The use of F-wave and sural potential in the diagnosis of subclinical diabetic neuropathy in Saudi patients

Taha S. Ahmed, PhD, *Mohammed O. Mekki,* MRCP, *Mohammad M. Kabiraj,* Mphil, *Hossain K. Reza,* PhD.

ABSTRACT

Objective: To compare nerve conduction parameters in asymptomatic diabetic patients and with no clinical signs of neuropathy and in control subjects.

Methods: Forty eight diabetic Saudi subjects (20 males, 28 females) and 48 age-and-sex-matched control subjects were studied. The mean age of patients ± standard deviation was 45.6±11.7 years. The mean duration of diabetes from time of diagnosis was 10.8±3.1 years, and their mean fasting plasma glucose was 8.5±0.9 mmol/l. Nerve conduction studies were performed on the right lower limb.

Results: In diabetic patients the tibial and peroneal nerve conduction velocity values were 48.6±4.7 and 46.3±5.2 m/s. They were not significantly different from controls ($p>0.01$). The tibial and peroneal distal motor latency values were 5.1±0.6 and 4.7±0.9 ms, and not significantly different from controls ($p>0.01$). The sural nerve distal sensory latency in patients was 3.2±0.7 ms and the sural sensory nerve action potential amplitude was 4.9±2.5 μV. These values were significantly different from controls ($p<0.01$). The tibial and peroneal minimal F-wave latency values in patients were 32.5±1.9 ms/m and 32.9±1.6 ms/m, and were significantly different from controls ($p<0.001$). The F-wave average duration values in patients were 11.8±1.5 ms for the tibial nerve and 9.0±1.4 ms for the peroneal nerve. These were significantly different from control ($p<0.001$).

Conclusion: The peroneal and tibial minimal F-latency and average F-duration provide the most sensitive nerve conduction; indicators for the diagnosis of subclinical neuropathy in diabetes.

Keywords: Nerve conduction, F-waves, sural sensory nerve action potential, neuropathy, diabetes.

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The prevalence of diabetes mellitus is on the rapid rise worldwide, the Kingdom of Saudi Arabia being no exception.[1,2] Its commonest neurologic complication is distal symmetric sensorimotor polyneuropathy (DPN), which can start as a subclinical neuropathy.[3,4] Subclinical diabetic neuropathy refers to the presence of nerve lesions attributable to diabetes mellitus in the absence of abnormal clinical manifestations but detectable by electrodiagnostic tests.[5] Changes in the sural sensory potential were generally claimed to take place before abnormalities in the tibial and peroneal motor conduction become detectable, and the sural potential was held to provide the earliest indication of the onset of mild neuropathy in diabetes mellitus.[6,7] More recently, however, changes in the F-wave minimal latency (F_{min})[8-10] or duration (F_{dur})[11] were also proposed as sensitive indicators for early diabetic polyneuropathy. The objective of this study is to compare the occurrence of changes in F-wave parameters (F_{min} and F_{dur}) and sural nerve potential in control subjects and in asymptomatic diabetic patients with no signs of polyneuropathy.

From the Department of Physiology (Ahmed, Reza), Department of Medicine (Mekki), College of Medicine, King Saud University, Department of Neurosciences (Kabiraj), Riyadh Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr Taha S. Ahmed, Department of Physiology, College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia. Fax. +966 (1) 467 1046. E-mail: taha_sadig@hotmail.com

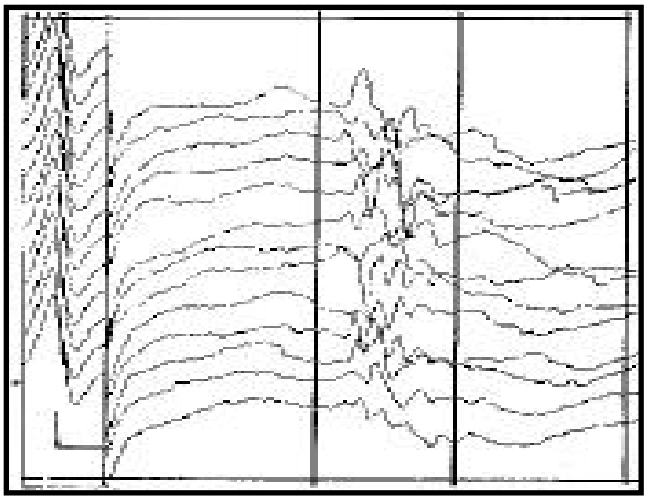

Figure 1 - F-wave recorded from the tibial nerve of a diabetic patients Stimulation at the ankle. Horizontal calibration bar = 10ms, vertical calibration bar = 10µV.

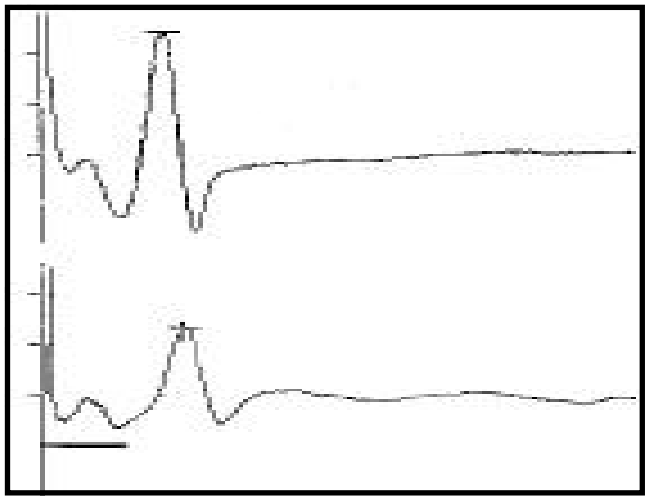

Figure 2 - Sural sensory potential recorded from a control subject (upper trace) and from a diabetic patient (lower trace). Horizontal calibration bar = 2ms, vertical division = 2µV.

Methods. In accordance with the recommendations for standardized classification of diabetic neuropathy[12-14] we examined first the symptom profile and performed a complete neurological examination on consecutive patients attending the diabetes clinic in King Khalid University Hospital between November 1998 and July 1999. The exclusion criteria included a duration of less than 5 years from first diagnosis, patients with signs of neuropathy, cardiac failure, thyroid disease or other endocrine disease in addition to diabetes, proliferative retinopathy and patients whose 24-hour urine collection contained more than 0.5 g of protein.

The nerve conduction studies were performed by the same examiner in order to eliminate inter-examiner variability[15,16] using the Nicolet Electromyography System (Nicolet Instruments, Wisconsin, USA). The room temperature was maintained at 25°C. The right lower limb was consistently used in all subjects for all measurements in this study. Moreover, the left ulnar and median nerves were tested in all subjects prior to the study. There was no evidence of median or ulnar neuropathy in these subjects.

The peroneal and tibial nerve motor studies were carried out using surface electrodes and conventional techniques.[17,18] For the peroneal study the active recording electrode was placed on the belly of extensor digitorum brevis (EDB) muscle. Stimulation was delivered at the ankle (9cm from the active recording electrode), below the head of the fibula and in the popliteal fossa. For the tibial nerve motor study the active recording electrode was placed over the abductor hallucis brevis (AHB) muscle, and stimulation was delivered at the ankle (9cm from the active recording electrode) and in the popliteal fossa.

The F-wave is a late response resulting from antidromic activation of motor neurons following supramaximal stimulation of a peripheral nerve.[19-21] For F-waves the peroneal and tibial nerves received 20 stimuli at a rate of 1.0Hz, in each case, at the ankle site, with the cathode being placed proximal to the anode. Each pulse was 0.1ms in duration and more than 60mA in intensity.[18,22] The F-wave was defined as the electrical potential exceeding 20µV in amplitude and having a latency of 40ms or more. [5,10,11] The latency of the first deflection from baseline was noted for each trace, and the shortest F-latency (F_{min}) was determined. The F_{min} value was then corrected for height [the value (ms)/height of subject (m)]. After that, the mean duration of the F-wave (F_{dur}) was estimated.[10,11]

The sural nerve antidromic sensory study was undertaken using surface electrodes. The active recording electrode was placed behind the lateral malleolus, and stimulation was delivered 14cm proximally on the posterior-lateral calf.[23] The latency was measured to the peak of the negative potential [23,24], and the amplitude was measured peak-to-peak. [16,25] Data were expressed as mean ± standard deviation (SD). The data was analyzed using the t-test, and simple linear regression was used for analyzing the correlation of the parameters with age and duration since diabetes was first diagnosed.

Results. Patients included in the study were 48 in number (20 males and 28 females). Their age ranged between 24 and 60 years (45.6±11.7, median 48 years) and the duration since they were first diagnosed as diabetic ranged between 5 and 19 years (10.8±3.1, median 9 years). Six of them had type I

Table 1 - The electrophysiological measurements given as mean±SD (number of nerves subjects) in control subjects and diabetic patients.

Parameter	Control Subjects	Diabetic Patients	p-value
Peroneal DML (ms)	4.6± 0.7 (48)	4.7±0.9 (48)	NS
Tibial DML (ms)	5.0±0.4 (48)	5.1±0.6 (48)	NS
Peroneal CV (m/s)	47.1±3.9 (48)	46.3±5.2 (48)	NS
Tibial CV (m/s)	48.8±4.1 (48)	48.6±4.7 (48)	NS
Peroneal F_{min} (ms/m)	29.3±1.3 (48)	32.9±1.6 (48)	<0.001
Tibial F_{min} (ms/m)	28.9±1.1 (48)	32.5±1.9 (48)	<0.001
Peroneal F_{dur} (ms)	6.4±1.3 (48)	9.0±1.4 (48)	<0.001
Tibial F_{dur} (ms)	9.6±1.0 (48)	11.8±1.5 (48)	<0.001
Sural DSL (ms)	2.9±0.3 (47)	3.2±0.7 (40)	<0.001
Sural Ampl (μV)	6.3±2.1 (47)	4.9±2.5 (40)	<0.001

DML - distal motor latency, CV = conduction velocity, F_{min} = F-wave minimal latency, F_{dur} = F=wave average duration, DSL = distal sensory latency, Ampl = amplitude of the nerve action potential, NS = not significant, SD = standard deviation

diabetes and the rest had type II diabetes. Their fasting plasma glucose (FPG) ranged between 7.2 and 11.5 mmol/l (8.5±0.9, median 8.5 mmol/l). The controls were 48 age-and-sex-matched to the diabetic subjects. They attended the medical clinics in King Khalid Hospital and King Abdulaziz Hospital for non-neurologic medical problems.

A summary of the values of electrophysiological parameters obtained from the normal subjects and diabetic patients is shown in Table 1. The mean values obtained from diabetic patients were considered significantly different from the control group if they fell outside ± 2SD of the control group mean values. The peroneal and tibial nerve distal motor latency (DML) and conduction velocity (CV) were comparable in the control and diabetic groups.

On the other hand, the F-wave parameters (F_{min} and F_{dur}) were clearly different in diabetic patients (Figure 1) when compared with the controls. The F-wave minimal latency was significantly longer ($p<0.001$) in diabetic patients than in controls. This was true for both the peroneal and tibial nerves (Table 1). Similarly, the F-wave average duration was significantly longer ($p<0.001$) in diabetic patients when compared to control values in case of either the peroneal or tibial nerve.

The sural nerve sensory potential was obtained in 47 out of 48 control subjects and in 40 out of 48 diabetic patients. The latency of this potential was significantly longer ($p<0.01$) in diabetic patients than in controls. The sural sensory nerve action potential (SNAP) amplitude was significantly smaller ($p<0.01$) in diabetic patients than in control subjects (Table 1 and Figure 2).

The correlation between values of various electrophysiological parameters and duration of diabetes from first diagnosis is shown in Table 2. The distal motor latencies and conduction velocities of the peroneal and tibial nerves showed no significant correlation with the disease duration in these asymptomatic patients. The sural sensory potentials, on the other hand, showed changes that correlated with the duration of diabetes. Their amplitude decreased ($p<0.05$) and latency increased ($p<0.05$, Table 2). The tibial nerve F-wave duration was also significantly increased ($p<0.01$) with increased disease duration. However, the highest correlations with disease duration were displayed by the minimal latencies of peroneal ($p<0.001$) and tibial ($p<0.001$) F-waves, and by the peroneal F-duration ($p<0.001$).

Table 3 shows the correlation between values of the electrophysiological parameters and age in both control subjects and diabetic patients. In the case of control subjects the only parameter which was increased with age was the peroneal F-wave minimal latency ($p<0.05$). It is noteworthy that this same parameter was far more increased with age in case of diabetic subjects ($p<0.001$). The peroneal and tibial distal motor latencies, as well as the tibial conduction velocity, showed no significant changes in correlation with advancing age, neither in control subjects nor in our asymptomatic diabetic patients. The peroneal conduction velocity, however, was significantly slowed down ($p<0.01$) in correlation with advancing age in the diabetic group. The sural nerve latency was increased with age ($p<0.01$) and its amplitude was also significantly reduced ($p<0.01$) with advancing age in the diabetic group. The peroneal and tibial minimal latencies were prolonged

Table 2 - The correlation between values of electrophysiological parameters and duration of disease in diabetic patients.

Parameter	Correlation Coefficient	p-value
Peroneal DML (ms)	0.1724	NS
Tibial DML (ms)	0.1514	NS
Peroneal CV (m/s)	-0.2430	NS
Tibial CV (m/s)	-0.1953	NS
Peroneal F_{min} (ms/m)	0.5163	<0.001
Tibial F_{min} (ms/m)	0.4298	<0.001
Peroneal F_{dur} (ms)	0.4132	<0.001
Tibial F_{dur} (ms)	0.3924	<0.01
Sural DSL (ms)	0.2863	<0.05
Sural Ampl (μV)	0.2911	<0.05

DML - distal motor latency, CV = conduction velocity, F_{min} = F-wave minimal latency, F_{dur} = F=wave average duration, DSL = distal sensory latency, Ampl = amplitude of the nerve action potential, NS = not significant

(p<0.001), and the peroneal and tibial F-wave durations increased (p<0.001) in correlation with increasing age in diabetic patients.

Discussion. There have been two earlier nerve conduction studies on diabetic patients in the Kingdom of Saudi Arabia.[26,27] The present study differs from them in two respects. First, in the present study careful history and clinical examination made it certain to exclude any patient with clinical neuropathy. By contrast, one of the earlier studies[26] stated that clinical examination revealed the presence of clinical neuropathy in 47% of the diabetic patients studied. The other study[27] made no mention of the findings on clinical examination, which makes one uncertain whether all patients included in that study had no signs of neuropathy. Second, one of the main objectives of the present work is to study changes in F-wave parameters (F_{min} and F_{dur}) in our subjects. These parameters were not measured in the earlier studies.

Since DPN is, by definition, a distal symmetrical polyneuropathy which starts in the lower limbs considerably earlier than in the upper limbs[28,29], the right lower limb was consistently used for measurements in our subjects. It is noteworthy that Fisher[21] found F_{min} fell within 95% of the true minimal latency when ten stimuli were used for the elicitation of the F-wave. Hence, twenty supramaximal stimuli employed for evocation of the F-wave in our study seemed more than adequate. In the present study, "contamination" of the F-wave by the axon reflex or H-response did not pose a practical problem, because supramaximal stimulation was used and because the characteristic features of these waves are different from those of the F-wave.[30-33]

In the diabetic subjects (Table 1) both of the F-wave parameters (F_{min} and F_{dur}) and the sural parameters (DSL and Ampl) disclosed abnormalities which were not detected by clinical examination or by conventional motor nerve conduction studies

Table 3 - The correlation between the values of electrophysiological parameters and age in control subjects and diabetic patients.

Parameter	Controls		Diabetics	
	Correlation Coefficient	p-value	Correlation Coefficient	p-value
Peroneal DML (ms)	0.1426	NS	0.1835	NS
Tibial DML (ms)	0.1135	NS	0.1601	NS
Peroneal CV (m/s)	-0.2028	NS	-0.3317	<0.01
Tibial CV (m/s)	-0.1024	NS	-0.2321	NS
Peroneal F_{min} (ms/m)	0.2748	<0.05	0.6750	<0.001
Tibial F_{min} (ms/m)	0.2351	NS	0.5514	<0.001
Peroneal F_{dur} (ms)	0.2443	NS	0.6471	<0.001
Tibial F_{dur} (ms)	0.2309	NS	0.5385	<0.001
Sural DSL (ms)	0.1945	NS	0.3458	<0.01
Sural Ampl (μV)	0.1789	NS	0.3469	<0.01

DML - distal motor latency, CV = conduction velocity, F_{min} = F-wave minimal latency, F_{dur} = F=wave average duration, DSL = distal sensory latency, Ampl = amplitude of the nerve action potential, NS = not significant

(DML and CV). The fact that F-wave parameters showed greater deviation ($p<0.001$) from normal values than sural parameters ($p<0.01$) implies that F-wave measurements are superior to sural measurements in terms of detection of subtle changes in nerve function. A unique feature of the F-wave is that it is associated with a depolarization that travels centrally antidromically to excite the cell body and then comes back orthodromically to be picked up by the peripherally-situated recording electrode. This relatively long to-and-fro journey of depolarization might make subtle nerve dysfunction more likely to be reflected in F-wave latency and duration than the one-way journey of depolarization in the classical nerve conduction studies. Moreover, the latter ones assess function on the distal segment of the nerve solely, whereas the F-wave assesses function in both proximal and distal segments of the nerve.[17,22] The significantly increased F_{dur} in diabetic patients (Table 1) probably reflected a temporal dispersion phenomenon where the F-wave complex became contaminated by presence of unmyelinated fibres amongst the healthy ones.[34]

The results (Table 2) indicate that the disease duration induces significant changes in F-wave parameters topmost, followed by sural parameters thereafter, and no changes in the conventional nerve conduction measurements at this stage of the disease where no overt clinical neuropathy is yet present. The peroneal F_{min} (Table 3) was the only electrophysiological parameter which showed deterioration in association with age in control subjects. This suggests the peroneal nerve, in particular, to be the most vulnerable to the effects of normal aging. In diabetic patients, on the other hand, aging was associated with domineering deterioration in F-wave parameters ($p<0.001$), and less severe changes in sural parameters ($p<0.01$) and peroneal CV ($p<0.01$). Tibial CV and the DML of both tibial and peroneal nerves did not show significant changes with age in these asymptomatic patients.

In view of our results we conclude that peroneal nerve and tibial nerve F_{min} and F_{dur} constitute the earliest nerve conduction studies which indicate the beginning of neuropathy in diabetic patients. However, such a conclusion should be corroborated by follow-up of these patients to determine how many of them in the future develop clinical neuropathy.

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