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Ulnar F-wave Study in the Detection of Subclinical Diabetic Neuropathy

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Abstract

Background Diabetic peripheral neuropathy (DPN) brought on by damage to the peripheral sensory and motor nerves. Since the F-wave passes through both the afferent and efferent pathways in the motor nerve, alterations in the F response parameters may indicate injury to either of these pathways.

Objective To explore the effectiveness of ulnar F-wave parameters in diagnosing subclinical neuropathy in patients with type 2 diabetes mellitus (T2DM).

Methods The study examined F-wave, glycated hemoglobin (HbA1c), and modified Toronto clinical neuropathy score (mTCNS), in addition to sural to radial amplitude ratio, sensory and motor conduction of upper and lower limb nerves, in 116 T2DM patients and 121 control participants.

Results In comparison to controls, DPN patients exhibit longer F-minimum (Fmin), F-maximum (Fmax), F-ratio (Fr), and modified F-ratio (mFr). Along with higher F-chronodispersion (Fc) and F-estimate (Fe), they also show lower F-persistence (Fp), F-wave conduction velocity (FWCV), and F-index (Fi). Patients with DPN have higher F-estimate (Fe) values than the controls, whereas patients without DPN have lower Fi. There was a strong correlation observed between several F-wave parameters and the mTCNS, disease duration, and HbA1c.

Conclusion Increased mFr value, longer Fm latency, and higher Fi value were useful in the early identification of subclinical DPN, while higher Fi value, FWCV slowing, and prolonged Fmin and Fmax latencies helped identify patients with clinical DPN. When separating diabetics with T2DM from those without DPN, the Fi value has the highest sensitivity and specificity.

Keywords DM, subclinical neuropathy, ulnar nerve, F-wave.

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List of abbreviations: AUC = Area under the curve, A-wave = Axon reflex, C7 = 7th Cervical vertebra, DM = Diabetes mellitus, DPN = Diabetic peripheral neuropathy, EDx = Electro diagnostic studies, EMG = Electromyography, Fc = F-wave Chronodispersion, Fe = F-wave estimate, Fi = F-wave index, Fmax = F-wave maximal latency, Fmin = F-wave minimal Latency, Fp = F-wave persistence, Fr = F-wave ratio, FWCV = F-wave conduction velocity, HbA1c = Glycated hemoglobin test, LSD = Least significant difference, mFr = Modified F-wave ratio, Ms = Millisecond, mTCNS = Modified Toronto Clinical Neuropathy Score, NCS = Nerve conduction study, ROC = Receiver operating characteristic curve, SRAR = Sural/radial amplitude ratio, T1DM = Type 1 Diabetes mellitus, T2DM = Type 2 Diabetes mellitus, µV = Microvolts

Introduction

Diabetic peripheral neuropathy (DPN) is one of the main microvascular complications of diabetes mellitus (DM). Sometimes, this could already be present at the time of diagnosis for type 2 diabetes mellitus (T2DM), while it appears in subjects with type 1 diabetes mellitus (T1DM) almost 10 years after the onset of the disease [1,2]. DPN is the most common and could affect almost 50%

of individuals with DM during their lifetime [3]. The impairment can involve both somatic fibers of the peripheral nervous system, with sensory-motor manifestations, as well as the autonomic system [4].

The diagnosis of DPN is mainly clinical with routine history taking could exclude other types and causes [5]. This could be sandwiched with neurophysiological examination of the peripheral nerves using nerve conduction studies (NCS) when the symptoms and signs are missing or other comorbid disease are present [4].

Since DPN is defined as "length-dependent" neuropathy because it affects the longest nerve fibers more frequently [6], thus the earliest abnormalities appear at the extremities of the lower limbs where the NCS of the sural nerve has been shown to be the most sensitive [7].

There is controversy regarding the fact that routine sensory and motor nerve conduction examinations are insufficient to detect DPN and subclinical neuropathies, and that F-wave examinations used in the detection of proximal nerve lesions can reveal abnormalities before routine conduction examinations and are more sensitive [8,9]. F-wave was obtained by applying a supramaximal antidromic stimulus to a motor neuron supplying the muscle. Unlike other conventional NCS which spares certain proximal nerve roots, F-waves are resultant small compound muscle action potentials which encompasses all nerve roots and are formed as a result of both orthodromic and antidromic stimulation [10].

The aims of this study were to look for the role of ulnar F-wave in diagnosing subclinical DPN and to test the diagnostic utility of different F-wave parameters in discriminating between the controls and patients with and without DPN.

Methods

A case-control study carried out at the Neurophysiology Department of Al-Imamein Al-Kadhimein Medical City in Baghdad, for the period from March 2023 to December 2023. The study was approved by the Iraqi Board for Medical Specialization (Order #240: 22/1/2023). All the participants were informed about the technique and the aim of the study and an informed consent was obtained from them.

Participants

A total of two hundred and forty-seven participants enrolled in this study, 126 of them were diagnosed to have T2DM according to the fasting plasma glucose and glycated hemoglobin (HbA1c) criteria [11]. They were 70 males and 56 females with an age range from 30 to 69 years. They were further subdivided into those with and without clinical DPN. Patients with cervical myelopathy, plexopathy, multifocal motor neuropathy, entrapment neuropathy, nerve injuries in the upper limb, with alcohol abuse, chronic renal failure and other systemic disease affecting the nerve function, those taking medications that could affect peripheral nerves system functions were excluded from the study. All the patients were referred by senior endocrinologist where they subjected to the measurement of HbA1c level and the modified Toronto clinical neuropathy score (mTCNS) [2,12].

Another 121 participants comprised 57 males and 64 females with an age range from 22 to 68 years serve as the control group.

Electrophysiological studies

A key point EMG machine (Medtronic, Denmark) was used throughout the study. The ambient temperature was around 25°C, and the skin temperature was maintained between 32°C and 34°C. According to the methods adopted by Preston and Shapiro [13], the sensory nerve conduction of the right median, ulnar, radial, and sural nerves, the motor nerve conduction of the right median, ulnar, peroneal, and tibial nerves, the F-wave and A-wave elicited by distal and proximal stimulation of the right ulnar nerve at wrist and elbow and the right sural/radial amplitude ratio (SRAR)

was also measured. Additionally, needle EMG studies of selected muscles in the upper and lower limbs.

F-wave measurement

A total of 10 stimuli were considered appropriate to explore the full potential of F-waves. To be clearly identifiable, F-waves should be at least 20 µV in peak-to-peak amplitude to differentiate them from background noise. The conventional stimulus intensity is 25% above maximal for eliciting a direct response. This provides a consistent physiologic environment for eliciting F-waves [(14)]. The following F-wave parameters were studied:

F-wave conduction velocity

F-wave conduction velocity (FWCV) is calculated according to the following equation: FWCV = D × 2 (mm)/ F – M – 1 (ms) [(15)] where, D represents the distance from the stimulus site to the spinal cord, F represents F-wave minimal latency obtained by wrist stimulation, M represents distal motor latency (DML) in ms. 1.0 ms represent the turnaround time.

F-wave ratio

The F-wave ratio (Fr) serves as a simple means of comparing the conduction characteristics between proximal and distal segment. It compares the conduction time from the spinal cord to the stimulus site to the remaining distal nerve segment to the muscle. It was calculated by the following equation: F ratio = F – M – 1 (ms) / M × 2 (ms) [(15)] where, F represents F-wave minimal latency at elbow, M represents proximal segment latency at elbow. 1.0 ms for the turnaround time.

Modified F-ratio latency

The modified F-wave ratio (mFr) is the ratio between the proximal segment latency time (spinal cord to elbow) and the DML (wrist to hypothenar muscle segment). It is calculated by the equation [(16)]: mFr = (F + DML – 2PML – 1)/ (2DML) where, F represent the F-wave latency time in msec (F obtained by wrist stimulation), DML in ms, PML represent the proximal segment latency (elbow to hypothenar muscle) in ms. 1.0 ms represent the turnaround time.

The F estimate

The F-wave estimate (Fe) takes into account the DML, the CV, and the patient's limb length in determining whether a prolonged F response is truly due to a lesion of the proximal nerve segment or merely reflects an abnormal DML or CV or an unusually tall patient. Fe is calculated according to the following formula [(13)]: Fe = (2D / CV) × 10 +1 ms+ DL where, D is the distance from the stimulation site to the spinal cord (cm), CV is the nerve conduction velocity (m/s), DL is the DML (ms). 10 is the conversion factor to ms.

Note: The turnaround time of 1 ms at the anterior horn cell is added to the equation.

F-wave index

F-wave index (Fi) taking into consideration all the F-wave parameters for more accurate in diagnosing cases with peripheral neuropathy and thereby minimizing the chances of missing the diagnosis. It is calculated according to the following equation [(17)]: Fi = [F-wave persistence (Fp) × Arm length] / [F-minimal Latency (Fmin) × F-wave chronodispersion (Fc) where, Fp is a measure of the number of F-waves obtained per the number of stimulations [(18)], Fc is a measure of the difference between the Fmin and F-wave maximal latency (Fmax) [(19)].

An obstetric tape measure was used for the upper limb length. The surface measurement from the stimulus point to the C7 spinous process with the limb extended and abducted 90 degrees pronated via the axilla and midclavicular point gives a close estimate of the nerve length.

The electrophysiologic settings for adequate display of F-waves were an amplifier gain of 200 or 500 µV per division and a sweep of 5 or 10 msec per division.

Statistical analysis

Statistical analyses were performed by using statistical package for social sciences (SPSS) software version 25.0 (SPSS, Chicago). Continuous data were subjected to normality test (Shapiro-Wilk test). Data with normal distribution were presented as mean and standard deviation (SD), and analyzed with Student t-test for two groups and analysis of variance (ANOVA) for more than two groups and abnormally distributed data were presented as median and range and analyzed with Man Whitney test and post hoc analysis was performed using least significant difference (LSD).

Categorical variables were expressed as number and percentage and analyzed with Chi-square test. Pearson's correlation test was used for the normally distributed data and Spearman's correlation for the non-normally distributed data to explore the possible correlation of different F-wave parameters with each of HbA1c level, disease duration, type of treatment, and mTCNS. Receiver operating characteristic curve (ROC) was used to evaluate different F-wave parameters in the context of discrimination between patients and controls. A p value less than 0.05 was considered to indicate a statistically significant difference.

Results

Demographic data

The study population's clinical and demographic data is presented in table (1). The age, sex, and occupation did not differ between the two groups. Fifty-six (44.44%) of the 126 patients were found to have DPN. The disease duration was 7.93±5.34 years. For the patient group, the mTCNS was 14.62±7.81 and the mean HbA1c level was 8.48±2.12 with a minimum of 5 and a maximum of 14. Just five patients received no treatment, compared to the majority of patients (87.3%) who were taking oral hypoglycemic medications.

Table 1. Demographic data of the study population (n=247)

Parameter		Patients (n=126)	Controls (n=121)	P value
Age (yr)	Mean±SD Range	53.35±8.27 30-69	46.04±9.87 22-68	0.133*
Sex	Males, n (%) Females, n (%)	70 (55.56%) 56 (44.44%)	57 (47.11%) 64 (52.89%)	0.115*
HbA1c level (%)	Mean±SD Range	8.48±2.12 5-14		
Modified TCNS	Mean±SD Range	14.62±7.81 2-31		
Electro diagnostic result	With Peripheral Neuropathy, n (%) Without Peripheral Neuropathy, n (%)	56(44.44%) 70(55.56%)		
Treatment	Oral hypoglycemic, n (%) Insulin, n (%) No, n (%)	110(87.3%) 11(8.73%) 5(3.97%)		

TCNS = Toronto clinical neuropathy score. * Unpaired ttest, ** Chi square test

Table 2 shows the demographic data of patients with and without DPN. No age and sex difference was presented between the two subgroups. The age and sex did not differ between the two groups. Patients with DPN showed significantly longer disease duration (p

=0.007), higher HbA1c level (p =0.006), and mTCNS (P <0.001) as compared to those without DPN.

Table 2. Demographic data of the patients with and without peripheral neuropathy (n=126)

Parameter		Peripheral Neuropathy With (n=56)	Without (n=70)	P value
Age (yr)	Mean±SD Range	53.8±8.15 32-69	52.99±8.4 30-68	0.759*
Sex	Males, n (%) Females, n (%)	35(62.5%) 21(37.5%)	35(50%) 35(50%)	0.161**
Duration of illness (yr)	Mean±SD Range	9.43±2.29 1-34	6.60±3.82 1-24	0.007*
HbA1c level (%)	Mean±SD Range	9.59±6.44 6-14	7.71±1.62 5-11	0.006*
Modified TCNS	Mean±SD Range	20.21±7.10 6-31	10.14±4.97 2-27	<0.001*

TCNS = Toronto clinical Neuropathy Score. * Unpaired ttest, ** Chi square test

Electrophysiological data

Patients vs Controls

Table 3 shows that the SRAR, Fp, FWCV, and Fi values of the patients were all significantly lower (p <0.001) than in the control group. Conversely, the patient group exhibited significantly higher (p <0.001) Fmin at the wrist, Fmax at the wrist, Fc, and Fe values than the control group. Furthermore, compared to the controls, the patients had evidently significant A-wave presence of (p = 0.011) but no significant difference in the Fr and mFr between the two groups).

Patients with DPN vsp without DPN

Table 4 shows that the SRAR, FWCV, and Fi values in the patients with DPN group were all significantly lower than in the patients without DPN group. Conversely, the patient with DPN group have significantly higher Fmin latency at the wrist, Fmin latency at the elbow, Fc, and mFr values than the patient without DPN group. There was no significant difference in the Fmax latency at the wrist, Fp, Fr, Fe and the presence of A-wave between the two subgroups.

Table 3. SRAR and ulnar F-wave parameters between all patients and controls

Parameter		Patients (n=126)	Controls (n=121)	P value
SRAR		0.32±0.32	0.57±0.19	0.001*
Fmin at Wrist (ms)		28.78±4.61	24.3±1.91	0.001*
Fmin at Elbow (ms)		24.63±4.33	21.29±1.86	0.001*
Fmax at Wrist (ms)		33.12±5.57	26.68±1.87	0.001*
F-persistence (%)		89.55±11.02	95.79±7.50	0.001*
Fc (ms)	Mean±SD	4.50±3.05	2.36±0.65	0.001**
	Median	4.0	2.3	
	Range	1.3-27.3	0.5-4.5	
FWCV (m/sec)		54.83±8.50	65.09±5.03	0.001*
F-wave ratio		1.14±0.27	0.99±0.20	0.067*
modified F-ratio		3.13±0.77	2.60±0.59	0.088*
F-wave index	Mean±SD	62.23±32.34	119.82±31.96	0.001**
	Median	55.28	112.28	
	Range	8.19-181.5	66.09-231.27	
F-wave estimate (ms)		29.51±6.39	26.90±3.16	0.001*
Presence of A wave	Yes	9 (7.14%)	1 (0.83%)	0.011***
	No			

SRAR = Sural/radial amplitude ratio; Fmin = F-wave minimum latency; Fmax = F-wave maximum latency; Fc = F-wave chronodispersion; FWCV = F-wave conduction velocity. * ANOVA test and ** for Kruskal Wallis test, *** Chi square test

Table 4. SRAR and Ulnar F-wave parameters between patients with and without PNP

Parameter		Peripheral Neuropathy		P value
		Without (n=70)	With (n=56)	
SRAR		0.59±0.20	0.18±0.10	0.026*
Fmin at Wrist (ms)		26.86±2.73	31.98±5.30	0.006*
Fmin at Elbow (ms)		22.86±2.30	27.58±5.26	0.001*
Fmax at Wrist (ms)		30.99±3.71	36.66±6.35	0.105*
F-persistence (%)		92.43±10.14	84.76±10.87	0.288*
Fc (ms)	Mean± SD	4.06±2.19	5.23±4.03	0.026**
	Median	3.6	4.35	
	Range	1.3-14.5	2.2-27.3	
FWCV (m/sec)		58. 23±7.69	49.17±6.59	0.019*
F-wave ratio		1.13±0.23	1.15±0.33	0.156*
modified F-ratio		3.08±0.63	3.22±0.96	0.023*
F-wave index	Mean± SD	72.11±34.96	45.76±18.15	0.001**
	Median	69.15	41.84	
	Range	12.9-181.5	8.19-83.97	
F-wave estimate (ms)		28.44±5.84	31.30±6.91	0.833*
Presence of A-wave	No	66(94.29%)	51(91.07%)	0.361***
	Yes	4(5.71%)	5(8.93%)	

SRAR = Sural/radial amplitude ratio; Fmin = F-wave minimum latency; Fmax = F-wave maximum latency; Fc= F-wave chronodispersion; FWCV = F-wave conduction velocity. * ANOVA test and ** for Kruskal Wallis test, *** Chi square test

Patients with and without DPN vs Controls

The Fmin at wrist was significantly different between the 3 groups. The Fmin at elbow, Fmax at wrist, Fc, and FWCV of patients with DPN were significantly prolonged when compared to the controls and to patients without DPN, whereas they were not different between controls and patients without DPN. The Fp, was significantly higher while the Fr, and Fe were significantly lower in the controls than those with DPN but not in patients without DPN, in addition, it was not significantly different between the two patient subgroups. The mFr was significantly lower and the Fi significantly higher in the controls than patients with and without DPN but they were not different within the patients themselves (Table 5).

Table 5. SRAR and Ulnar F-wave Parameters between Controls and Patients with and without PNP

Parameter		Controls(n=121)	Patients		P value
			Without DPN(n=70)	With DPN(n=56)	
SRAR		0.57±0.19	0.59±0.20	0.18±0.10	0.216*
Fmin at Wrist (ms)		24.3±1.91[a]	26.86±2.73[b]	31.98±5.30[c]	0.001*
Fmin at Elbow (ms)		21.29±1.86[a]	22.86±2.30[a]	27.58±5.26[b]	0.001*
Fmax at Wrist (ms)		26.68±1.87[a]	30.99±3.71[a]	36.66±6.35[b]	0.001*
F-persistence (%)		95.79±7.50[a]	92.43±10.14[ab]	84.76±10.87[b]	0.001*
Fc (ms)	Mean ±SD	2.36±0.65	4.06±2.19	5.23±4.03	0.001**
	Median	2.3[a]	3.6[a]	4.35[b]	
	Range	0.5-3.5	1.3-14.5	2.2-27.3	
FWCV (m/sec)		65.09±5.03[a]	58.23±7.69[a]	49.17±6.59[b]	0.001*
F-wave ratio		0.99±0.20[a]	1.13±0.23[ab]	1.15±0.33[b]	0.001*
modified F-ratio (ms)		2.60±0.59[a]	3.08±0.63[b]	3.22±0.96[b]	0.001*
F-wave index	Mean±SD	131.68±25.15	72.11±34.96	45.76±18.15	0.001**
	Median	127.35[a]	69.15[b]	41.84[b]	
	Range	98.55-231.27	12.9-181.5	8.19-83.97	
F-wave estimate, ms		26.90±3.16[a]	28.44±5.84[ab]	31.30±6.91[b]	0.001*
Presence of A-wave	No	120 (99.17%)	66 (94.29%)	51 (91.07%)	0.361***

SRAR = sural/radial amplitude ratio; Fmin = F-wave minimum latency; Fmax = F-wave maximum latency; Fc= F-wave Chrono dispersion; FWCV = F-wave conduction velocity; DPN = diabetic peripheral neuropathy. The data are presented as Mean±SD or median and range. Different small letters indicate significant difference. * ANOVA test and ** for Kruskal Wallis test, *** Chi square test

Correlation analysis

In figure (1), the HbA1c level in the patients group was positively correlated with the Fmin, Fmax, Fc (r =0.419, p <0.001; r = 0.402, p <0.001; r = 0.276, p =0.003; r = 0.204, respectively) and negatively with FWCV, mFr, and Fi with the HbA1c level (r = -0.388, p <0.001; r = -0.223, p = 0.018; r = -0.199, p =0.036, respectively).

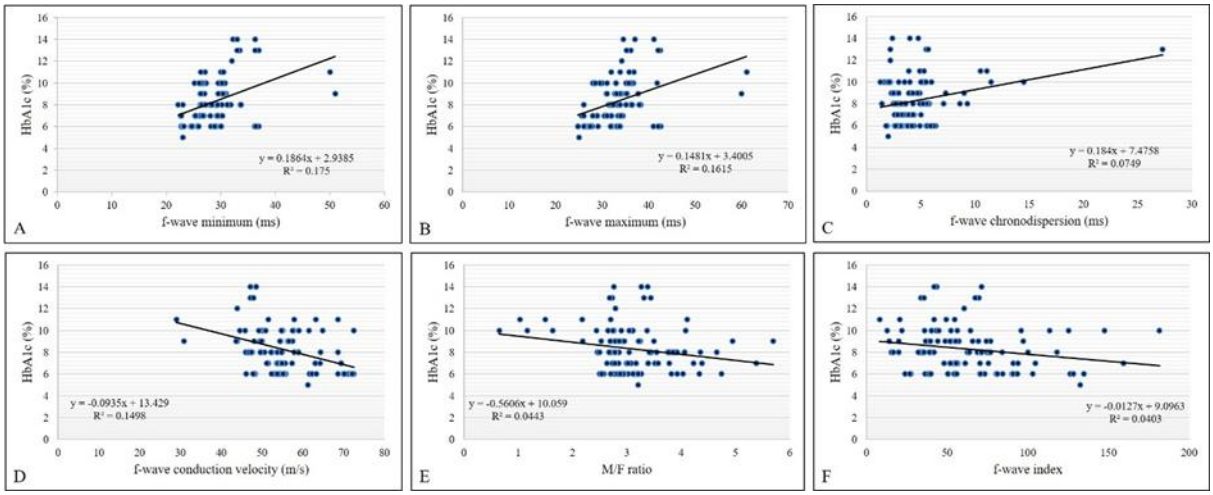

Figure 1. Scatter plot and regression line between HbA1c level and ulnar Fmin latency (A), Fmax latency (B), F-wave chronodispersion (C), FWCV (D), F-wave ratio (E), and F-wave index (F) within the patient group

Figure 2, show that the Fi was negatively correlated with the disease duration (r = -0.219, p = 0.021) while the Fe was positively correlated with the disease duration (r = 0.243, p = 0.010).

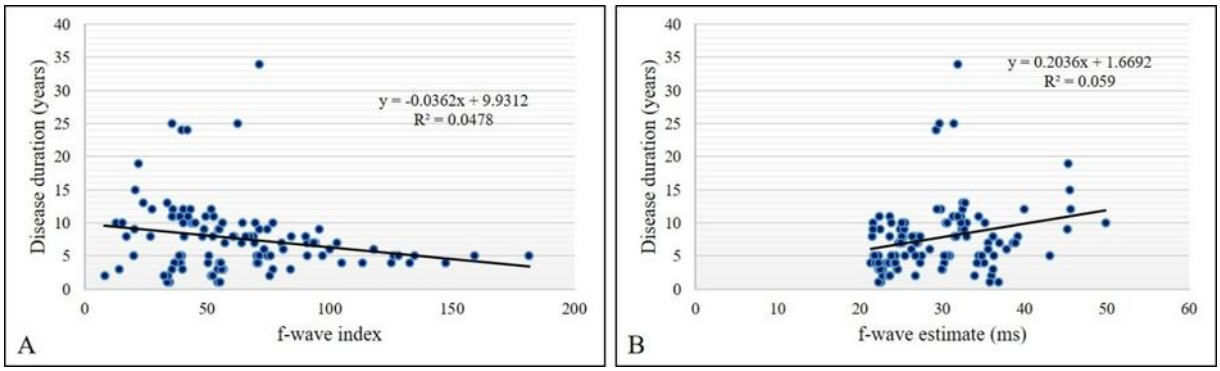

Figure 2. Scatter plot and regression line between disease duration and ulnar F-wave index (A) and F-wave estimate (B) within the patients group

The Fmin, Fmax, and Fc all show positive relationships with mTCNS (r = 0.489, p = 0.001; r = 0.443, p = 0.001; r = 0.249, p = 0.008). In contrast to the aforementioned findings, the mTCNS was negatively correlated with Fp (r = -0.240, p = 0.011), FWCV (r = -0.543, p = 0.001), and Fi (r = -0.259, p = 0.006) as shown in figure (3)

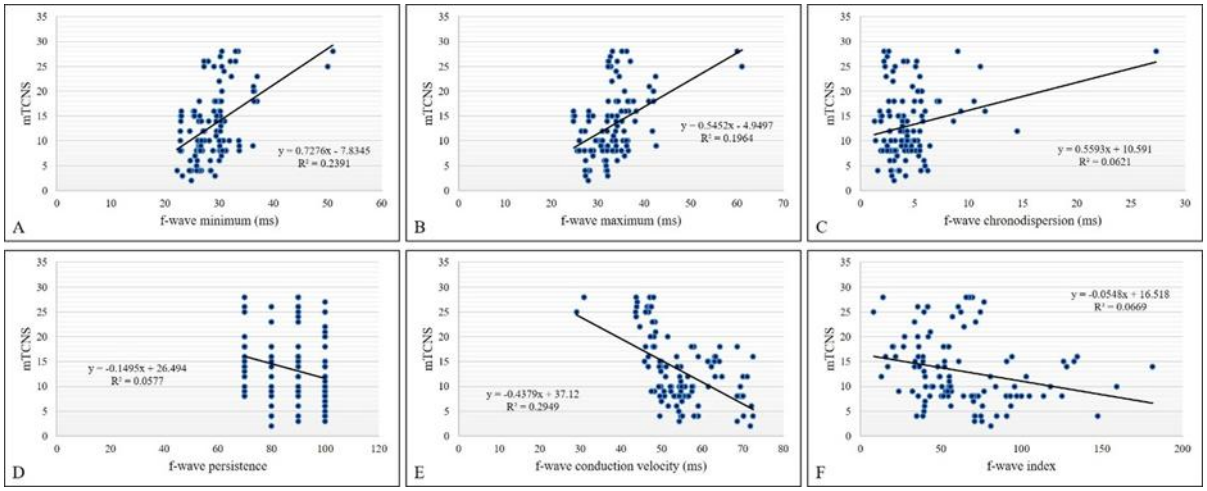

Figure 3. Scatter plot and regression line between mTCNS and ulnar F-min latency (A), F-max latency (B), F-wave Chrono dispersion (C), F-wave persistence (D), FWCV (E), and F-wave index (F) within the patient group

ROC curve

Controls versus all diabetic patients

Using the ROC curve, the FWCV area under the curve (AUC) was 0.837, 95% confidence interval (CI) = 0.780-0.894, p <0.001. At a cut-off value of FWCV = 61.57m/s, the test's sensitivity and specificity were 79% and 79%, respectively. The AUC for Fp was 0.662, 95% CI= 0.592-0.733, p <0.001. The test's sensitivity and specificity were 70% and 58%, respectively, at a cut-off value of Fp = 95.

For Fe, the AUC was 0.415, 95% CI = 0.336-0.493, p <0.024. The test's sensitivity and specificity were 47% and 99%, respectively, at a cut-off value of Fe = 27.06. The AUC for Fmin latency was 0.838, 95% CI= 0.787-0.890, p <0.001. The test's sensitivity and specificity were 77% and 74%, respectively, at a cut-off value of Fmin latency = 25.85ms. The AUC for Fmax latency was 0.898, 95% CI= 0.857-0.940, p <0.001. The test's sensitivity and specificity were 82% and 79%, respectively, at a cut-off value of Fmax latency = 28.25.

The AUC for Fc was 0.845, 95% CI= 0.794-0.896, p <0.001. The test's sensitivity and specificity were 78% and 69%, respectively, at a cut-off value of F-wave Fc = 7.75. The AUC for Fi was 0.945, 95% CI= 0.911-0.979, p <0.001. The test's sensitivity and specificity were 91% and 91%, respectively, at a cut-off value of Fi = 103.23 (Figure 4)

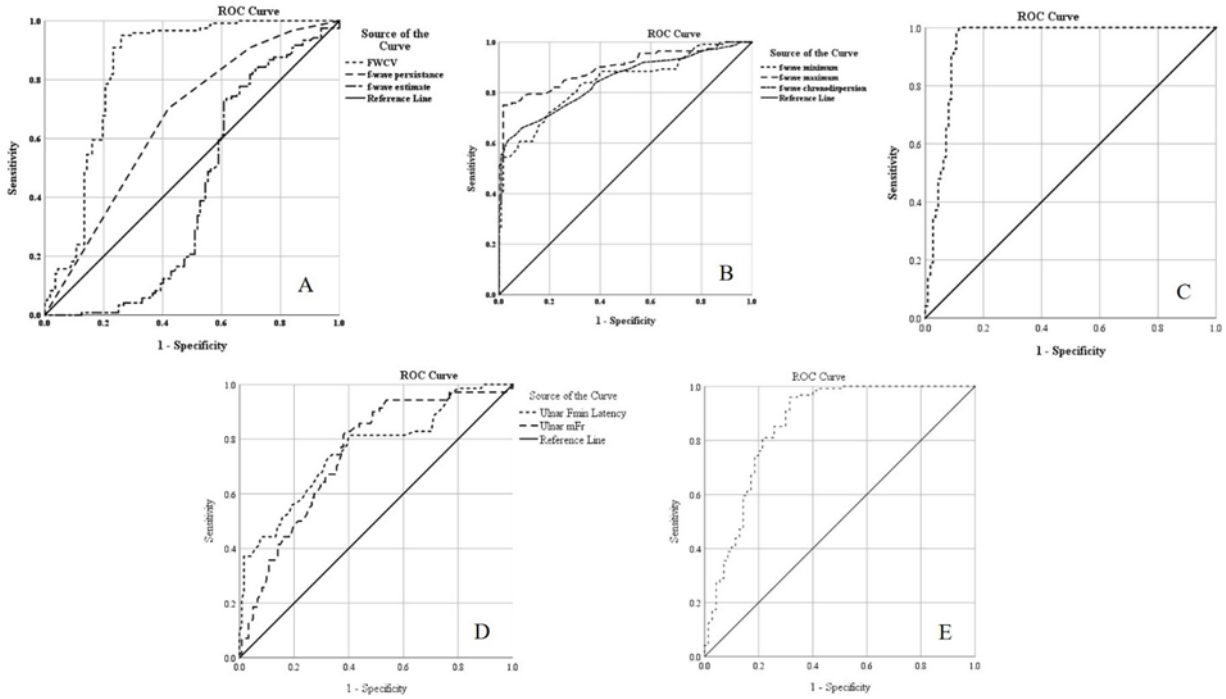

Figure 4. ROC curve of FWCV, F-wave persistence, and F-wave estimate in the context of discrimination between patients and controls (A), Fmin and Fmax latencies, and F-wave chronodispersion in the context of discrimination between patients and controls (B), F-wave index in the context of discrimination between patients and controls (C), Ulnar Fmin Latency and mFr in the context of discrimination between controls and patients without DPN (D), and Ulnar F-wave index in the context of discrimination between controls and patients without DPN (E)

Controls versus patients without DPN

The AUC for Fmin latency was 0.758, 95% CI= 0.685-0.831, p <0.001. The test's sensitivity and specificity were 74% and 66%, respectively, at a cut-off value of Fmin latency = 25.15. The AUC for mFr was 0.745, 95% CI= 0.674-0.816, p <0.001. The test's sensitivity
and specificity were 74% and 63%, respectively, at a cut-off value of mFr = 2.75. The AUC for Fi was 0.856, 95% CI= 0.794-0.919, p <0.001. The test's sensitivity and specificity were 80% and 79%, respectively, at a cut-off value of Fi = 94.29.

Discussion

The F-wave

The study found that the diabetics' Fmin (at the wrist or elbow) and Fmax latencies were longer than the controls. These results were consistent with numerous studies [9,20,21]. Furthermore, Fmin at wrist in diabetic patient without DPN subgroup were longer than the control group.

Between the groups under study, there were significant differences in both Fc and Fp values. Early in the disease's progression, there is a marked increase in the Fmax latency relative to the Fmin latency, which raises the Fc value [22]. The study's findings, which show that Fmax latency has a higher sensitivity and specificity than Fmin latency, further corroborate this. Prolonged Fmin and Fmax latencies, as well as Fc, were recognized as indicators of lower motor neuron damage [16,23].

Changes in F response parameters may indicate damage to any portion of the afferent or efferent pathway in the motor nerve, as F-wave travels in both of these pathways [13,24]. Furthermore, F-wave aids in the diagnosis of

conditions involving long nerve distances, such as DPN [18,25].

The decrement in Fp of the diabetic patient in the current study may indicated a depletion of motor neurons and motor axons respectively. Many studies were in line with such finding which further supports the findings of this study [26,27].

The patients' FWCV was significantly lower in the current study than in the controls, indicating a slowing throughout the entire nerve length. This finding was in harmony with the results of other studies [28,29].

Between the groups under study, Fr and mFr were longer in patients with DPN than control group, the result resembles the study of Kimura [15]. Furthermore, mFr aid in early diagnosis of sub clinical DPN in diabetic patients, this study showed that the mFr was longer in diabetics without DPN group than control.

When other significant F-wave parameters (Fp, the numerator, and the two denominators Fmin and Fc) in the equation of Fi are taken into account, the value of Fi in the current study was significantly lower in patients with DPN when compared to the controls. Other researchers also found that diabetic patients had lower Fi values [17,30]. Also, the value of Fi was significantly lower in the patients without DPN when compared to the controls.

Moreover, the study's patients with DPN exhibit noticeably higher Fe levels when compared to the control value. To the best of our knowledge, there was no comparable data about this finding.

The A-wave

Presence of A-wave was evident in patients with DPN, although in the minority of them (7.14%). A-wave is an abnormal late response following the compound muscle action potential during routine motor nerve conduction studies recorded in F-wave studies with supramaximal stimuli, and distinguished by its constant shape and latency [31].

A-wave was suggested to be a sign of underlying neuropathy, which is commonly present in a variety of neurogenic disorders, such as motor neuron diseases, demyelinating neuropathies, axonal neuropathies, and radiculopathies [32,33]. A-waves have recently been found to occur more frequently in patients with distal DPN, ranging from 32% to 45.9% [34,35]. It is worth noting that A-wave occur in only one out of 121 healthy subjects. Such findings have been reported [35]. This seemed to favor the pathological origin of A-waves and have a higher risk of developing neuropathy in the future [36].

Correlation analysis

F-wave parameters demonstrated a weak to moderate statistically significant relationship with HbA1c and disease duration upon application of the Pearson correlation statistic. Agarwal et al. [18] and Shaji et al. [37] also reported similar findings. This could be the result of the 7.93±5.34 years that the mean illness duration was in our cases. Increased production of glycosylation end products, metabolic disturbances, endothelial damage, and oxidative products are linked to long-term diabetes.

Only 8 patients in the current study presented with DPN and had a duration of more than 15 years, which it is in harmony to Oguejiofor et al. finding of a higher prevalence of neuropathy in those with DM duration of more than 15 years [38]. Conversely to current study findings, Kulkarni et al. [39] showed that no parameter was correlated with the HbA1c level. This could be because the latter study only included 24 patients, which is an extremely small sample size.

Moreover, the Fp showed no significant correlation with the duration of the disease or the HbA1c level. This runs counter to Shaji et al. findings [37]. This disparity may be caused by the patients in the current study having a wide range of HbA1c levels (5%-14%) and disease durations (one year to 34 years).

Additionally, a significant correlation was found between the majority of F-wave parameters and mTCNS, suggesting that a higher disease score corresponds with longer Fmin and Fmax latencies, Fc, and lower Fp and Fi.

The sensitivity and specificity of F-wave

The F-wave parameters that demonstrate higher sensitivity and specificity in differentiating between the patients and controls of the current study are Fi, Fmax, FWCV, and Fmin, in descending order of preference. Fi has the highest sensitivity and specificity, according to other researchers' findings [17,30].

Others have also reported higher sensitivity and specificity for the FWCV [26]. On theoretical base, only one fiber that generates an F-wave has its conduction delayed, then alteration can be detected by analyzing the Fmax and Fmin latencies. Furthermore, the Fmin latency may be normal if at least one fast-conducting fiber is not significantly changed [40,41].

In this study, the Fc latencies were less sensitive than the Fmax and Fmin latencies. This is most likely due to the fact that Fmin and Fmax latencies were prolonged in some patients, as the data showed, and since Fc is the difference of these parameters, it might still within the normal range. This is consistent with the findings of Nobrega et al. [22] but at odds with Panayiotopoulos and Chroni [23] findings, who believe that Fc is a useful metric for identifying changes in the peripheral nervous system.

This study showed the F-wave parameters that demonstrate higher sensitivity and specificity in differentiating between the patients without DPN and controls of the current study are Fi, Fmin and mFr, in descending order of preference.

Among limitation in the current study is the absent data of HbA1c level in the control group.

In conclusion, the study concludes that Fi value decrement, FWCV slowing, and prolonged Fmin and Fmax latencies were helpful in identifying patients with clinical DPN. Increased mFr value, longer Fmin latency, and Fi value decrement were helpful in the early identification of subclinical DPN. When it comes to differentiating between diabetics without DPN and those with T2DM from the controls, the Fi value has the highest sensitivity and specificity.

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Author contribution

All stated authors contributed directly, significantly, and intellectually to the work and consented it to be published.

Conflict of interest

The authors declare that there is no conflict of interest.

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