Ratio of Motor Nerve Conduction Velocity to F-Wave Conduction Velocity in Diabetic Neuropathy

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OBJECTIVE — To investigate the usefulness of a new parameter, the ratio of motor nerve conduction velocity to F-wave conduction velocity (M/F ratio), for the differential diagnosis of diabetic neuropathy.

RESEARCH DESIGN AND METHODS — Nerve conduction studies were conducted in 95 patients with diabetic neuropathy, 44 nondiabetic patients with peripheral neuropathy, and 24 normal control subjects. Nondiabetic patients with neuropathy were grouped by clinical diagnosis as follows: segmental demyelination (n = 15), axonal neuropathy (n = 11), alcoholic polyneuropathy (n = 4), and other polyneuropathy (n = 14). Motor nerve conduction velocity (MCV) of post-tibial nerves, sensory nerve conduction velocity (SCV) of sural nerves, and F-wave conduction velocity (FWCV) of post-tibial nerves were measured by standardized techniques. The M/F ratio was calculated from these measurements.

RESULTS — The MCV and SCV of diabetic patients were significantly slower and the M/F ratio was significantly lower than those of normal subjects: MCV, 43.7 ± 5.4 vs. 47.1 ± 2.9 m/s, $P < 0.001$; SCV, 44.7 ± 11.1 vs. 48.3 ± 5.7 m/s, $P < 0.05$; M/F ratio, 0.84 ± 0.09 vs. 0.90 ± 0.06, $P < 0.001$. The FWCV of nondiabetic patients with neuropathy was significantly slower (40.0 ± 6.3 vs. 48.3 ± 4.0 m/s, $P < 0.001$) and the M/F ratio was significantly higher (1.04 ± 0.12, $P < 0.001$) than that of normal subjects, respectively. Although MCV, SCV, and FWCV were correlated with age in normal control subjects, the M/F ratio was independent of age in the diabetic as well as the nondiabetic patients with neuropathy.

CONCLUSIONS — Results suggest that the M/F ratio, which is influenced by the neuronal damages in the distal segment of peripheral nerves, is useful in the differential diagnosis of diabetic neuropathy.

Diabetic polyneuropathy, a common complication of diabetes, is diagnosed by symptoms, signs, physical examination, nerve conduction studies, and other neurophysiological methods. Although nerve conduction studies are useful in the diagnosis and evaluation of diabetic neuropathy, there are difficulties in using them for the differential diagnosis of peripheral neuropathy because the pathological changes of diabetic neuropathy are varied. As a result, diabetic neuropathy is diagnosed essentially by excluding various other possible causes of neuropathy (1).

The F-wave is a late muscle response that results from the antidromic activation of one or a small number of motor neurons following electrical stimulation of a peripheral nerve (2). Kimura et al. (3) focused on use of the F-wave because it allows assessment of the proximal nerve segment, which is not accessible by the conventional nerve conduction studies. They reported that the F ratio, calculated from the latency of proximal and distal segments of peripheral nerves, was smaller in diabetic patients than in control subjects. They suggested that the distal segment is more dominantly damaged in diabetic polyneuropathy (3).

We studied the specificity of a new F-wave parameter, the ratio of motor nerve conduction velocity to F-wave conduction velocity (M/F ratio), in diagnosing diabetic neuropathy to the exclusion of other peripheral neuropathies.

RESEARCH DESIGN AND METHODS

Subjects

We studied a total of 163 subjects in the following groups: 95 patients with clinical or subclinical diabetic neuropathy with diffuse symmetrical peripheral neuropathy (51 men, 44 women; mean age 60 ± 10 years), 44 nondiabetic patients with peripheral neuropathy (32 men, 12 women; mean age 48 ± 21 years), and 24 normal control subjects (11 men, 13 women; mean age 62 ± 12 years). The criteria for the diagnosis of diabetic polyneuropathy were at least two abnormalities among clinical symptoms, neurological examinations, electrodiagnostic studies, quantitative sensory testing, and autonomic function testing. Patients with subclinical diabetic neuropathy were identified by completing the above criteria, except for clinical symptoms. Patients were excluded if clinical evaluations revealed severe renal complications, carpal tunnel syndrome, nerve root compression, or mononeuropathy.

The diabetes group consisted of 78 patients with NIDDM (40 men, 38 women; mean age 63 ± 8 years; HbA_{1c} 8.0 ± 1.9%), and 17 patients with IDDM (11 men, 6 women; mean age 49 ± 10 years; HbA_{1c} 9.4 ± 1.6%). The mean duration of diabetes was 13.9 ± 8.8 years.

The 44 patients with nondiabetic peripheral neuropathy were grouped according to the following diagnoses: *1*) fif-

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Abbreviations: FWCV, F-wave conduction velocity; MCV, motor nerve conduction velocity; M/F ratio, ratio of MCV to FWCV; SCV, sensory nerve conduction velocity; SMON, subacute myelo-optico-neuropathy.

Table 1—*Nerve conduction studies*

	Diabetes	Neuropathy	Control
n	95	44	24
MCV of post-tibial nerves (m/s)	43.7 ± 5.4*§	45.9 ± 4.7	47.1 ± 2.9
SCV of sural nerves (m/s)	44.7 ± 11.1†	47.8 ± 8.3	48.3 ± 5.7
FWCV of post-tibial nerve (m/s)	47.3 ± 5.9‡	40.0 ± 6.3*	48.3 ± 4.0
M/F ratio	0.84 ± 0.09*‡	1.04 ± 0.12*	0.90 ± 0.06

Data are means ± SD. *$P < 0.001$ vs. control; †$P < 0.05$ vs. control; ‡$P < 0.001$ vs. neuropathy; §$P < 0.05$ vs. neuropathy.

teen patients with segmental demyelination, nine with Guillain-Barré syndrome, five with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), and one with hereditary motor and sensory neuropathy (HMSN), type 1; 2) eleven patients with axonal neuropathy, five with toxic neuropathy, one with vitamin deficiency neuropathy, one with subacute myelo-optico-neuropathy (SMON), two with ischemic neuropathy, and two with amyloid neuropathy; 3) four patients with alcoholic polyneuropathy; and 4) fourteen patients with other polyneuropathy. All patients were diagnosed and treated at the Department of Neurology, Kyoto Prefectural University of Medicine.

Nerve conduction study

The protocol for electrodiagnosis recommended by the American Diabetes Association was used (4). MCV of post-tibial nerves and SCV of sural nerves were measured. For MCV of the post-tibial nerves, supramaximal stimuli were applied to the ankle and knee, and the compound muscle action potential was recorded from surface electrodes placed over the abductor hallucis muscle. Motor nerve conduction time, which is defined as the difference between the proximal and distal motor nerve latencies, in this instance, gave the motor nerve conduction velocity (MVC) of the knee-to-ankle segment of the leg, when divided into the knee-to-ankle distance. For sensory nerve conduction velocity (SCV) of the sural nerves, surface electrodes were placed adjacent to the lateral malleolus of the ankle, and stimulation was applied 13 cm proximal to the active electrode.

F responses were recorded from post-tibial nerves by use of the same electrode arrangement as for MCV studies, employing shocks of supramaximal intensity to the ankle. A total of 16 F-waves were recorded, and minimal F-wave latency was determined (5). F-wave conduction velocity (FWCV) in the segment to and from the spinal cord was calculated as $(D \times 2)/(F-M-1)$. D was the distance from the ankle stimulus site to the spinal cord, measured as the surface distance to the T12 spinous process via the greater trochanter of the femur. M/F, MCV divided by FWCV, represented the ratio of conduction velocity of the distal portion to that of the entire length of the post-tibial nerve.

Statistical analysis

Data are presented as mean ± SD. Results of the nerve conduction studies were evaluated by unpaired Student's *t* test, and single correlations between variables were assessed by Pearson's coefficient of correlation. A level of $P < 0.05$ was accepted as statistically significant.

RESULTS — There were no significant differences in age between the diabetic patients and control subjects, but the group with nondiabetic polyneuropathy was younger than either the diabetic patients ($P < 0.001$) or the control subjects ($P < 0.01$).

Nerve conduction studies

The MCV of post-tibial nerves and SCV of sural nerves in the diabetic patients were slower than those of the normal control subjects (Table 1). Although there was no significant difference between diabetic patients and normal control subjects in FWCV of post-tibial nerves, the M/F ratio in the diabetic patients was significantly smaller than that of normal control subjects.

There was no significant difference in MCV of post-tibial nerves and SCV of sural nerves between the nondiabetic patients with neuropathy and normal control subjects. The FWCV of the post-tibial nerves in the nondiabetic patients was slower than that of normal subjects; the calculated M/F ratio was larger than that of normal control subjects.

Among the nondiabetic patients with peripheral neuropathy, the M/F ratio was also significantly larger (segmental demyelination, 1.05 ± 0.11, $P < 0.001$; alcoholic neuropathy, 1.032 ± 0.01, $P < 0.001$; axonal neuropathy, 1.01 ± 0.13, $P < 0.05$) than that of normal control subjects. The FWCV was significantly slower (segmental demyelination, 38.7 ± 4.8 m/s, $P < 0.001$; alcoholic neuropathy, 41.0 ± 7.0 m/s, $P < 0.01$) than that of normal control subjects.

Correlation between age and nerve conduction variables (Table 2)

The M/F ratio was not correlated with age in normal control subjects, although there were significant negative correlations among age and motor, sensory, and F-wave conduction velocities. In the diabetic patients, however, conduction velocities and the M/F ratio were not correlated with age. The M/F ratio in the patients with nondiabetic polyneuropathy was also not correlated with age. The M/F ratio was not affected by sex and height of the subjects.

Feasibility of using the M/F ratio in the differential diagnosis of diabetic neuropathy

We compared study groups for the incidence of abnormality in MCV, SCV, FWCV, or the M/F ratio to test the specificity of each parameter in the diagnosis of diabetic neuropathy (Fig. 1). A value greater than the mean + 2 SD or less than mean − 2 SD of the control value was considered abnormal. High incidences of abnormalities in

Table 2—*Correlation between age and nerve conduction variables*

	Diabetes (n = 95)		Neuropathy (n = 44)		Control (n = 24)	
Variable	*r*	*P* value	*r*	*P* value	*r*	*P* value
MCV	0.0672	<1	−0.3187	<0.1	−0.5627	<0.01
SCV	0.0400	<1	−0.1884	<0.5	−0.5164	<0.02
FWCV	0.0336	<1	−0.3215	<0.1	−0.7349	<0.002
M/F ratio	0.0279	<1	0.2757	<0.1	0.2352	<0.5

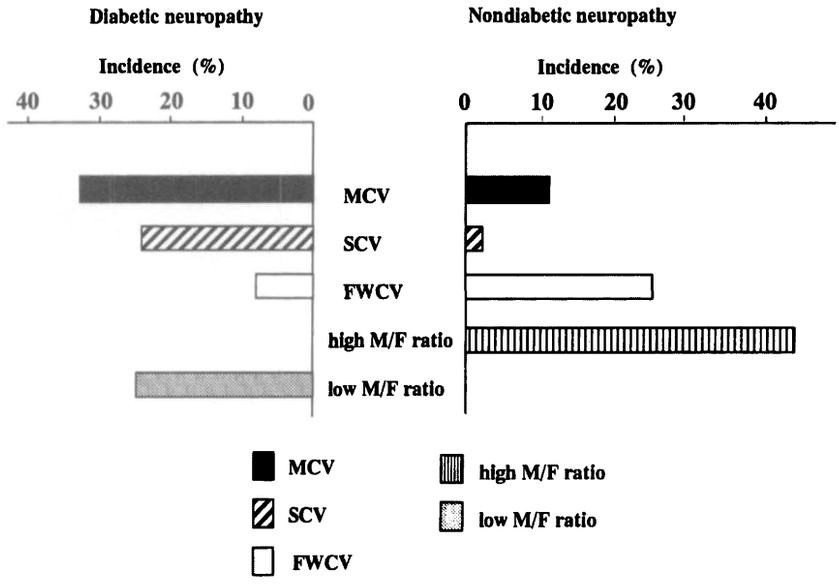

Figure 1—*Incidence of abnormal values of MCV, SCV (greater than the mean + 2 SD), high value for the M/F ratio (greater than the mean + 2 SD), and low value for the M/F ratio (less than the mean − 2 SD) in patients with diabetic neuropathy or in nondiabetic patients with peripheral neuropathy.*

MCV and SCV were present in the diabetic patients, whereas a high incidence of an abnormality in FWCV was present in the patients with nondiabetic neuropathy. A low incidence of an abnormality in SCV was detected in the nondiabetic patients with neuropathy. A striking contrast was evident when we compared the incidence of an M/F ratio greater than mean + 2 SD (high M/F ratio) and that of an M/F ratio less than mean − 2 SD (low M/F ratio). About 20% of the patients with diabetic neuropathy had a low M/F ratio but none of these patients had a high M/F ratio. In contrast, about 48% of the nondiabetic patients with neuropathy had a high M/F ratio, whereas none of these patients had a low M/F ratio.

CONCLUSIONS — The main advantage of F-wave methodology has been in the detection of peripheral neuropathies in which F-waves may show clinically significant and measurable changes even before conventional nerve conduction studies are informative (2). This is because the slowing of nerve conduction is maximized by F-waves traveling for long distances over the entire length of the nerve. Different patterns of F-wave abnormality have been demonstrated in patients with various peripheral nerve disorders (2), as well as in diabetic neuropathy (6,7). Although F-response latency was considered a sensitive indicator of peripheral neuropathy (8), amplitude and duration in ulnar nerve F response were the other sensitive parameters for the detection of mild diabetic neuropathy in type 1 diabetes (7). F-wave study added to conventional nerve conduction studies should provide more information that is useful in diagnosing the early stages of diabetic neuropathy.

Another application of F-wave measurement is in the evaluation of proximal nerve lesions (9). F-wave studies can provide useful information about patients who have lumbar or cervical root compression (10) or the carpal tunnel syndrome (9). It would be useful to exclude complications like radiculopathy in patients with diabetes.

While several useful F-wave parameters have been reported, the routine application of F-waves is mainly limited to latency measurement. Kimura et al. (3) suggested that the latency ratio of the proximal to the distal segment (F ratio) was reduced in diabetic patients. They concluded that motor conduction abnormalities in diabetic polyneuropathy were diffuse over the entire length of the nerve, but were more intense in the distal than in the proximal segment.

In this study, we proposed the M/F ratio as a new parameter that would have some advantages over the parameters previously determined by conventional nerve conduction or F-wave studies. The M/F ratio is not affected by age, whereas MCV, SCV (4), and F-wave latency (11) may be influenced by age. M/F ratio proved useful for the differential diagnosis of diabetic neuropathy. Subgroups of various pathological patterns of peripheral neuropathy, such as segmental demyelination, axonal neuropathy, SMON, and alcoholic neuropathy, can be differentiated from that of diabetic neuropathy on the basis of the M/F ratio. Although the incidence of an abnormal M/F ratio was relatively low, its assessment together with the SCV or FWCV provided a more specific diagnosis of diabetic neuropathy.

The pathological changes in diabetic neuropathy are so complicated, that some studies have cited electrophysiological and pathological evidence of segmental demyelination as the primary lesion (12). However, other studies have shown axonal damage to be the initiating event (13). Because segmental demyelination and axonal damage coexist in patients with diabetic neuropathy (14), nerve conduction studies, which primarily reflect the functional status of large myelinated nerve fibers, reveal various patterns. The F ratio and the M/F ratio have been used in an effort to clarify these patterns. Kimura's F ratio and our M/F ratio are similar. Use of the entire FWCV would increase sensitivity to longitudinal, heterogeneous, and subtle changes in the peripheral nerves, rather than to proximal-to-distal changes. Exactly why the M/F ratio should be able to discriminate diabetic neuropathy from nondiabetic neuropathy is unclear. Studies of additional patients with an analysis of the pathological changes, together with electrophysiological studies, are indicated. Our findings suggest that the M/F ratio is a useful parameter for the differential diagnosis of diabetic neuropathy.

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