The Usefulness of Minimal F-wave Latency and Sural/Radial Amplitude Ratio in Diabetic Polyneuropathy

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——— Abstract ———

The possibility of whether minimal F-wave latency and a simple ratio between the sural and superficial radial sensory response amplitudes may provide a useful electrodiagnostic test in diabetic patients was investigated in this report. To evaluate the diagnostic sensitivity of minimal F-wave latency, the Z-scores of the minimal F-wave latency, motor nerve conduction velocity (MCV), amplitude of compound muscle action potentials (CMAP), and distal latency (DL) of the median, ulnar, tibial, and peroneal nerve were compared in 37 diabetic patients. For the median, ulnar, and tibial nerves, the Z scores of the minimal F-wave latency were significantly larger than those of the MCV. In addition for all four motor nerves, the Z scores of the minimal F-wave latency were significantly larger than those for the CMAP amplitude. Furthermore, 19 subjects showing abnormal results in the standard sensory nerve conduction study had a significantly lower sural/radial amplitude ratio (SRAR), and 84% of them had an SRAR of less than 0.5. In conclusion, minimal F-wave latency and the ratio between the amplitudes of the sural and superficial radial sensory nerve action potential are sensitive measures for the detection of nerve pathology and should be considered in electrophysiologic studies of diabetic polyneuropathy.

Key Words: Minimal F-wave latency, sural/radial amplitude ratio, diagnostic sensitivity, diabetic polyneuropathy

INTRODUCTION

Diabetic polyneuropathy is characterized by a combined axonal loss and demyelinating sensorimotor peripheral neuropathy. To investigate this condition, nerve conduction studies with the determination of latency and velocity, are commonly used as they are considered to be the most sensitive, reliable, noninvasive, and objective means.[1-4] Standard nerve conduction studies usually suffice in securing a diagnosis when moderate to severe symptoms are present. However, in some patients with more mild symptoms, electrodiagnostic diagnosis may be more difficult. Axonal loss, which is believed to be the cause of most symptoms and clinical deficits of diabetic polyneuropathy, is characterized by a distal to proximal gradient of severity, with the longest nerves of

the lower extremities being affected earlier than the more proximal, upper extremity nerves.[5-7] Thus, an early reduction in the sural amplitude relative to the radial might be anticipated. Clinically, many patients with diabetic polyneuropathy complain of sensory symptoms. Diabetic polyneuropathy is believed to affect mainly the distal nerve segments, while sensory nerve conduction, especially the sural nerve, is considered to be more impaired than motor nerve conduction.[8] For this reason, F-wave studies have been considered to be of limited value in patients with subclinical diabetic neuropathy.[9] However, it has been recently reported that F-wave determinations in diabetic patients are very reliable.[10] As a consequence, the diagnostic sensitivity of the minimal F-wave latency was compared with other standard nerve conduction parameters such as motor nerve conduction velocity (MCV), amplitude of compound muscle action potentials (CMAP), and distal latency (DL). Furthermore whether or not minimal F-wave latency and a simple ratio between the sural and radial sensory response amplitudes might provide a useful electrodiagnostic test in patients with diabetic neuropathy was investigated.

MATERIALS AND METHODS

Patients

For nerve conduction studies, 50 consecutive diabetic patients that were referred to our electrodiagnostic laboratory over a 6-month period were identified. The majority of patients were referred to this laboratory because of pain and/or a tingling sense or paresthesia. These are all common symptoms of diabetic polyneuropathy, and some patients were referred to this laboratory as part of a clinical screening process for diabetic complications.

All patients underwent a detailed neurologic examination of both the upper and lower extremities. Patients were required to have at least two of the following:

(1) symptoms of paresthesia or dysesthesia;

(2) reduced vibratory sense below the knee;

(3) reduced ankle jerk compared to knee jerk and;

(4) reduced discrimination and light touch sense distally in the legs.

Subjects were excluded for any of the following reasons:

(1) electromyographic evidence of lumbosacral polyradiculopathy;

(2) clinical or electromyographic results suggesting the presence of a proximal diabetic neuropathy;

(3) concomitant diseases which could affect peripheral nerve function such as malnutrition or alcoholic hepatitis;

(4) clinical or electrophysiologic evidence of sciatic, peroneal, sural, or tibial mononeuropathy and;

(5) clinical or electrophysiological evidence of carpal tunnel syndrome and lumbosacral plexopathy.

After exclusion of these subjects, the final number of eligible patients in this study was 37 (25 women and 12 men aged 57 ± 10 years). The patients that complained of symptoms such as paresthesia, dysesthesia and burning sense numbered 33 (89% of total subjects). All patients had type 2 diabetes mellitus and the mean duration of the disease was 6.2 ± 5.6 years.

Nerve conduction studies

Nerve conduction studies of the median, ulnar, tibial, peroneal, sural, and superficial radial nerves were included. All studies were performed with surface recordings, using the standardized technique per-

formed by Ma and Liveson.[11] The nerves were stimulated using 0.1-ms electric pulses with a supramaximal intensity to elicit the maximum amplitude of CMAPs and SNAPs (sensory nerve action potentials). The temperature of both the upper and lower extremities were equalized and maintained at $31-34°C$. For the F response, 20 stimuli were given at a frequency of 1/s. An F-wave was defined as an action potential of an amplitude exceeding $20 \mu V$ and a latency within a reasonable range for the investigated nerve, excluding spurious voluntary activity. The latency to the onset of the first deflection from the baseline was recorded for each trace, and the shortest latency was determined (minimal F-wave latency).

For comparing the amplitude of the sural with those of the superficial radial nerves, all sural and superficial radial nerve stimulation was carried out 13 cm proximally in the midcalf, and 10 cm proximally along the radius, respectively. In addition, the disc electrode imbedded in a plastic bar was used as a constant distance between the active and reference electrode.

For each nerve, the results from only one side were included. In all, 148 motor nerves and 37 sural and superficial radial nerves from 37 patients were studied.

Calculation and statistical analyses

The results of motor nerve conduction studies were expressed as Z scores [Z=(result value-age and height matched normal mean value)/standard deviation] using age and height matched normal mean value and standard deviation.[11,12] For comparisons of the different conduction parameters (minimal F-wave latency, MCV, amplitude of CMAP), a paired student's t-test with the Bonferroni-corrected limit of significance was applied. The Z-score of the conduction velocities and response amplitudes were multiplied by -1 in order to compare the minimal F-wave latency results. The relationships between the various parameters were obtained using Pearson product-moment correlations. The sural/radial amplitude ratios (SRAR) were calculated by dividing the highest sural amplitude by the highest radial amplitude obtained.

RESULTS

The results of the motor nerve conduction studies,

Table 1. Z Scores (mean ± SD) of Minimal F-wave Latency (F-lat), Nerve Conduction Velocity (MCV), Amplitude (MAMP), and Distal Latency (DL) of the Median, Ulnar, Tibial, and Peroneal Nerve

Z-Scores	Nerve			
	Median	Ulnar	Tibial	Peroneal
F-lat	2.31 ± 1.34	2.02 ± 1.19	2.31 ± 1.21	2.34 ± 1.27
MCV	0.71 ± 1.36*	1.13 ± 1.31*	1.72 ± 1.23*	2.02 ± 1.38
MAMP	0.05 ± 0.92*	−0.11 ± 0.84*	0.64 ± 0.74*	0.58 ± 0.89*
DL	1.39 ± 3.79	0.05 ± 1.09*	0.65 ± 0.99*	0.03 ± 1.43*

* $p < 0.05$.
For comparison of F-lat, the Z scores of MCV and MAMP were multiplied by -1.
Asterisk means significant difference between the Z-score of F-lat and that of MCV, MAMP, DL in each nerve.
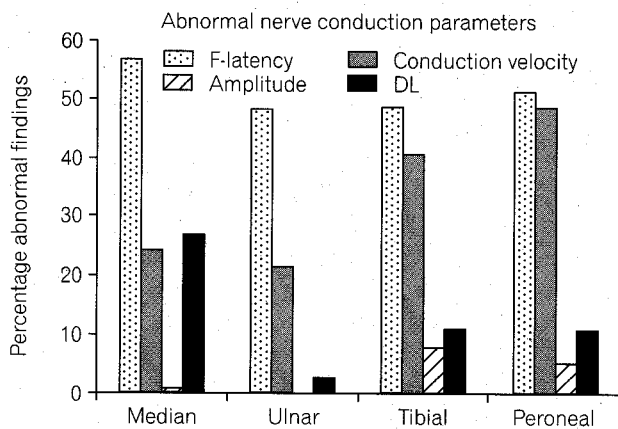

Fig. 1. The percentage of patients with abnormal findings of the minimal F-wave latency, nerve conduction velocity, amplitude of the compound muscle action potential, and distal latency (DL) of the mendian, ulnar, tibial, and peroneal nerve. Normal finding: $-2 \leq$ Z score ≤ 2. Abnormal finding: Z score > 2 or < 2.

Table 2. The Frequency of Normal Findings in Relation to Abnormal Findings (Normal Finding: Abnormal Finding) (%) for the Parameters (1) Minimal F-wave Latency (F-lat), (2) Nerve Conduction Velocity (MCV) of the Median, Ulnar, Tibial, and Peroneal Motor Nerve

Nerve	Abnormal MCV Normal F-Lat	Abnormal F-lat Normal MCV
Median	22 (9)	67 (21)
Ulnar	0 (8)	56 (18)
Tibial	0 (15)	18 (18)
Peroneal	11 (18)	21 (19)

The number of patients with abnormal findings is given for each nerve in parenthesis.
NF, there was no abnormal finding.
Normal: $-2 \leq$ Z score ≤ 2.
Abnormal: Z score > 2 or < 2.

including F-waves, are shown in Table 1 and Fig. 1. The minimal F-wave latency had a larger Z score than the MCV of the median, ulnar, and tibial nerves, and was larger than the Z scores for the amplitude of the CMAP in all four motor nerves (Table 1). There was a significant correlation between the Z scores for minimal F-wave latency and MCV in all four motor nerves. The correlation coefficients were $\gamma = -0.41$ (p < 0.05), $\gamma = -0.66$ (p < 0.01), $\gamma = -0.76$ (p < 0.01), and $\gamma = -0.69$ (p < 0.01), for the median, ulnar, tibial, and peroneal nerve, respectively. The number of abnormal nerves (Z score > 2 or < 2) was larger for minimal F-wave latency than for the MCV and the amplitude of the CMAP of all four nerves (Fig. 1). For the nerves with normal MCV, 67,

56, 18, and 21% (median, ulnar, tibial, and peroneal nerve respectively) had abnormal minimal F-wave latencies. By comparison, 22, 0, 0, 11% of the nerves (median, ulnar, tibial, and peroneal nerve respectively) with normal minimal F-wave latency had abnormal MCVs (Table 2).

Patients showing abnormal findings in the standard sensory nerve conduction study had significantly lower SRARs (0.34 ± 0.39) (p < 0.05), and 84% of them had an SRAR of less than 0.5. As well, 50% of the subjects showing normal findings in standard sensory nerve conduction study had an SRAR of less than 0.5. Altogether, 67% of patients showing polyneuropathic symptoms had an SRAR of less than 0.5 (Table 3).

Table 3. Sural/Radial Amplitude Ratio in Relation to the
Standard Sensory Nerve Conduction Study

Standard sensory nerve conduction study	Sural/radial amplitude ratio (No. of patients)		Mean±SD
	<0.5 (%)	≥0.5 (%)	
Normal (n=18)	9 (24)	9 (24)	0.57±0.26
Abnormal (n=19)	16 (43)	3 (8)	0.34±0.39*
Total (n=37)	25 (67)	12 (12)	

* $p < 0.05$.

DISCUSSION

In this study, we found that in patients with diabetic neuropathy, the minimal F-wave latency was a more sensitive indication of nerve conduction abnormalities than either MCV or the amplitude of motor nerves in the upper and the lower extremities. In addition, the sural/radial amplitude ratio of 84% of patients showing abnormal in standard sensory nerve conduction study was less than 0.5. Additionally, the patient's ratio was significantly lower if his/her result of standard sensory nerve conduction result was abnormal.

For the median, ulnar, peroneal and tibial motor nerves, the Z scores of the minimal F-wave latency were significantly larger than those of the MCV. This observation may not necessarily be related to more severe pathological changes along more proximal parts of the motor nerve. It may be the result of inherent methodological problems.

In most previous electrophysiological studies of diabetic patients, the F-wave has been applied primarily to assessing the function of the proximal part of the motor nerves.[6,13,14] However, there have been conflicting results.

Some authors have found no difference between the proximal and distal parts, while others have reported that the distal parts reveal a slight, but significantly more pronounced reduction in the MCV.[6,13] A reduction in the conduction velocity, a selective loss of the fastest axon, or decreased excitability of the anterior horn cells may explain the increased minimal F-wave latency. Since each motor neuron elicits an F-wave following 1−5% of the stimulation, a decreased excitability in patients will result in even

fewer F-waves. It can be argued, therefore, that 20 stimuli are insufficient to obtain a representative population of F-waves and this may eventuate in a false result of increased latency. However, Fisher found that the minimal F-wave latency was within 95% of the true minimal latency when 10 stimuli were applied.[15] In our study, the increased minimal F-wave latency appears to be mainly due to changes in conduction velocity because the minimal F-wave latency value correlated strongly with the MCV value.

In recent years, the use of amplitude measurements has been recommended for clinical trials of diabetic polyneuropathy. This is because they more closely reflect the axonal loss, which is the pathological alteration resulting in the sensory and motor disturbances in diabetic polyneuropathy.[16] In this study, the Z-scores of the CMAP amplitude were smaller than those of the MCV and minimal F-wave latency, and these findings may reflect a relatively intact axonal pathology. However, the large variation in reference amplitude values results in relatively small Z-scores and the amplitude of CMAP is thought to be an insensitive parameter in detecting abnormalities in individual patients.

For diabetic patients with subclinical neuropathy, about 50% demonstrate either an abnormality of the SNAP amplitude or conduction velocity.[17] In addition, in this study, only 19 patients (51%) showed abnormal standard sensory nerve conduction, even though all patients participating in the study had clinical evidence of polyneuropathy. Seward et al. suggested that the sural/radial amplitude ratio (SRAR) is a sensitive, specific electrodiagnostic test for mild axonal polyneuropathy, and that a critical ratio of less than 0.4 has a specificity of 90% and a sensitivity of 90%.[18] Polyneuropathy is characterized by the distal degeneration of neurons.[19] and typically the longest axons are the first to be affected first. The process of degeneration gradually extends proximally, involving the feet and lower legs before the longest nerves of the arm become affected,[5-7] it therefore may be useful to test the SRAR when detecting polyneuropathy in diabetic patients as in these previous studies. In our study, subjects showing abnormal results in standard sensory nerve conduction had a significantly lower SRAR (p<0.05), and 84% of them had an SRAR of less than 0.5. Moreover, 50% of the subjects showing normal findings in standard sensory nerve conduction study also had an SRAR of less than 0.5.

However, SRAR as a test for diabetic polyneuropathy has several limitations. First, as the SRAR relies on two separate nerves being studied, any mild isolated neuropathy of either nerve could distort the ratio. Furthermore, the ratio may also be distorted in diabetic patients with significant demyelinating components to their polyneuropathy. Bromberg and Alberts reported a relative sparing of the sural sensory response amplitude when compared to the median nerve in patients with acute and chronic inflammatory demyelinating polyneuropathy.[20] Finally, the technical precision with which each of the sensory responses is recorded is crucial for achieving an accurate ratio. In each subject, several attempts were made to maximize the response amplitude. Actually, the sural nerve has a strong correlation of decreasing amplitude with increasing age. However, a previous study showed that the SRAR had no definite correlation with age and the authors suggested that the reductions in sensory amplitude with increasing age were, in part, due to nerve cell loss presumably at the level of the dorsal root ganglion rather than it being a solely length-dependent process.[18]

In conclusion, for detecting polyneuropathy in diabetic patients, minimal F-wave latency is a more sensitive parameter than both the conduction velocity of motor nerve fibers and the amplitude of motor nerves. Therefore, F-wave studies should be a routine part of electrophysiological investigations of diabetic patients. In addition, a sural/radial amplitude ratio must be considered to be as an additional sensory nerve conduction study. Patients with suspected polyneuropathy in whom the sural amplitude response is not clearly diagnostic may particularly benefit from this simple test.

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