytic Procedure and Post-LIT Treatment

We performed cerebral angiography via a femoral approach. The LIT was performed when clinical, CT, and angiographic criteria were completely met and written informed consent was obtained from the patient or a family member. An infusion microcatheter with a single end hole was placed on the distal portion of the MCA thrombus by using a steerable microguidewire through a 6-French guiding catheter. Maximum dose of 420,000IU of urokinase (Urokinase 60,000IU, Mitsubishi Pharma Corporation) was infused manually at the rate of 35 mL/hr through the microcatheter. Simultaneously, mechanical disruption of the clot was performed by using a flexible microguidewire with a tip angle of 90 degrees (GT wire TERMO, 0.016 or 0.012 in). Penetration and fragmentation of the thrombus were achieved by gently advancing and rotating the tip of microguidewire. The LIT was stopped when the infusion time from the start of LIT exceeded 1 hour or when the operator confirmed that the artery was recanalized by >50% of the area perfused by the initial occluded artery during capillary, as seen in the lateral view.

The protocol required that no anticoagulants or antiplatelet agents were administered for 24 hours after treatment and that arterial blood pressure was monitored during the first 24 hours. When systolic blood pressure increased to >180 mmHg after LIT, IV antihypertensive drugs were continuously infused for at least 48 hours.

Clinical Variables and Outcome Measures

We assessed a history of hypertension (previous systolic ≥160 mmHg or diastolic ≥95 mmHg or receiving antihypertensive drugs), diabetes mellitus (fasting blood sugar >7.7 mmol/L, random blood sugar >11.1 mmol/L, or receiving insulin or oral hypoglycemic agents), hypercholesterolemia (total cholesterol ≥220 mg/dL or receiving antihyperlipidemic agents), smoking or alcohol habit, and anticoagulant and antiplatelet therapy before stroke onset. Grades of collateral flows and vessel recanalization were assessed by using cerebral angiography. All the angiograms were analyzed by a stroke neurologist without knowing the final result. The grades of collaterals were simply classified as poor (<50% of the occluded vascular territory was caused by collaterals) and good (collateral flows via leptomeningeal anastomoses allowed >50% filling of the territory distal to the occlusion). The achieved vessel recanalization was classified as described by Mori et al (10) and Yamaguchi et al (11). Vessel recanalization was classified into two groups. The lesion was categorized to be low grade if no or slight recanalization was perfusing <50% of the ischemic area. The grade of vessel recanalization was considered to be high grade when reperfusion covering >50% of the ischemic area was achieved.

Early signs revealed by initial CT were defined on the basis of loss of insular ribbon and cortical ribbon effacement. The presence or absence of hemorrhagic transformation was evaluated by follow-up CT performed >24 hours after LIT. SICH was diagnosed when hemorrhagic transformation was confirmed by CT and NIHSS score increased by ≥4 or when level of consciousness deteriorated by 1 point compared with before LIT.

Neurologic severity was assessed immediately, at 24 hours, and at 1 month after LIT by using NIHSS scores. Outcome at discharge was assessed by using the mRS and the Barthel index scores. Number of deaths during the hospital stay was monitored.

Statistical Analysis

All values are expressed as mean ± SD for parametric values or as a median (range) for nonparametric values. Comparisons among groups were made by analysis of variance and then Mann-Whitney U test. The χ^2 test was conducted for the analysis of discrete variables. $P < 0.05$ was considered to be statistically significant. Logistic regression analysis was used to evaluate the contribution of the various factors to the outcome.

Table 1: Characteristics of patients undergoing local intra-arterial thrombolysis

Age, mean (SD), yr	65 (13)
Men, %	80.8
Cardioembolic stroke, %	92.3
Atrial fibrillation, %	76.9
Occlusion of M1 segment, %	42.3
History of risk factors, %	
Hypertension	57.7
Diabetes mellitus	19.2
Hypercholesterolemia	19.2
Smoking	46.2
Alcohol	42.3
Time to admission, mean (SD), hr	0.96 (0.87)
Time to starting LIT, mean (SD), hr	3.78 (1.17)
Early CT sign, %	46.2
Previous anticoagulant therapy, %	26.9
Previous antiplatelet therapy, %	15.4
Symptomatic hemorrhage, %	0
Baseline NIHSS score, median (range)	18 (6–23)
NIHSS score after LIT, median (range)	
Immediately	15 (3–22)
24 hr later	12 (2–22)
1 month later	6 (0–16)
BI score at discharge, median (range)	95 (0–100)
mRS score at discharge, median (range)	2 (0–5)
Deaths, %	0
Hospital stay, mean (SD), days	50 (23)

Note.—LIT indicates local intra-arterial thrombolysis; NIHSS, National Institutes of Health Stroke Scale; BI, Barthel index; mRS, modified Rankin scale.

Results

Demographics and Clinical Data

The baseline characteristics of the 26 patients who underwent LIT are shown in Table 1. LIT was commenced 3.78 ± 1.17 hours after stroke onset. Hemorrhagic transformation in 11 patients (42.4%) was revealed by CT. However, no patients developed SICH or died. The median of the baseline NIHSS score was 18 (range, score of 6–23) at admission and became 6 (range, score of 0–16) 1 month later. Stroke recurred in two patients during their hospital stay. The median mRS score was 2 (range, score of 0–5), and the median Barthel index score was 95 (range, score of 0–100) at the time of discharge.

Outcome Data

Thirteen of 26 patients achieved good outcomes (mRS score, ≤2), and the other 13 had poor outcomes (mRS score, ≥3). The median baseline NIHSS scores were not different between the two groups (median score of 16 versus median score of 18). Patients with poor outcomes experienced no recurrence of stroke and no major complication, such as pneumonia or heart failure, during their hospital stay. The length of hospital stay was longer for patients with poor outcomes than for those with good outcomes (61 versus 38 days). Patients with good outcomes were younger (age 57.3 years ± 13.1 for good outcome group versus age 72.5 years ± 6.2 for poor outcome group), had hypertension less frequently (38.5% versus 76.9%), had an alcohol habit more frequently (61.5% versus 23.0%), M1 occlusion (61.5% versus 23.1%), good collaterals (61.5% versus 15.4%), and good recanalization (69.2% versus 30.7%). No differences were observed based on sex, baseline NIHSS scores, time to admission, time to LIT commencement, frequency of early signs revealed by CT, antiplatelet or anticoagulant therapy before stroke, hemorrhagic transformation on CT, blood pressure levels, or dose of urokinase or heparin between the two groups (Table 2). The antihypertensive agents were IV infused in four patients with good outcomes (31%) and in six patients with poor outcomes (46%). No differences were noted in arterial blood pressure after LIT between the two groups (Table 2). No patient received anticoagulants or antiplatelet agents for 24 hours after treatment.

Figure 1 shows the evolution of the NIHSS scores after LIT in patients with good and poor outcomes. The NIHSS scores of patients with good outcomes improved immediately after LIT. On the other hand, this immediate improvement was not observed for those with poor outcomes. The median NIHSS score was 9 (range, score of 3–19) for the good outcome group and 18 (range, score of 13–22) for the poor outcome group immediately after LIT ($P = .001$). The NIHSS scores of 11 patients (85%) with good outcomes improved immediately after LIT by ≥2. On the other hand, such an improvement was noted for only one patient with poor outcome. The differences in the median NIHSS scores between the two groups gradually increased with time. Thus, the NIHSS scores were 7 (range, score of 2–19) for the patients with good outcomes and 18 (range, score of 10–22) for the patients with poor outcomes after 24 hours ($P = .001$). One month later, the scores were 2 (range, score of 0–9) versus 10 (range, score of 6–18) ($P < .0001$). The Barthel index score in the good outcome group was 100 for all patients at discharge, whereas in the poor outcome group, the median Barthel index score was 40 (range, score of 0–90) ($P < .0001$). The median mRS score at discharge was 1 (range, score of 0–2) in the patients with good outcomes and 4 (range, score of 3–5) in the patients with poor outcomes ($P < .0001$).

Logistic Regression Analysis

Univariate analysis showed that the variables associated with good outcome (mRS score, ≤2) at discharge were age, good collaterals, occlusion of M1 segment, alcohol habit, no history of hypertension, high grade recanalization, and improvement of NIHSS score by ≥2 immediately after LIT (ΔNIHSS score, ≥2) (Tables 3 and 4). We selected factors in baseline characteristics, such as age, good collaterals, occlusion of M1 segment, alcohol habit, and nonhypertension, as independent factors for multivariate analysis with a logistic regression model for good outcome (Table 3, Model 1). The analyses showed no factors to be significant.

Table 2: Demographic and clinical variables for patients undergoing local intra-arterial thrombolysis

Variable	mRS Score ≤2 (n = 13)	mRS Score ≥3 (n = 13)	*P* Value
Age, mean (SD), yr	57 (13)	73 (6)	.0003
Men, %	84.6	76.9	>.9999
History of risk factors, %			
Hypertension	38.5	76.9	.047
Diabetes mellitus	15.4	23.0	>.9999
Hypercholesterolemia	23.1	15.4	>.9999
Smoking	61.5	30.8	.116
Alcohol	61.5	23.0	.047
Previous anticoagulant therapy, %	38.5	15.4	.378
Previous antiplatelet therapy, %	23.0	7.6	.593
Time to admission, mean (SD), hr	1.06 (0.95)	0.85 (0.81)	.519
Time to starting LIT, mean (SD), hr	3.81 (1.23)	3.75 (1.15)	.858
Time to end LIT, mean (SD), hr	4.86 (1.11)	4.85 (1.22)	.739
Baseline NIHSS score, median (range)	16 (6–22)	18 (9–23)	.757
Blood pressure at admission, mean (SD), mmHg			
Systolic	149 (32)	151 (23)	.741
Diastolic	86 (15)	83 (9)	.739
Early CT sign, %	53.8	38.5	.431
Occlusion of M1 segment, %	61.5	23.1	.047
Collateral flow (≥50%), %	61.5	15.4	.016
Dose of urokinase, mean (SD), $\times 10^4$ IU	40.6 (11.6)	36 (14.9)	.527
Dose of heparin, mean (SD), $\times 10^3$ IU	3.8 (2.8)	3.3 (2.1)	.723
Recanalization (≥50%), %	69.2	30.7	.049
Hemorrhagic transformation on CT, %	38.5	46.2	.691
Use of antihypertensive drug, %	31	46	.973
Blood pressure after LIT (with/without antihypertensive drug), mean (SD), mmHg			
Systolic	138 (10)	132 (23)	.275
Diastolic	73 (10)	76 (8)	.572
Hospital stay, mean (SD), days	38 (9)	61 (26)	.014

Note.—mRS indicates modified Rankin scale; LIT, local intra-arterial thrombolysis; NIHSS, National Institutes of Health Stroke Scale.

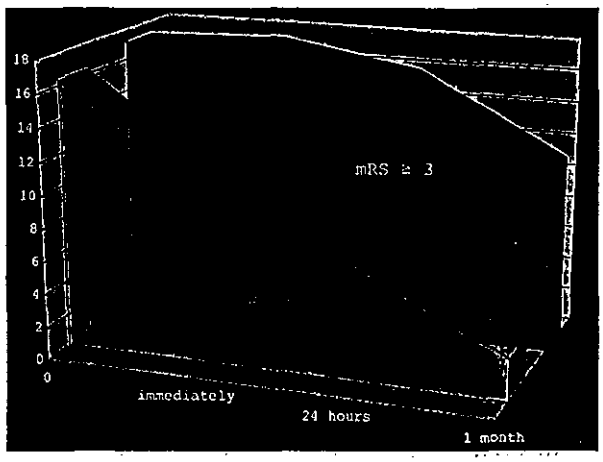

FIG 1. Progression of NIHSS scores of patients with good outcomes and those with poor outcomes.

In a Model 2 analysis, we added ΔNIHSS score ≥ 2 and high grade recanalization to factors of age and good collaterals that showed $P < .2$ in the Model 1 multivariate analysis as an independent factors (for multivariate analysis with a logistic regression model) for good outcome (Table 4). As a result, ΔNIHSS ≥ 2 was the only significant predictor for favorable outcome.

Discussion

The National Institute of Neurologic Disorders and Stroke rt-PA trial revealed that SICH occurred in the rt-PA group 10 times more often than in the placebo group (1). Other randomized controlled trials reported that SICH occurred in 8% to 20% of patients (2–6). In our study, in which LIT was performed only in patients with embolic MCA occlusion, no cases of SICH (95% confidence interval, 0.871–1) or death occurred. Levy et al (7) reported that a predictor of SICH was a high mean blood pressure before IV tissue plasminogen activator treatment. Kidwell et al (8) found that in patients who had undergone LIT, the NIHSS score in the SICH group was higher than in the non-SICH group (mean NIHSS scores, 20 in SICH versus 15 in non-SICH). Other predictors of hemorrhagic transformation were longer time to recanalization, lower platelet count, and higher glucose level. The inclusion and exclusion criteria for LIT in our study were similar to those of the National Institute of Neurologic Disorders and Stroke rt-PA trial except for the time window, and we strictly followed the American Heart Association guidelines (3). As a result, patients with excessively high baseline NIHSS scores (scores > 29) were excluded from the study. In our study, 50% of the patients had mRS scores ≤2 at discharge, whereas 40% of the patients in the Prolyse in Acute Cerebral Thromboembolism II study had

Table 3: Logistic regression analysis for pretreatment predictors of favorable outcome in patients undergoing local intra-arterial thrombolysis (Model 1)

Variable	Univariate			Multivariate		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age <60 yr	5.1	1.02–30.06	.027	7.8	0.49–308.36	.182
Good collaterals	8.8	1.55–74.68	.016	6.1	0.53–102.44	.166
Occlusion of M1 segment	5.3	1.04–33.91	.047	5.4	0.41–139.85	.218
Alcohol habit (+)	5.3	1.04–33.91	.047	3.5	0.22–95.49	.377
Hypertension (−)	5.3	1.04–33.91	.047	2.3	0.19–29.67	.483

Note.—OR indicates odds ratio; CI, confidence interval.

Table 4: Logistic regression analysis for predictors of favorable outcome for patients undergoing local intra-arterial thrombolysis (Model 2)

Variable	Univariate			Multivariate		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
ΔNIHSS score ≥2	65.9	7.46–1656.23	.001	38.8	2.40–2112.46	.024
High grade recanalization	10.3	1.37–216.38	.049	18.0	0.59–1538.90	.126
Age <60 yr	5.1	1.02–30.06	.027	7.7	0.32–296.83	.265
Good collaterals	8.8	1.55–74.68	.016	6.0	0.18–522.90	.261

Note.—OR indicates odds ratio; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale.
*ΔNIHSS score was calculated by subtracting immediate NIHSS score from baseline NIHSS score.

mRS scores ≤2 at day 90. Therefore, strict application of the criteria for the management of patients with LIT seems to be essential to obtain favorable outcomes and to avoid SICH. Additionally, antihypertensive medicine was aggressively infused through an IV route in patients who had high systolic blood pressure >180 mmHg after LIT. None of our patients had blood pressure >180 mmHg after antihypertensive treatment. It was suggested that control of blood pressure after LIT was also an important factor against SICH.

Bendszus et al (12) reported artery factors related to good outcomes in patients who had undergone LIT of MCA and internal carotid artery occlusion. They noted that presence of leptomeningeal collaterals and successful recanalization after LIT correlated with good outcome, whereas the interval from stroke onset to LIT was not related to it. However, their series had a 10% incidence of SICH. Arnold et al (13) reported that a low NIHSS score at admission and good vessel recanalization were independently associated with good outcome, and SICH occurred in 7% of patients. In the Prolyse in Acute Cerebral Thromboembolism II study, it was reported that outcome is associated with history of cerebrovascular disease, hypertension, and diabetes (14).

In our study, as in previous reports, the good outcome group was younger and had a higher rate of good collaterals and higher grade recanalization than the poor outcome group. In addition, the good outcome group had few cases of hypertension, as in the Prolyse in Acute Cerebral Thromboembolism II study, and alcohol habit and M1 occlusion were frequent. Aronowski et al (15) reported that a low dose of ethanol plus caffeine reduced infarct volume in a rat model of transient MCA occlusion. Although the optimal dose of alcohol was unknown, our result suggested that alcohol was a neuroprotective factor in the thrombolytic therapy. It seems very interesting that in our study, 62% of the good outcome group had M1 occlusion, compared with only 23% of the group with mRS ≥3. Gönner et al (16) indicated that good outcomes were achieved in 57% of patients with occlusion of M1 and perforators. On the other hand, all patients who had M1 occlusion without involving perforators or an M2 occlusion achieved good outcomes (100%). All our patients had M1 distal occlusions without perforator involvement. Although the rate of recanalization was not significantly different between patients with M1 occlusion and those with M2 occlusion, the patients with M1 occlusion had good collaterals (90%) compared with the patients with M2 occlusion (6%). The grade of collaterals may be more important for later outcome than the site of arterial occlusion.

No study has reported in detail on the evolution of NIHSS scores after LIT. In the good outcome group, the NIHSS score improved immediately after LIT and then continued to improve gradually. On the other hand, in the poor outcome group, the NIHSS score remained stable for nearly 24 hours (Fig 1). Multiple logistic regression analysis revealed that ΔNIHSS immediately after LIT was the only independent factor for good outcome. Thus, later outcome can be predicted by a change in NIHSS score (ΔNIHSS) immediately after LIT.

The present study had some limitations. First, it was an observational study. We cannot compare our results with those of patients who did not undergo LIT. Therefore, the effect of LIT for MCA occlusion is unclear. Second, our study size was small, so care must be taken in the interpretation of the analyses.

Conclusion

Strict criteria should be applied in selecting patients with MCA occlusion for LIT to avoid SICH. Favorable outcome at a later time or discharge may be predicted by improvement in NIHSS score immediately after LIT. These observations should be confirmed in large prospective randomized controlled trials.

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Transcranial Color-Coded Real-Time Sonographic Criteria for Occlusion of the Middle Cerebral Artery in Acute Ischemic Stroke

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BACKGROUND AND PURPOSE: **Transcranial color-coded real-time sonography (TCCS) is a useful tool to evaluate disease of the middle cerebral artery (MCA). This study was undertaken to identify TCCS criteria for the diagnosis of MCA stem and MCA branch occlusions.**

METHODS: **TCCS and digital subtraction angiography were performed in 55 consecutive patients with acute stroke: 10 with MCA stem occlusion, the MO group; eight with MCA branch occlusion, the MB group; and 37 with nonocclusive lesions, the control group. We measured the end-diastolic velocity (EDV) of the bilateral MCA stems and calculated the end-diastolic ratio by dividing the EDV of the unaffected side by that of the affected side.**

RESULTS: **EDV was highest in the control group, and end-diastolic ratio was highest in the MO group. An EDV of >25 cm/s indicated a nonocclusive lesion in the MCA, with a positive predictive value of 98.4%, a negative predictive value of 81.0%, and an accuracy of 93.9%. An EDV of ≤25 cm/s with an end-diastolic ratio of <2.7 indicated an MCA branch occlusion with a positive predictive value of 85.7%, a negative predictive value of 97.2%, and an accuracy of 95.3%. An EDV of ≤25 cm/s with an end-diastolic ratio of ≥2.7 indicated MCA stem occlusion with a positive predictive value of 100%, a negative predictive value of 100%, and an accuracy of 100%.**

CONCLUSION: **We developed TCCS criteria for the diagnosis of MCA diseases. MCA flow velocity detected by means of TCCS can help identify MCA stem occlusion as well as MCA branch occlusion.**

In the early 1990s, transcranial color-coded real-time sonography (TCCS) was introduced as a new method for imaging the basal cerebral arteries (1–3). TCCS is a noninvasive, easy-to-repeat, diagnostic technique that is widely used for the evaluation of cerebral hemodynamics. As a result of combining the B-mode facility and the color-coded Doppler facility, the brain vessels can be clearly displayed. Furthermore, since the angle of insonation can be measured and corrected for, one can obtain velocity measurements that are closer to true values (4, 5). Thus, TCCS is a useful tool in evaluating vascular diseases of the middle cerebral arteries (MCAs), particularly in patients with ischemic stroke.

However, only a few reports have described the diagnosis of MCA stem occlusion with TCCS (6, 7). In fact, TCCS criteria for MCA occlusion, particularly MCA branch occlusion, have not yet been established. MCA branch occlusion frequently occurs in patients with acute ischemic stroke. Therefore, it is important to be able to evaluate the MCA branch occlusion as well as the MCA stem occlusion when one is deciding on a patient's therapy.

Peripheral resistance, which is found after the point of measurement, is thought to reflect blood flow velocity; the higher peripheral resistance, the lower the blood flow velocity. Therefore, we hypothesized that the blood velocity in the MCA stem of patients with MCA branch occlusion is lower than that in patients without MCA occlusion and that it is higher than that of patients with MCA stem occlusion. The aim of the current study was to establish TCCS criteria for determining the specific sites of MCA occlusion.

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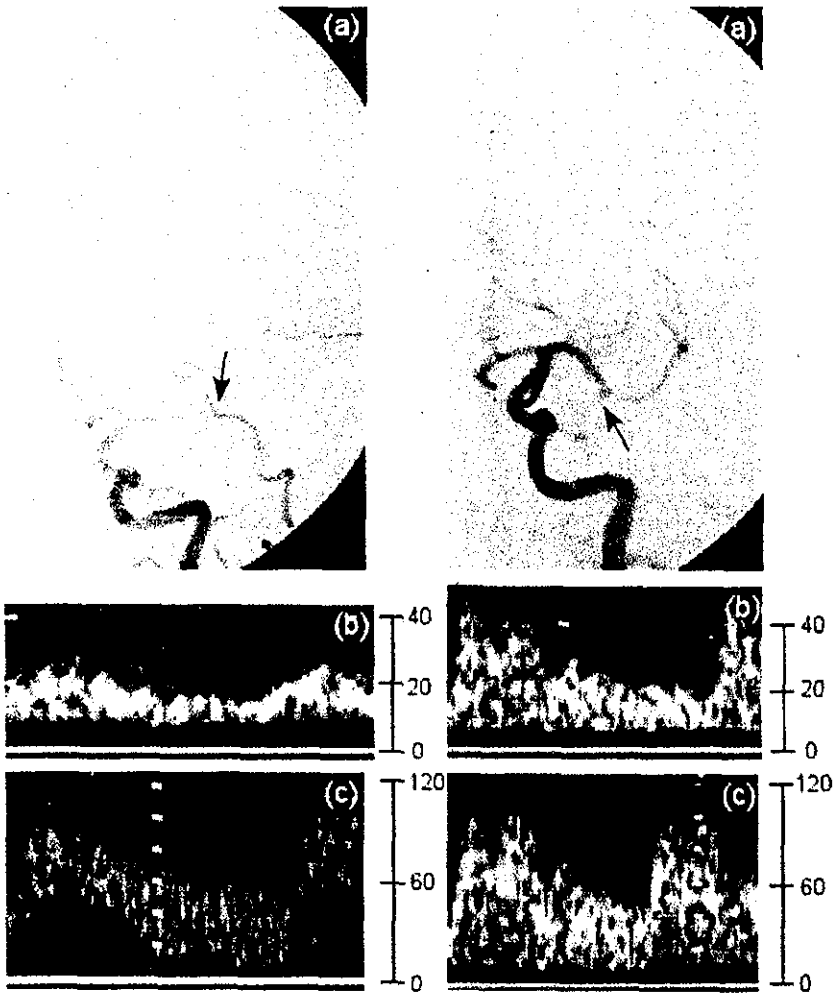

FIG 1. Left anteroposterior carotid angiograms in representative cases evaluated with cerebral angiography and TCCS. Y axis is represented blood flow velocity (cm/s). *Left* image shows occlusion of the horizontal portion of the left MCA (*a*). Occlusion site overlies the external carotid artery branch. Doppler waveforms of the *left (b) and right (c)* MCAs show EDVs of 14.5 and 49.9 cm/s, respectively. *Right* image shows occlusion of the branch in the left MCA (*a*). Doppler waveforms of the left (*b*) and right (c) MCAs show EDVs of 18.2 and 44.6 cm/s, respectively.

Methods

We prospectively performed TCCS in 66 consecutive patients with acute stroke who underwent intra-arterial digital subtraction angiography (DSA). TCCS examinations were performed 24 hours before and after the intra-arterial DSA study. Eleven patients (three with occlusion or a severe stenosis in internal carotid artery, six with MCA stem stenosis, and two with proximal MCA occlusion) were excluded from this study. Patients with proximal MCA occlusion were excluded because TCCS could not display the flow signal of the MCA, and thus the flow velocity could not be measured. Therefore, 55 patients were enrolled. Their stroke subtypes were as follows: two patients had a lacunar stroke, 10 had atherothrombotic stroke, 20 had cardioembolic stroke, one had a transient ischemic attack, 18 had other types of ischemic stroke, three had hemorrhagic stroke, and one had amourosis fugax.

The study protocol followed all principles outlined in the Declaration of Helsinki. Selective angiography was performed by using biplane DSA (Angio Rex Super-G and DFP-2000A; Toshiba, Tokyo, Japan). All examinations were performed by means of transbrachial or transfemoral catheterization in accordance with the Seldinger method. Standard anteroposterior and lateral images were routinely obtained.

According to the DSA results, we assigned the patients as follows: Patients with an MCA stem occlusion were the MO group, patients with an MCA branch occlusion were the MB group, and patients with no occlusive or stenotic MCA lesions were the control group.

TCCS was performed by using a unit (Sonos 5500; Philips Medical Systems, Japan, Tokyo) with a 1.0–3.0-MHz sector scan. The transtemporal acoustic window was used to visualize the MCA stem in real time by using color signals. We obtained color Doppler flow images and measured flow velocity at the MCAs. Patients were examined first in the left lateral decubitus position and then in the right lateral decubitus position. Particular care was taken to identify an appropriate straight-vessel segment of the MCA by means of tilting, rotating, or shifting the transducer. A 1.9-mm, range-gated, pulsed Doppler sample volume was used to measure the blood flow velocity in the MCA stem. The sample volume was moved slowly from the proximal to the distal position along the horizontal segment of the MCA and displayed as a color flow image on B-mode images. We chose the measured point where the blood flow velocity was the highest. Then we measured the mean end-diastolic velocity (EDV) over five consecutive cardiac cycles. Angle correction was applied when the correction angle did not exceed 60°. Furthermore, the side-to-side ratio of the end-diastolic flow velocity (end-diastolic ratio) was calculated by dividing the velocity of the unaffected side by that of the affected side in the MO and MB groups. We also detected the end-diastolic ratio of patients in the control group by dividing the higher MCA velocity by the lower one.

The age and blood flow velocity data for each group were expressed as the mean ± SD. Statistical comparisons of velocity differences within each group were performed by using one-way factorial analysis of variance and then Scheffé multiple comparison tests. Sensitivity-specificity curve analysis was applied to obtain cutoff values for EDV to distinguish the MO or MB group from the control group and for the end-diastolic ratio to differ-

entiate the MO group from the MB group. A P value of $< .05$ was accepted as indicating a significant difference.

Results

We performed intra-arterial DSA in 55 patients (46 men and nine women; mean age, 63.8 ± 13.1 years). TCCS depicted bilateral MCA flow signals in 43 patients. However, TCCS depicted only unilateral MCA flow signal intensity in the other 12 patients. Consequently, the EDV of 98 vessels was measured. Occlusive lesions were present in 10 patients with a unilateral mid-to-distal occlusion of MCA stem, seven patients with a unilateral MCA branch occlusion, one patient with bilateral MCA branch occlusions, and 37 patients without a significant occlusion or stenosis. Thus, the groups consisted of patients with an occlusion of the MCA stem (MO group, $n = 10$), those with an occlusion of the MCA branch (MB group, $n = 8$), and patients with no occlusive lesions (control group, $n = 37$).

We did not detect MCA flow on the right side in the patient with bilateral MCA branch occlusions. Typical waveforms obtained in the MO and MB groups are shown in Figure 1.

The end-diastolic ratio was calculated for all patients in whom bilateral MCAs were detected. Scattergrams of the EDV and the end-diastolic ratio for each group are shown in Figure 2. EDV was significantly higher in the control group (40.5 ± 11.5 cm/s) than in the MO group (12.2 ± 3.6 cm/s, $P < .001$) or MB group (19.6 ± 4.8 cm/s, $P < .001$). The end-diastolic ratio (4.2 ± 1.5) of the MO group was significantly greater than that of the MB group (1.8 ± 0.5, $P < .001$) or control group (1.2 ± 0.1, $P < .001$).

On sensitivity-specificity curve analysis, the optimal threshold value of EDV for differentiating the MO and MB groups from the control group was 25 cm/s (Fig 3A). A positive predictive value of 81.0%, a negative predictive value of 98.4%, and an accuracy of 93.9% were calculated for the optimal threshold value. The optimal threshold value of the end-diastolic ratio for discriminating the MO group from the MB group was 2.7 (Fig 3B), with a positive predictive value of 100%, a negative predictive value of 100%, and an accuracy of 100%.

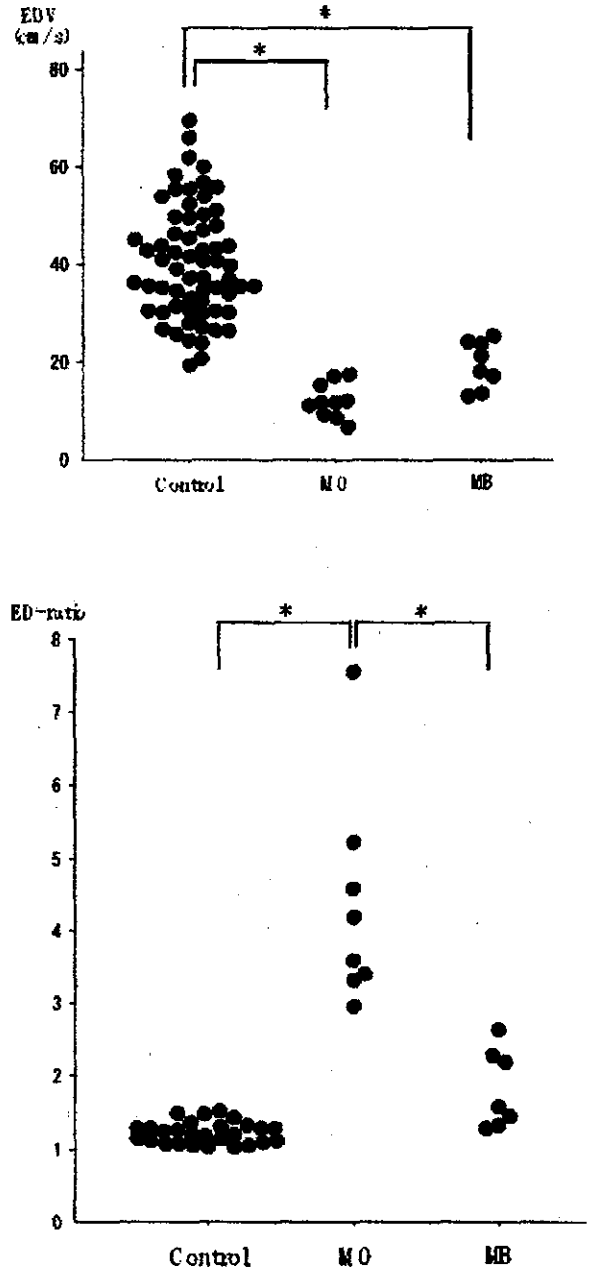

FIG 2. Scattergrams. *Top*, Mean EDVs (±2 SDs) for the control, MO, and MB groups are 40.5 ± 11.5, 12.2 ± 3.6, and 19.6 ± 4.8, respectively ($P < .001$, Scheffé test). *Bottom*, Mean end-diastolic ratios (±2 SDs) for the control, MO, and MB groups are 1.2 ± 0.1, 4.2 ± 1.5, and 1.8 ± 0.5, respectively ($P < .001$, Scheffé test).

Discussion

To our knowledge, this is the first study to develop TCCS criteria for diagnosing MCA stem occlusion and MCA branch occlusion. Kimura et al (7) reported that the end-diastolic ratio of patients with an MCA stem occlusion might increase to >1.9. In the present study, the end-diastolic ratio in the MO group was higher than 1.9, and this is compatible with the previous report by Kimura et al. Because they did not report TCCS criteria for determining MCA branch occlusion, the results of our MB group cannot be compared with their results.

Sensitivity-specificity curve analysis demonstrated an optimal threshold EDV value of 25 cm/s for differentiating MO and MB patients from control patients. In the MO and MB groups, 17 (94.4%) of 18 patients had an EDV <25 cm/s. However, of 37 patients in the control group, four (10.8%) had an EDV < 25 cm/s. Therefore, if the EDV is <25 cm/s, one cannot always identify the group (MO, MB, or control) to which the patient belongs. This is a limitation of our study. We have already reported that the end-diastolic ratio of control group patients was <1.9, even if EDV was under 25 cm/s (7). Therefore, the

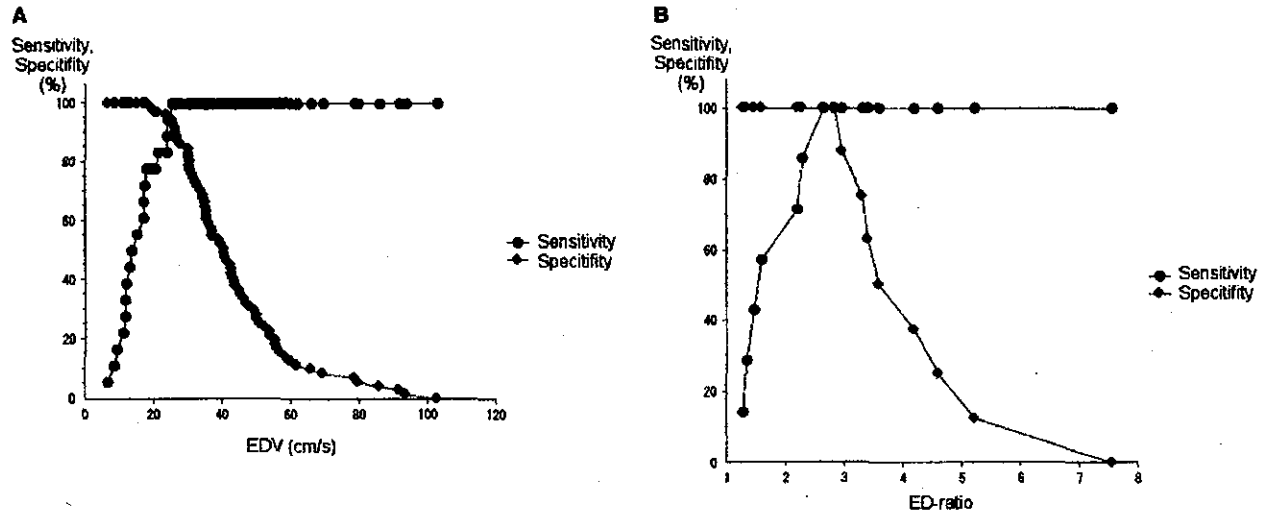

FIG 3. Sensitivity-specificity curves.
A, Predicting MO or MB by EDV. Optimal threshold value for EDV is 25 cm/s.
B, Differentiating MO from MB by the end-diastolic ratio. Optimal threshold value for the ratio is 2.7.

end-diastolic ratio should be useful in deciding if patients with EDV of ≤25 cm/s have an occlusive MCA lesion.

In the present study, we observed no differences in the end-diastolic ratio between the MB group and the control group. Therefore, the end-diastolic ratio alone is insufficient to diagnose an MCA branch occlusion. However, an end-diastolic ratio of 2.7 perfectly distinguished the MO group from the MB group. By using both the EDV and the end-diastolic ratio, we could distinguish the MB group from the control and MO groups. These results can be explained by the differences in the peripheral resistances among the MO, MB, and control groups. We conclude that the TCCS criteria of an EDV of ≤25 cm/s and an end-diastolic ratio of <2.7 indicates an MCA branch occlusion and that an EDV of ≤ 25 cm/s and an end-diastolic ratio of ≥2.7 indicates an MCA stem occlusion. The diagnostic algorithm for MCA stem and branch occlusion is shown in Figure 4.

A few patients could not be examined because of inadequate insonation windows during TCCS. The failure rate increased with age and was higher in women because of the higher prevalence of temporal hyperosteosis (8). Furthermore, the detection rate of intracranial artery flow signal intensity by using transcranial Doppler imaging is lower in Japanese patients than in white patients (9). Contrast agents can increase the detection rate of the MCA with TCCS (8, 10–13). Therefore, use of a contrast agent may help in diagnosing MCA diseases if the MCA flow cannot be detected with conventional TCCS.

When intravenous thrombolysis with tissue plasminogen activator (t-PA) is given to ischemic stroke patients within 3 hours of stroke onset, long-term outcomes improve (14). The Prolyse in Acute Cerebral Thromboembolism (PROACT) II study (15) demonstrated a significant benefit from treatment with intra-arterial prourokinase in patients with MCA occlusion treated within 6 hours of stroke onset.

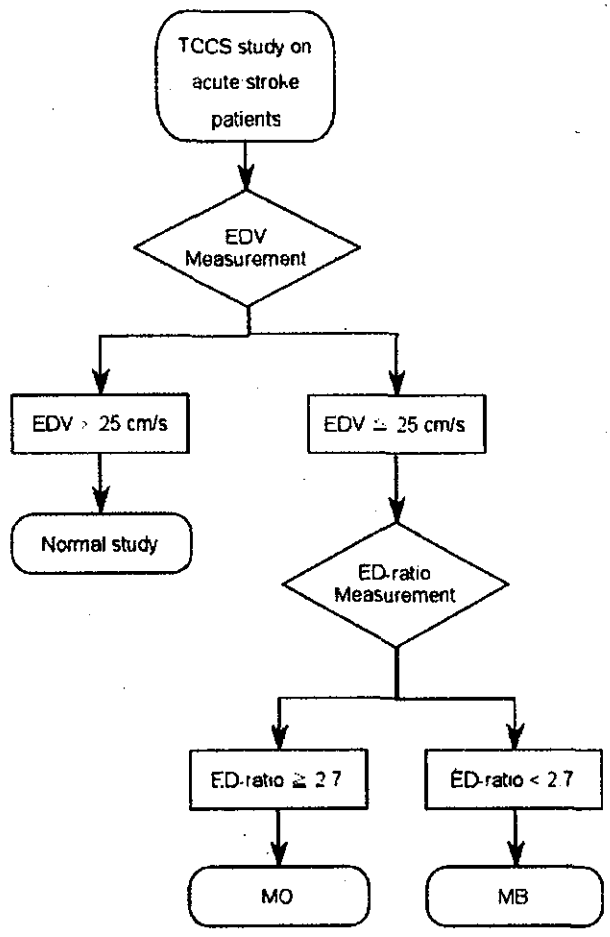

FIG 4. Algorithm for diagnosing MO and MB by using the EDV and end-diastolic ratio on TCCS.

Therefore, our TCCS criteria for MCA diseases may be useful in determining whether we perform the intra-arterial or venous thrombolysis in patents with hyperacute stroke. Furthermore, Eggers et al (16)